ABSTRACT BOOK

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SCIENCE FOR SIGHT

OCTOBER 10-13

EUROPEAN ASSOCIATION FOR VISION AND EYE RESEARCH


EVER
European Association for Vision and Eye Research

EVER

Travel grants for best paper

We are pleased to announce that the following 11 members have received a travel grant of 500 EUR each from the EVER sections:

- ACB - Kai KAARNIRANTA - Finland
  4481 - AICAR induces effectively autophagy clearance in ARPE-19 cells
- COS - Benoit CHAPELLIER - France
  2631 - Meganuclease targeting HSV-1 limits viral endothelitis in vivo
- EOVS - Cécile DELETTRE - France
  4285 - Characterization of visual impairment in a Wfs1 mouse model of Wolfram syndrome
- G - Thuy Linh TRAN - Denmark
  2651 - Aquaporins in glaucoma eyes
- IM - Arnaud SAUER - France
  2843 - IL-17A as a possible target of anti-inflammatory and anti-parasitic treatment in toxoplasmic uveitis
- LC - Germain BARREAU - France
  3483 - Intracameral cefuroxime injection at the end of cataract surgery reduces the incidence of endophthalmitis, a French study
- MBGE - Xiaohe YAN - Germany
  2464 - A mutation in peroxidasin causes microphalmia and anterior segment dysgenesis in mice
- NSPH - Guzel BIKBOVA - Japan
  4475 - Neuroprotective and regenerative effect of neurotrophin-4 on neuronal degeneration induced by advanced glycation end-products in adult rat retinas
- PBP - Amandio ROCHA DE SOUSA - Portugal
  4263 - Ghrelin's expression in the eye and its implication in the reduction of intraocular pressure
- PO - Pathma RAMASAMY - Ireland
  3282 - Proteomic analysis of uveal melanoma
- RV - Agnes BOLTZ - Austria
  3664 - Relevance of complement factor H polymorphisms in the response to intravitreal bevacizumab in exudative age-related macular degeneration

ALTA EFICACIA

Alta Eficacia Tecnología SL, Spain, travel grant

Alta Eficacia Tecnología is pleased to announce a travel grant of 400 EUR for the best paper in the VEP section

- Stamatina KABANAROU - Greece
  2422 - Colour contrast sensitivity and electrophysiological abnormalities in patients undergoing long term desferrioxamine treatment

SUOMEN SILMÄLÄÄKÄRIYHDISTYS RY
FINLANDS ÖGONLÄKARFÖRENING RF

The Finnish Ophthalmological Society 100th Anniversary Travel Grants

The Finnish Ophthalmological Society is pleased to announce a travel grant of 1.000 EUR to the following groups of authors

- F079 - Polyphenolic compounds reduce inflammation in ARPE-19 cells
  HäNLER M, SUURONEN T, SALMINEN A, KAARNIRANTA K, KAUPPINEN A–Kuopio
- 2842 - Inflammasome activation by oxidative stress in ARPE-19 cells
  KAUPPINEN A, LAAKSO N, KINNUNEN K, SALMINEN A, KAARNIRANTA K–Kuopio

EVER LECTURE

Visual fields for EVER - and more

MARTIN L
Mälardalen University (Eskilstuna)

Purpose

Visual field examinations are essential in eye care, especially in patients with glaucoma or neuro-ophthalmological disorders. During the last three decades an explosive development has led to automation of examination procedure, new stimulus modalities and a spread of the methods outside eye clinics. Recently, the advent of other physiological tests and imaging methods has presented new ways for analysis of the visual system. The lecture will highlight some of the factors influencing the choice of method, considering the medical situation, patient characteristics and the care setting.

Conclusions

Optimum use of available examination techniques requires good understanding of the methods positive and negative predictive value, the disease prevalence and course, and the "real-world" consequences for the individual patient

Heritage of Ophthalmology: a Philatelic view

ZEYEN T
University Hospital (Leuven)

Stamp collecting is one of the world's most popular hobbies. Many collectors limit their scope to particular countries or themes. For obvious reasons I chose to collect stamps related to ophthalmology. Searching for them and learning about their back story has been a pleasant way to discover parts of the heritage of ophthalmology. I will present photographs of a selection of my stamps introducing our forerunners, showing famous ophthalmologists, ophthalmologists who chose a different path and well-known blind people, representing eye diseases and aids for blind, and commemorating important congresses.

KEYNOTE LECTURE

New treatments for age related macular degeneration

MILLER J
Mass Eye and Ear and Mass General Hospital (Boston)

Treatment of age related macular degeneration (AMD) has progressed dramatically in the last 10 years, particularly in the neovascular stage of the disease. This has been accomplished in part through greater understanding of the pathophysiology of neovascular AMD and the role of VEGF in vessel growth and leakage. Anti-VEGF treatment halts vision loss in more than 90% of patients, and leads to vision improvement in a third. Ideally, however, we would like to develop treatments that can prevent AMD or halt its progression as well as to prevent any vision loss, and this requires greater understanding of the earliest events in AMD. Genetic studies have identified associations with the CFH gene and HTRA-1 gene amongst others, suggesting key pathways in the disease process. Delineating the dysfunction in these pathways through additional genetic and functional studies, and then developing effective interventions, is the current goal of AMD research. In addition, investigators seek to refine our current therapies as well as to improve current diagnostic modalities in order to better characterize the phenotype of AMD patients. Finally, since photoreceptor loss is the ultimate cause of vision loss in patients with AMD as well as other retinal disorders, investigations are ongoing to identify the molecular pathways of photoreceptor cell death and test therapies that might be used for neuroprotection.
Methods

Genetics and treatment of Stargardt disease

ALLIKMETS R
Ophthalmology (New York)
Pathology & Cell Biology (New York)

Purpose

When the adenosine triphosphate (ATP)-binding cassette (ABC) transporter gene, ABCA4 (originally named ABCR), was cloned and characterized in 1997 as the causal gene for autosomal recessive Stargardt disease (STGD) it seemed as if just another missing link was added to the extensive table of genetic determinants of rare monogenic retinal dystrophies. Now, 14 years later, the ABCA4 gene continues to emerge as the predominant determinant of a wide variety of retinal degeneration phenotypes, such as STGD, cone-rod dystrophy, retinitis pigmentosa, and age-related macular degeneration.

Methods

A combination of genetic, molecular biology, gene- and small molecule therapy approaches.

Results

ABCA4 has caused exciting and sometimes intense discussions among ophthalmologists and geneticists, resulting in more than 300 publications during this time. In my presentation I will summarize our current knowledge of the role of ABCA4 in retinal disease and review the substantial progress in diagnostic and therapeutic applications for ABCA4-associated disorders which most recently seemed impossible.

Conclusions

Although ACBA4 has proven to be a complex and difficult research and therapeutic target, I hope to convince the audience that treatment of all ABCA4-associated disorders, and especially STGD, should be possible in the near future.

KEYNOTE LECTURE

Diced Alu: Canning the blinding inflammasome

AMBATI J
Department of Ophthalmology and Visual Sciences (Lexington)

Purpose

To determine the mechanisms of retinal pigmented epithelium (RPE) cell death induced by DICER1 deficient and Alu RNA accumulation, which are observed in human geographic atrophy RPE.

Methods

Human and mouse RPE cell culture studies were combined with in vivo mouse models of RPE degeneration induced by DICER1 targeting or Alu RNA exposure.

Results

DICER1 deficit or Alu RNA exposure activates the NLRP3 inflammasome and triggers TLR-independent MyD88 signaling via IL18 in the RPE. Genetic or pharmacological inhibition of inflammasome components (NLRP3, Pycard, Caspase-1), MyD88, or IL18 prevents RPE degeneration induced by DICER1 loss or Alu RNA exposure. Human GA RPE contains elevated amounts of NLRP3,
PYCARD, and IL18 and evidence of increased Caspase-1 and MyD88 activation.

Conclusions

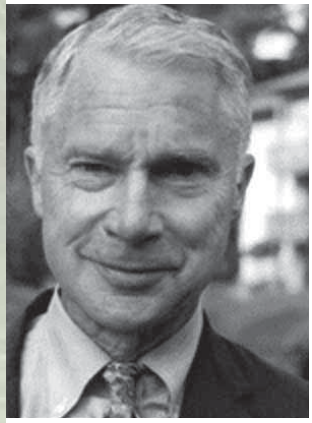
These findings provide a rationale for targeting the NLRP3 inflammasome and IL18/MyD88 pathways in GA.

Acta Ophthalmologica

The changing roles of perimetry and perimeters in glaucoma management

HEIJL A
Lund University, Department of Ophthalmology (Malmö)

OPHTHALMIC RESEARCH LECTURE



Ophthalmic Research

Priorities of Ophthalmic Research

SPAETH G
Wills Eye Institute (Philadelphia)

Purpose

The purpose of this presentation is to examine critically several of the fundamental considerations regarding research, focusing on ophthalmic research. Time and resources are limited. Paradoxically, they appear to be increasingly so. In such an environment it would seem to be important to perform research that is " useful." Who is best suited to decide what is "useful?" Does limiting the freedom of investigators to study what they wish result in dampening creativity? Who should determine – if anybody – priorities of research?

Methods

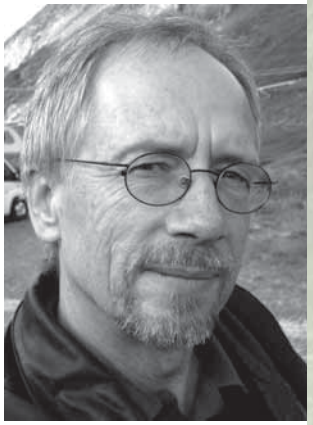
Historical and literature review, with personal opinions informing (or biasing) the conclusions.

Results

The concept of "academic freedom" has long been protected by academic communities, more vigorously in some cultures than others. On the other hand, limits at least since the time of Socrates have been placed on research and commentary; these limits have been imposed by cultural mores, and by communities such as various religious groups, by economically powerful people and industries, and governments. The medical and scientific communities also have imposed limits. Who should set these? How responsible has the medical community been?

Conclusions

Freedom is most likely to be allowed when that freedom leads to outcomes the community considers in their best interest. Critical reappraisal of the appropriateness of deciding priorities of research is needed. Is the concept of the "clinical an/scientist" viable?
Suggestions will be given as to how to preserve or increase the creativity of research and yet promote the study of issues that are useful, relevant and likely to lead to a "better world."



From chickens to humans - learning about the puzzles of myopia

SCHAEFFEL F
Eberhardt Karls Universität (Tübingen)

After it was found that the growing vertebrate eye uses the focus of the retinal image to fine-tune its axial length to the focal length of the optics, it seemed as if the solution of the problem of myopia was in close reach. While a lot was learned about the fascinating details of biological mechanisms coordinating eye growth by vision from animal experiments, it is still a puzzle why eyes of children start to deviate from the correct path and become too long. Currently, a major challenge is to find out which details of visual experience in kids may have a similar effect as wearing a negative lens or a diffuser - since these are the two treatments that induce axial myopia in animal models. The talk will also review some current attempts to slow down the progression of myopia once it had already started.

Courses

• 1511
Pathophysiology of uveitis

DICK A
Bristol

Purpose This talk will overview the pathophysiology of non-infectious uveitis in relation to recent SUN (standardised uveitis nomenclature) disease classification.

Methods The experimental and translational human evidence of autoimmunity and activation of immunity will be discussed. In addition the talk will highlight the pathways and mechanisms of tissue damage that results in sight-threatening disease.

Results Traditionally, despite active immune regulatory mechanisms operative within the ocular environment, inflammation still occurs. Activated antigen and non-antigen specific T cells are generated in uveitis. The interplay with innate immunity and in particular cells of myeloid lineage both systemically and within the local environment dictate the severity and extent of pathology we observe

Conclusion The understanding of immune responses during the uveitis open many avenues to potential novel immunotherapies that not only suppress inflammation but attempt to redress immune balance, tolerance and local homeostasis within ocular tissues

• 1512
Classification of uveitis

ANDROUDI S
Thessaloniki

Purpose Classification and standardization of uveitis is important, as it enhances the precision and comparability of clinical research from different centers and assists in the development of a complete picture of the course of the disorders and their response to treatment

Methods Attempts have been made to standardize some aspects of uveitis, and various classification criteria, inflammation grading schema, and outcomes criteria have been described.

Results The most widely used classification of uveitis is the one devised by the International Uveitis Study Group (IUSG) in 1987, based on the anatomical location of the inflammation. This classification includes anterior uveitis (iritis, iridocyclitis, and anterior cyclitis), intermediate uveitis (pars planitis, posterior cyclitis, and hyalitis), posterior uveitis (focal, multifocal, or diffuse choroiditis, chorioretinitis, retinitis, and neuroretinitis) or panuveitis (anterior chamber, vitreous, retina, and choroid).In 2005, the Standardization of Uveitis Nomenclature (SUN) Working Group standardized a grading schema for aspects of intraocular intraocular inflammation, that is, anterior chamber cells, anterior chamber flare, and vitreous haze, was developed. Standardized definitions of outcomes, including reporting visual acuity outcomes, were approved.

Conclusion Today's uveitis nomenclature has been revised regarding the anatomical location and the grade of inflammation, and supplemented by the inclusion of definitions for onset, duration and course.

• 1513
Symptoms and signs of anterior uveitis

NERI P, ARAPI I, CAPUANO V, PIRANI V
The Eye Clinic, Polytechnic University of Marche, Ancona

Purpose To review the symptoms and signs of anterior ueveitis (AU), based on the anatomic classification of uveitis, iritis and iridocyclitis.

Methods Review of symptoms and signs of AU.

Results Perikeratic injection, cells and flare in the anterior chamber, small keratic precipitates (KPs) are peculiar findings of alternating unilateral acute non-granulomatous anterior uveitis, which is commonly described in association with HLA-B27 antigen and spondyloarthropaties. In such cases, fibrinous exudate or hypopyon can also occur. Patients presenting acute anterior uveitis typically show red eyes, photophobia, ocular pain, and often blurred vision. In chronic anterior uveitis, the onset is usually subtle and patients may be asymptomatic until the development of complications. Viral anterior uveitis is typically unilateral, characterized by recurrent episodes of anterior uveitis. Endotheliitis, high intraocular pressure, and patchy/sectoral iris atrophy are also present. Chronic flare, Koeppe and Busacca nodules of the iris, medium-size KPs or large mutton-fat KPs, peripheral anterior synechiae and broad-based posterior synechiae represent hallmarks of granulomatous anterior uveitis which tends to chronicity. Juvenile Idipoathic Arthritis (JIA)-associated anterior uveitis is peculiarly a bilateral non-granulomatous chronic anterior uveitis, frequently worsened by several complications.

Conclusion The typology of AU influences its clinical presentation: the clinical findings can vary on the basis of its acute or chronic, granulomatous or non-granulomatous nature. Specific AU subtypes are characterized by a large number of distinct ocular signs.

• 1514
Symptoms and signs of posterior uveitis

KHAIRALLAH M, KAHLOUN R
Ophthalmology, Monastir

Purpose Posterior uveitis (PU) is an important anatomic form of uveitis in which the primary site of infl ammation is the choroid or retina, with or without subsequent vitreous involvement.

Methods Review of symptoms and signs of PU.

Results The onset of PU can be sudden or insidious, involving one or both eyes. Most common ocular symptoms include blurred vision, loss of vision, and floaters. PU is usually associated with vitritis. Both vitreous cells and fl are should be graded according to standardized grading systems. Other vitreous changes may include vitreous strands, vitreous hemorrhage, vitreous traction, and posterior vitreous detachment. Depending on the primary site of inflammation, PU can present in the form of retinitis, choroiditis, retinochoroiditis, or chorioretinitis. Retinal and/or choroidal inflammation can be focal, multifocal, or more diff use, involving the periphery or posterior pole. It is important to distinguish between active and inactive chorioretinal disease. Retinal vasculitis can occur in the setting of several PU entities involving retinal veins or arteries. It appears as focal, multifocal, or diff use vascular cuffing or sheathing. Other retinal vasculitic changes include retinal hemorrhages, features of retinal vascular occlusion, retinal/optic disc neovascularization, and aneurysms. Macular involvement may result from direct inflammatory infiltration, macular edema, serous retinal detachment, retinal ischemia, epiretinal membrane, or macular hole. Optic nerve involvement may include optic disc hyperemia, optic disc edema, optic neuritis, neuroretinitis, optic disc exudate, and optic disc granuloma.

Conclusion Clinician should be aware of the array of ocular symptoms of signs and their importance in orienting work-up.

• 1515
Laboratory work-up and specialized investigations

PLEYER U
Charité - Universitätsmedizin Berlin, Berlin

Based on the anatomical involvement of the eye intraocular inflammation is classified into anterior, intermediate, posterior and panuveitis. All subtypes of uveitis are potentially related to infectious and noninfectious etiologies.This presentation will assist the participants in accurately diagnosing uveitis in a step latter approach including physical and laboratory investigations.In addition, a tailored approach based on confounding clinical observations with specialized investigations will help to further differentiate clinical entities. In cases of suspected intraocular infections the option of intraocular fluid evaluation for antibody testing and polymerase chain testing against the causative agent will be presented. Taken together, this part of the course will provide a rational decision-making strategy for diagnosis of patients with uveitis.

• 1516
Imaging in uveitis: techniques and indications

HERBORT CP (1, 2)
(1) Inflammatory Eye Diseases, Centre for Ophthalmic Specialised Care, Lausanne
(2) University of Lausanne, Lausanne

Purpose To present the array of the main imaging methods used or that should be used in the investigation of uveitis and specify their respective indications.

Methods Review of the different imaging modalities as well as laser flare photometry (LFP).

Results Imaging work-up of (posterior) uveitis automatically and routinely always comprised FA and more recently OCT. FA usually does not bring new unknown elements as it gives information on the superficial structures accessible to fundus examination but it allows more precise appraisal of the pathology of these superficial structures such as retinal vasculitis, macular oedema, retinal ischemia, subretinal fluid, retinal neovessels as well as optic disc inflammation. OCT gives morphologic quasi-histologic details of the retina, especially useful because it is non-invasive and allows close follow-up. FAF gives information on inflammation induced changes on the retinal pigment epithelium and photoreceptor outer segments but FAF still needs to be better standardized if possible at all. Mostly, these methods fail to give information on the choroid, at least as often involved as the retina, which can only be explored by ICGA. Unlike FA and OCT, ICGA very often shows occult unknown elements. It is therefore obvious that ICGA should be included in routine imaging work-up of those cases of posterior uveitis where angiography is deemed necessary and choroiditis cannot be excluded.

Conclusion Classical imaging methods and newer modalities together with LFP transformed uveitis monitoring into a precise clinical science, as long as these methods are used which unfortunately is far from being the case.

• 1521

Preparation, fixation, embedding, sectioning and staining – basic requirements of morphological tissue investigation

KNOP N, KNOP E
Ocular Surface Center Berlin, Dept. for Cell- and Neurobiology, Charite – Universitätsmedizin Berlin, Berlin

Purpose A thorough understanding of the body construction of different cell types and tissues (referred to as "morphology", i.e. structural study), is a prerequisite for understanding of physiology, pathology and clinics. Morphology is usually performed by use of imaging techniques, referred to as microscopy, and respective techniques for pre-treatment (preparation) of the object of interest (tissue specimen).

Methods We will explain and discuss different imaging and preparation techniques for the morphological analysis of tissues, with a focus on ocular tissues.

Results There is a wide variety of morphological techniques that can be differentiated by their resolution or by imaging medium into e.g. conventional light microscopy (LM) and electron microscopy (EM). More recent developments include confocal laser scanning-, optical coherence- (OCT), multi-photon- and acoustic microscopy, that may allow inspection of living tissues at a microscopical/ cellular level. Conventional morphology (histology) requires a respective preparation that consists of tissue fixation to stop natural post mortal degradation and typically requires embedding of the fixed tissue into a medium that can be sectioned, followed by the actual sectioning, as well as measures to increase contrast, e.g. by staining. This also applies to transmission electron microscopy (TEM) whereas scanning electron microscopy (SEM), that displays surfaces, requires the stabilisation of tissue against the energy of the electron beam.

Conclusion Knowledge of morphological techniques allows to chose the right technique for your question in order to perform morphological investigation with an optimal result.

• 1522

Immunohistochemical identification of tissue antigens – principal methological requirements, considerations and results

KNOP E, KNOP N
Ocular Surface Center Berlin, Dept. for Cell- and Neurobiology, Charite – Universitätsmedizin Berlin, Berlin

Purpose To identify specific components (antigens, i.e. protein or polysaccharide macromolecules) of tissues and cells, these are labelled by specific antibodies (AB). Their localization is visualized by marker molecules. Such techniques are known as immunohistochemistry (IHC).

Methods We will explain and discuss different techniques for the IHC labelling in histological specimens on a light microscopical level in order to discuss their advantages and disadvantages.

Results AB are generated after injection into an animal and are used directly (polyclonal AB) or after plasma-cell fusion with tumor cells to produce monoclonal AB. AB are incubated on tissue sections, on cells in culture, or on complete tissues. Pre-treatment of the tissue can block unwanted reactivities, or permeabilize the cells for improved AB entry, or re-activates antigens (antigen-retrieval) that were masked by tissue fixation. Direct IHC uses an AB that directly carries a marker and results in simple, quick procedures. Indirect techniques, in contrast, amplify the primary AB by secondary AB and/or tertiary reagents and result in more laborious techniques with improved sensitivity and staining intensity. Markers are often enzymes for production of a visible color signal or fluorescent molecules. It is also possible to perform simultaneous staining of different antigens on the same section in order to show co-localization of different antigens and to suggest/verify interaction of factors in a biological process.

Conclusion IHC is a widely used technique to identify specific macromolecules together with their localization in the tissue and thus provides important information on cell biology.

• 1523

Immuno electron microscopy – tracking the sub-cellular localization of antigens in high resolution

AKHTAR S
Cornea Research Chair, Department of Optometry, College of Applied Medical Sciences, King Saud University, Riyadh

Purpose Any antigen to which an antibody can be generated can be localized, at sub-cellular level and viewed under very high magnification by immuno-electron microscopy (immune-EM). The applications of EM immunocytochemistry are very wide ranging.

Methods A particular antigen is localized by primary antibody (monoclonal or polyclonal) within a tissue. The primary antibody is visualized using a secondary antibody, the gold conjugates of 5 or 10nm size. The gold particles are opaque and can be seen under an electron microscope. The antibody can be used on pre-embedded or post embedded tissue. In the pre-embedding method, a fresh thin piece of tissue is treated with primary and secondary antibodies. In the post-embedding method, primary and secondary antibodies are used on ultrathin sections. The immunocytochemistry is also carried out on cryosection. Double immune labeling is also carried out by some authors.

Results A number of extracellular matrix proteins and non-collagenous glycoproteins, such as collagen, elastin, fibronectin, laminin, keratan sulphate proteoglycan, BKS1, chondroitin sulphate, keratoepithilin have been demonstrated by the immuno-EM procedure. A number of cellular proteins such as keratoepithelin and actin were also shown by immuno-EM.

Conclusion Immuno-EM is a very powerful technique since it combines the specificity and flexibility of immunocytochemistry with the resolution at high magnification of electron microscopy. Acknowledgement: Supported by National Plan for Science and Technology, KSU, Riyadh.

• 1524

Morphological techniques for endothelial cell analysis of corneal grafts

THURET G
Saint Etienne

ABSTRACT NOT PROVIDED

• 1531
Herpetic eye disease

VASSILEVA P
SOBAL "Prof. Pashev", MU-Sofia, Sofia

Purpose Human herpes viral infection is a major cause of morbidity worldwide and a frequent cause of ocular pathology – conjunctivitis, keratitis, scleritis, uveitis, optic neuritis. It is a recurrent disease and the complications may lead to blindness.

Methods Diverse clinical picture with various manifestations, risk factors and diagnostic problems are discussed in a retrospective review of 120 consecutive patients with herpetic eye infection referred to our hospital for a year. Pathogenesis and classification of ocular herpetic disease are analyzed. 50 patients (42%) had stromal keratitis. Symptoms and signs of recurrence were documented in 34 patients (28%). Herpes simplex infection was observed in 85 patients (71%) and varicella zoster virus in 35 patients (29%). Therapeutic approach depended on clinical form and stage.

Results Controversies in optimal management and current treatment strategy are demonstrated. Treatment of complications, including severe cases with corneal perforation are presented.

Conclusion Systemic antiviral treatment demonstrate beneficial effect in our series of patients. Importance of differentiating HSV and VZV is emphasized. But still to date scientifically proven answers on herpetic eye disease are very limited.

• 1532
Diagnosis

BODAGHI B
Paris

ABSTRACT NOT PROVIDED

• 1533
Treatment: medical therapy

HERGELDZHIEVA T (1, 2)
(1) University Eye Hospital "Prof. Pashev", Sofia
(2) Medical University, Sofia

Purpose To present the current medical treatment of herpetic eye disease (HED).

Methods Electronic search of PubMed using the terms randomized clinical trials, treatment, herpes, and eye was performed.

Results For herpes simplex virus (HSV) epithelial keratitis, trifluridine and acyclovir are more effective than idoxuridine or vidarabine. Brivudine and ganciclovir are at least as effective as acyclovir. The effectiveness of corneal epithelial débridement is improved by an antiviral agent. For HSV stromal keratitis, topical corticosteroids in addition to a topical antiviral agent are effective in managing HSV stromal keratitis. Topical cyclosporine A in conjunction with prophylactic antivirals is an alternative treatment for HSV stromal keratitis, especially in cases of non-necrotizing disease not controlled by corticosteroids or in cases with side effects from steroid treatment. In patients with necrotizing HSV stromal keratitis, amniotic membrane transplantation with postoperative antivirals and corticosteroids are recommended when antivirals alone do not control the disease. For HSV iridocyclitis, a study's results show a trend for a benefit from oral acyclovir in addition to topical corticosteroids. For ophthalmic herpes zoster, oral antiviral drugs at the first signs of infection are recommended for all patients. The monotherapy with antiviral ointment is insufficient. For metaherpetic eye disease, antiviral agents are generally contraindicated and resurfacing therapy and/or surgical reconstruction should be considered.

Conclusion Appropriate and timely treatment of different forms of HED benefits better visual prognosis and improved quality of life.

• 1534
Treatment: surgical methods

DEKARIS I, RATKOVIC M, PALIK M, DRACA N
University Eye Hospital Svjetlost, Zagreb

Purpose Herpetic keratitis may lead to a significant corneal scaring and loss of vision which often leads to surgical treatment, which can be both penetrating (PKP) and deep anterior lamellar keratoplasty (DALK). However, the survival of corneal grafts is hampered by the presence of neovascularization (NV) and possible recurrence of herpetic disease. In our prospective study we have used bevacizumab treatment at the end of surgery, aiming to decrease corneal NV,and consequently to increase graft survival rate.

Methods Twelve high-risk eyes undergoing PKP due to post-herpetic corneal scar were progressively followed up for 17.54 months (range 6-24). There were 7 females and 5 males of average age 51 and 44.28 years, respectively. All surgeries were ended by subconjunctival bevacizumab injection (25 mg/ml) under the NV. Grafts were prospectively examined for their clearance, presence of NV and endothelial cells density (ECD) loss.

Results At the end of follow-up 11 out of 12 (91.7%) of corneal grafts remained clear; corneal NV reduction was found in all eyes and ECD loss at 24 months was 26.63%. Two out of 12 (16.6%) of patients had herpetic recurrence in their graft, which was successfully treated with systemic acyclovir.

Conclusion Subconjunctival bevacizumab may offer an adjunctive measure during surgical treatment of post-herpetic corneal scars. This might be explained by suppression of the angiogenic potential mediated by VEGF in such patients.

• 1541

Limbal stem cell transplantation techniques

DUA H
Nottingham

ABSTRACT NOT PROVIDED

• 1542

Modern pterygium surgery

GICQUEL JJ
Poitiers

Pterigyum is the most common surgically managed ocular surface disorder. The primary Goals are to prevent recurrences in advanced cases and get a proper esthetic result in younger patients with less symptomatic casesThere has been 1 article every month for the last 4 decades on the subject…Bare sclera technique should be avoided at all costs, because it involves too many recurrences. Hence will discuss other techniques, such as conjonctivo-limbalautograft (sutured or glued), conjunctival graft, amniotic membrane and the use of anti-mitotic drugs.

• 1543

Anterior and posterior lamellar keratoplasty

NUBILE M
Chieti

ABSTRACT NOT PROVIDED

• 1544

Corneal collagen cross linking: traditional vs transepithelial

MENCUCCI R
Florence

ABSTRACT NOT PROVIDED

• 1545

Indications and limitations of amniotic membrane transplantation

YEUNG A
Nottingham

ABSTRACT NOT PROVIDED

• 1551

How to localise retinal tears ?

KOROBELNIK JF
Bordeaux

ABSTRACT NOT PROVIDED

• 1552

To analyse the role of vitreous in a retinal detachment

BERROD JP
Nancy

ABSTRACT NOT PROVIDED

• 1553

How to remove subretinal fluid?

POURNARAS CJ
Geneva

Purpose Rhegmatogenous retinal detachments (RRD) can be repaired surgically using non-drainage techniques. However,removal of subretinal fluid (SRF) remains an important surgical step in retinal detachments treated by scleral buckling, particularly in cases of bullous detachments, inferior breaks, proliferative vitreoretinopathy, high myopia, chronic detachments, cases with poor retinal pigment epithelium function and eyes intolerant to sustained intraocular pressure rise.

Methods Conventional drainage techniques include passive needle drainage of subretinal fluid through a 3 to 4 mm radial sclerotomy within the bed of the buckle and closure with a preplaced suture. Many modified SRF drainage techniques have been described.Internal subretinal fluid drainage with simultaneous automated air-fluid infusion is an important part of modern vitreoretinal surgery.

Results Needle drainage, where the needle shaft is observed using an indirect ophthalmoscope, seemed to be associated with a higher success rate than conventional drainage. The most common complications of subretinal fluid drainage include subretinal hemorrhage, retinal incarceration, and retinal perforation.Using perfluorocarbon liquid or infusion of low-molecular weight silicone oil as a peroperative tool, retinal flattening posterior to equator is an important step of the vitreoretinal approach and internal drainage for the treatment of RRD. Subretinal fluid is drained through a preexisting retinal break or an intentionally created drainage retinotomy using an extrusion cannula. It allows the immediate and complete reattachment of the retina and enables laser endocoagulation of the breaks. If the original retinal break can be treated by laser photocoagulation or cryopexy, the subretinal fluid is not necessarily removed completely.

• 1554

How to prevent proliferative vitreoretinopathy ?

JONAS JB
Mannheim

Purpose Proliferative vitreoretinopathy (PVR) is a serious complication of any rhegmatogenous retinal detachment.

Methods Besides an early intervention to close the retinal defect by either an episcleral buckling procedure or by vitrectomy and internal tamponade, additional medical regimens may be sought after to prevent the proliferation of intravitreally intruded retinal pigment epithelium cells and other cells.

Results Itravitreal medical therapy, including drugs such as triamcinolone, microplasmin or anti-VEGF drugs ma ybe discussed for their rol ein the prevention of PVR.

Conclusion Potential procedures to reduce the risk of PVR will be discussed.

• 1555

How to prevent postoperative complication?

CREUZOT C
Department of Ophthalmology, Dijon

Retinal detachment can lead to early and delayed post-operative complications. The purpose of the course is to present the different complications following retinal detachment surgery with their appropriate treatments.The postoperative complications will be divided according to the presentation of the patient (ie inflamed, painful eye or white painless eye) with or without visual loss.Then, IOP measurement and the results from slit lamp and fundus exam will provide us with the main signs useful for diagnosis. With a painful red eye, the main severe diagnoses will be the different causes of increased IOP and endophthalmitis. The main cause of increased ocular pressure is related to the internal tamponade used during surgery (gas or silicone). However, the diagnosis of the presence of silicone in the anterior chamber should be difficult. Hyphema or cataract due to gas should prevent us from a good fundus examination.This course will mainly focus on the different early and more delayed complications after retinal detachment surgery and will try to give some rules to decrease this risk.

• 1561

Eyelid tumours : The relative value of clinical signs

LASUDRY J
Ophthalmology, Hôpital académique Erasme, Université Libre de Bruxelles, Brussels

Purpose Despite the fact that the majority of eyelid tumours are benign, proper management in daily practice requires to detect the malignant ones.

Methods A few clinical behaviour criteria are usually examined to support the hypothesis of a malignancy, however most are of limited reliability.

Results In any case of doubt, biopsy is recommended, which is readily done in the outpatient setting, to reach a pathologic diagnosis, and to draw the appropriate management plan.

Conclusion In all malignant cases, complete carcinologic control is required.

• 1562

Bases of pathological diagnosis of eyelid tumours

LOEFFLER K
Universitäts-Augenklinik Bonn, Bonn

Purpose This presentation will discuss a variety of tumours of the eyelid and adjacent conjunctiva both clinically and histopathologically.

Methods Clinical features of some "usual" and "unusual" tumours will be correlated with histopathologic findings.

Results In many cases, the clinical diagnosis based on certain morphologic criteria and patient's history will be correct. However, it is not infrequent that only histopathologic examination will reveal the exact diagnosis and help to further manage the patient appropriately.

Conclusion The correct diagnosis of eyelid lesions can usually be established using appropriate clinical features but histopathology is mandatory to confirm this since "surprises" are more frequent than we might assume.

• 1563

Margins or not margins

MOURIAUX F
Caen

Purpose Management of malignant eyelid tumors needs to be individualized, taking into account patient factors, tumor characteristics, and histological subtype. Several treatment modalities have been proposed, but surgical excision with monitoring of excision margins has the highest cure rate. The basis of ideal resection margins is almost completely from retrospective data. Moreover, resection margins of basal cell carcinoma are less extensive than spindle cell carcinoma, Merkel carcinoma or others. In another hand, Mohs surgery or complete surgical excision with frozen-section control of the margins offers the lowest tumor-recurrence rate.

Methods The course will discuss of margins, Mohs and Frozen-section control in malignant eyelid tumors especially for basal cell carcinoma

• 1564

Bases of surgery for eyelid reconstruction

BRISCOE D
Emek Medical Center, Afula

Purpose Eyelid defects can be complex and often demand individual approaches in order to achieve a successful functional and cosmetic reconstruction. The course gives the basis of understanding and experience of the issues involved in rebuilding an eyelid. Course participants will be equipped with simple principles of understanding that will make this task much more simple.

Methods Key principles of reconstruction including area and location of the defect, layers, support, anchorage, vascular supply, and the use of flaps and grafts, are discussed in detail. Numerous cases with graphic photographs and diagrams are presented and their reconstruction possibilities worked out interactively with the course participants.

• 1611
Infectious uveitis

KESTELYN P
Ghent

ABSTRACT NOT PROVIDED

• 1612
B27-associated uveitis

WILLERMAIN F
Brussels

B27 associated uveitis is a very frequent form of non infectious intraocular inflammation which account for approximately 50 % of acute anterior uveitis. Its main clinical features, natural history and association with seronegative arthritis are well known. B27 associated uveitis are thus often considered as an easy diagnosis. However, several aspects of the disease remain challenging and debated. This lecture will insist on the most controversial aspects of the work up, treatment, and management of ocular complications of B27 associated uveitis.

• 1613
Behçet disease, sarcoidosis, VKH

ABU EL ASRAR A
Riyadh

ABSTRACT NOT PROVIDED

• 1614
White dot syndromes

MARKOMICHELAKIS N
Athens

ABSTRACT NOT PROVIDED

• 1615

Paediatric uveitis

BODAGHI B
Ophthalmology, Paris

The etiology and treatment of uveitis in children remains different from adults. Infectious and auto-immune conditions must be identified. Juvenile idiopathic arthritis-associated uveitis is the main etiology of chronic anterior uveitis. Pars planitis is another frequent etiology of bilateral auto-immune uveitis. On the other hand, toxoplasmic retinochoroiditis, ocular toxocariasis and cat scratch disease should be excluded in children with unilateral posterior uveitis. Case reports will be presented in order to illustrate th management of different pediatric uveitis entities. Methods

• 1621
Experimental glaucoma models

KALESNYKAS G
Kuopio

Purpose To introduce in vivo methods for experimental glaucoma research.

Methods Animal models with natural elevation of intraocular pressure (IOP) and genetic manipulation to raise IOP will be discussed. Experimental elevation of IOP in rats and mice will be presented in more detail.

Results Up to 30% of retinal ganglion cell (RGC) loss during a 3-week period can be achieved with rat laser photocoagulation model. Similarly, experimental elevation of IOP in mice can result in up to 30% RGC axon loss in the optic nerve with a 6-week follow-up.

Conclusion The age and strain of animals should be considered in experimental glaucoma research.

• 1622
Methods to study neuroprotection

ZACK DJ
Baltimore

ABSTRACT NOT PROVIDED

• 1623
Experimental models of intraocular inflammation

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(2) Duke-NUS, SRP Neuroscience and Behavioral Disorders, Singapore
(3) Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Purpose Intra-ocular surgery is usually followed in the near term post-operative perios by a course of steroids or NSAIDS. However, the nature of post-surgical inflammation is not well known due to the problems with developing an useful model. This talk describes the issues and outcomes using a mouse model of cataract surgery.

Methods Cataract surgery was simulated by an approach 0.4mm posterior ttp to the limbus using a sapphire knife. Pupillary dilation was achieved by using 1% tropicamide and 2.5% phenylephrine. A corneal incision, of ca.30–60°, was made, and 1% sodium hyaluronate was inserted into the anterior chamber. The corneal incision was then extended to ca.90°, and an anterior curvilinear continuous capsulorrhexis was performed and lens was removed by forceps. The anterior chamber was filled with 1% sodium hyaluronate, and the corneal wound was closed using interrupted sutures. Topical 2.5% phenylephrine, 1% tropicamide, and 1% atropine were administered at the end of the surgery. Antibiotics were administered after surgery three times/day.

Results In vivo confocal microscopic analysis showed cell infiltration was not observed in the anterior chamber in the control eye, but seen in the wounded eye at PO day 1(66±5 cells). Cells in the anterior chamber peaked at day 3 (316±52 cells), and decreased over time to day 7 (3±1 cells). RT-PCR showed that S100A8/9 mRNA levels in the iris were up-regulated significantly ($p<0.05$) at PO day 1, peaked at day 3, and remained elevated to day 7. mRNA levels of S100A8/9 in the cornea, HMGB1 in the cornea and iris increased significantly ($p<0.05$) at PO day 1 and decreased over time. Immunostaining for S100A8/9 and HMGB1 corroborated the RT-PCR results. There was no detectable S100A8/9 or HMGB1 in the unwounded iris. The expression of S100A8/9 and HMGB1 was stimulated in the cornea stroma and iris, with a peak at PO day 3, and decreasing over time.

Conclusion A mouse model and potentially other animal models of cataract surgery could be useful to develop new methods for control of intra-ocular inflammation.

• 1624
Oxygen induced retinopathy (OIR) mouse model

UUSITALO-JÄRVINEN H (1, 2)
(1) University of Tampere, Department of Ophthalmology, Tampere
(2) Tampere University Hospital, Department of Ophthalmology, Tampere

Purpose To introduce mouse model for oxygen induced retinopathy (OIR).

Methods Newborn mice are exposed to 75 % oxygen at P7 for 5 days. High oxygen level leads to regression of retinal vasculature and large avascular areas of retina. At P12, upon return to normoxia avascular retinal areas become ischemic. Ischemia drives revascularization of the retina and formation of pre-retinal neovascularization.

Results The rate of revascularization and the amount of pre-retinal neovascularization can be analyzed and quantified from retinal flat-mount preparations and cross sections.

Conclusion OIR model is a highly reproducible in vivo model for the studies on hypoxia driven angiogenesis.

• 1631
Femtosecond laser and microkeratome preparation of ultrathin (UT) DSAEK Grafts, the six months clinical results

MURTA J, ROSA A, QUADRADO M, BRITO S, CARDOSO A
Ophthalmology-University Hospital, Faculty Medicine, University Coimbra, Coimbra

Purpose To evaluate the use of a femtosecond laser and a mechanical microkeratome to prepare ultrathin posterior corneal disks for Descemet stripping automated endothelial keratoplasty (DSAEK) and to assess associated visual results, disk thickness and endothelial cell loss.

Methods This clinical study involved ultrathin DSAEK tissue preparation used in 28 patients with endothelial dysfunction. The first cut was performed with an Intralase FS60 laser and the second cut with a Moria CBm 300- microkeratome. The thickness of the first cut was modified for each cornea to obtain a final graft thickness of 120 µm. Post-op central graft thickness was performed with corneal laser tomography (Spectralis). Central endothelial cell density (ECD) was calculated before, 3 and 6 months after surgery.

Results Final graft thickness was 92.9+28.5 µm, 83.1+23.6 µm, 77.2+16.9 µm and 74.3+27.5 µm at one week, one three and six months post-op, respectively. No loss of corneas due to irregular cuts or perforation during preparation. The mean BSCVA was 0.4, 0.5, 0.7 and 0.7(0.39, 0.35, 0.16 and 0.17 LogMAR) after one week, one, three and six months post-op, respectively. A 26.3% and 31.2% endothelial cell loss was observed after 3 and 6 months of the surgery, respectively. Significant positive correlation between BCVA (logMAR) and central graft thickness at 1 and 3 months was observed (r=0.76,p=0.01; r=0.73,p=0.01) as well as between BCVA (logMAR) at 3 months and preoperative central graft thickness (r=0.82,p=0.007; Spearman correlation). Patients without bullous keratopathy achieved better visual outcome at 3 months (p=0.04, Mann-Whitney test).

Conclusion Femtosecond laser and microkeratome can be used sequentially to prepare custom ultrathin DSAEK grafts with no loss of corneas. This procedure minimizes the variability inherent to microkeratomes and allows very quick recovery of visual acuity after posterior lamellar keratoplasty.

• 1632
Femtolaser assisted preparation and quality of endothelial button

BOURGES JL
Paris

ABSTRACT NOT PROVIDED

• 1633
FEMTO-DSEK: is endothelial cut possible?

BAIKOFF G
Marseille

The interest of the Femtosecond laser is its ability to cut parallel and regular corneal surfaces with great precision. The most common example we have is its routine use for lasik flaps for which the standard thickness is around 100µm.The difficulty of deep cuts with the Femtolaser gave rise to a number of irregularities, leading the author to use a posterior trans endothelial cut. The advantage of the VisuMax is that it applies very little pressure on the endothelium, the endothelial cells undergo very little alteration and with a cell loss of approximately 5% to 7%.After surgery (endothelial graft) the smoothness of the cut is not perfect (high resolution OCT) and a number of endothelial graft irregularities are visible. These irregularities can be due to the viscoelastic interface used to protect the endothelium when the aplanation cone comes into contact with the graft or else due to the bubbles that appear to be more important in the posterior stromal tissue than in the anterior one. The corneal graft is still swollen and the slack substance of this posterior tissue has a different reaction than when cutting a lasik flap in the anterior stromal tissue which is much denser. A certain number of methods are possible in order to try and reduce these irregularities. They will be discussed during the presentation.

• 1634
Endothelial cell viability of endothelial lenticules

THURET G (1, 2), HE Z (1), CAMPOLMI N (1, 2), HA THI BM (1), PISELLI S (1), DUMOLLARD JM (1, 3), PEOC'H M (1, 3), MURAINE M (4), TOUBEAU D (4), GAIN P (1, 2)
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(2) Department of Ophthalmology, University Hospital, Saint-Etienne
(3) Department of Pathology, University Hospital, Saint-Etienne
(4) Department of Ophthalmology and Eye Bank, University Hospital, Rouen

Purpose Despite concerns about the attrition of the post-operative endothelial cell density (ECD), endothelial keratoplasty, whatever the method of lenticule preparation has gain popularity over penetrating keratoplasty because of a short/medium-term favourable benefit/risk balance. Because the long and very long-term issues may mostly depend on the endothelial cell (EC) pool brought by the graft, and because the supplementary handling necessary to cut the lenticules may stress EC, we focused our attention on the EC viability of endothelial lenticules

Methods Systematic review of the literature and experimental data from our laboratory

Results We indentified in PubMed, articles where EC viability was assessed after lenticule preparation, and those with post-operative clinical data. Methods of EC assessment and interpretation were analysed. Experimental assessment using a specifically designed triple Hoechst/Ethidium/Calcein staining coupled with image analysis of the whole graft surface provide a precise objective determination of the viable ECD (vECD), the only which is important for the recipient.

Conclusion Almost all published series show that the preparation of endothelial lenticules trigger a significant EC loss. Reduction of initial ECD is liable to have long or very long-term functional consequences, that remain to be investigate (maximal published follow-up is only of 4-5 years). Experimental data, especially the vECD, allow a precise quantification of the phenomenon and therefore comparison between different cutting techniques. There are strong bodies of evidence proving that we don't graft as many EC as we think

• 1635

Rho Kinase Inhibitors: the end of endothelial keratoplasty?

GICQUEL JJ
Poitiers

The human corneal endothelium shows poor regenerative abilities. In cases of pseudophakic bullous keratopathy or Fuchs' dystrophy, descemet striping automated keratoplasty brings considerable clinical benefits. However there are still allograft rejections and the shortage of donor corneas is a problem that still needs to be solved. The Rho/Rho kinase (ROCK) inhibitors may help establishing ex vivo endothelial cell cultures and may also give birth to new pharmacological treatments of corneal endothelial dysfunction.

• 1641
Corneal bacterial infections

GICQUEL JJ
Poitiers

Because of their potential to permanently impair vision or perforate the eye, bacterial corneal ulcers are an ophthalmologic emergency. They usually follow an insult (sometimes minor) in the corneal epithelium that provides an entry for bacteria. The increased use of soft contact lenses in recent years has led to an important rise in the occurrence of bacterial ulcers (especially aggressive Gram- bacteria). In this course you will learn about the new concepts in bacterial ulcers diagnosis and treatment.

• 1642
Herpes and zoster keratitis

LABETOULLE M
Ophthalmology, Bicetre Hospital, South Paris University, Le Kremlin Bicêtre

The two leading causes of viral infection of the cornea with potential severely impaired visual acuity are the Herpes Simplex Virus (HSV) and the Varicella-zoster Virus (VZV). Both of them are able to become latent in the trigeminal ganglia, before reactivation and migration along the trigeminal fibers innervating the cornea. The clinical settings of keratitis may vary from an epithelial defect (dendritic of geographic) to a more severe disease involving the stroma and/or the endothelium. Most of first episodes of HSV keratitis occur from the second to the fifth decade of life, and associated skin lesions are not frequent. In contrast, VZV keratitis mostly occurs after the sixth decade, as an associated finding of herpes zoster ophthalmicus (HZO). However, recent studies have highlighted the possibility of HSV keratitis in elderly, while other studies reported VZV keratitis in children, either isolated or associated with HZO. The curative options for treatment of HSV keratitis are now well established, but the preventive regimens of antiviral drugs still have to be optimized, since the most popular treatment, based on the results of the HEDS study, only reduces the rate of relapses in a two-fold manner. For VZV, vaccines against chickenpox and HZO may significantly change the epidemiologic data when they will be more frequently used in European countries.

• 1643
Infectious keratitis in children

BREMOND-GIGNAC D
Ophthalmology, University Hospital, Picardie Jules Verne University (Amiens)
INSERM UMRS 968, Vision Institute, Paris VI University (Paris)

Purpose Infectious keratitis in children is not common but can cause a severe visual impairment if late diagnosed with delayed treatment established or with weak efficacy. The course aims to better define diagnosis, epidemiology evolution and treatment in keratitis in children.

Methods In children, infectious keratitis can be difficult to diagnose because the pathology can develop without pain. In addition blepharospasm is often observed and the examination may be difficult to perform. The examination of a keratitis, ulceration or severe ulcer could be difficult to individualize. The treatment should be provided earlier and aims to eliminate the bacteria, virus ou fungal pathogens.

Results Clinical forms bacterial, chlamydia, viral, amoebae or fungal need to be recognized, in order to treat and avoid sight-threatening issue. The specific epidemiology of pathogens will be detailed according to the age.

Conclusion Risks of visual impairment and amblyopia must be integrated. Topical antibiotics adapted to the symptoms will be studied with practical aspects, diverse clinical cases and considering quality of life of the children and parents

• 1644
Infectious crystalline keratopathy and its management

DUA H
Nottingham

ABSTRACT NOT PROVIDED

• 1651

Do not forget your slit lamp

BRON A
Dijon

During their residency, young ophthalmologists are fascinated by all the imaging techniques now available almost everywhere. It is fair to acknowledge that the yield of these techniques in the screening, the diagnosis and the follow-up of ocular hypertensive and glaucoma patients is invaluable. However before embarking to the prescription and the interpretation of these techniques it is mandatory to carefully retrieve the symptoms and signs of the patients. Ophthalmologists are still medical doctors and not only technicians. Therefore they cannot forget the basis of a medical examination. Like the stethoscope for general practitioners and cardiologists, the slit-lamp is a key step of the examination for ocular diseases by ophthalmologists.In this course, young ophthalmologists will find a check list to help them in retrieving medical history, symptoms and a check list for the slit-lamp examination from the lids to the optic nerve head. This rapid and systematic approach is designed to help them to improve their daily clinical practice with glaucoma patients.

• 1652

How to become familiar with gonioscopy?

HOMMER A
Vienna

Gonioscopy is an essential examination in Glaucoma care. There is no other technique available that can replace it. Differential diagnosis of the different types of glaucoma is not possible without it. This course will highlight the different lenses, examination technique, findings and classifications. It will be shown with Videos, Computer animation as well as clinical cases.

• 1653

Visual field examination in daily practice

ZEYEN T
Leuven

Automated perimetry is the most important functional test in glaucoma patients. This course will teach which programs and strategies to use, how to instruct patients and avoid artifacts, and how to use the available software to interpret worsening of visual field defects and calculate rates of change. Finally, consensus statements will be provided on the usefulness of non-conventional perimetric tests.

• 1654

How to evaluate structure in glaucomas?

SUNARIC MEGEVAND G
Rothschild Foundation, Geneva

This course is designed for young ophthalmologists and will give the opportunity to discuss aspects of the structure and structural changes of the optic nerve head and the retinal nerve fiber layer related to glaucoma and the alteration of the visual function related to this disease. In the last few years there is increasing evidence of the importance of structural measurements particularly early in the disease, and combining information from structure and function can significantly improve detection and assessment of glaucoma progression. Different tools and new technologies for measuring structural changes will be discussed in details such as stereo- photographs, HRT, GDx and OCT.

• 1661

A step-by-step approach to examining eye movements

BORRUAT FX
Lausanne

The eyes move in order either to keep track of an object of interest or to change visual attention from an object to another. There are several types of eye movements, each of them can be altered due to different mechanisms and pathologies. Patients with eye movement disorders can be either symptomatic (diplopia, oscillopsia) or asymptomatic. This presentation will summarize the infranuclear, nuclear and supranuclear pathways of oculomotility with an emphasis on fixation, saccades, pursuit, convergence and basic examination of the vestibulo-ocular reflex. Guidelines for an examination of eye movements in clinical practice will be provided with video presentations of both normal and abnormal situations.At the end of the session, participants should be able to examine eye movements adequately and recognize abnormal fixation, defective pursuit, and inappropriate saccades.

• 1662

Cranial nerves 3,4 and 6: from brainstem to orbit

KAWASAKI A
Lausanne

Purpose To review the pertinent anatomy of the ocular motor cranial nerves in correlation with their clinical presentation

Methods didactic lecture and cass

Results The nucleus of the oculomotor nerve (CN3) is composed of several subnuclei. The central caudal subnucleus innervates the levator palpebrae bilaterally. Fibers from the superior rectus subnucleus decussate and innervate the SR muscle of the contralateral eye. Axonal fascicles from each subnucleus remain topographically arranged as they traverse the midbrain. Autonomic fibers (pupil and accommodation) orient dorsomedially in the peripheral nerve as it exits the peduncles of the ventral midbrain. The clinical presentation of a nuclear, fascicular and peripheral lesion of CN3 are distinctive and localizing. The trochlear nerve (CN4) is the smallest cranial nerve yet has the longest pathway. It is susceptible during closed head injury. The abducens nerve (CN6) exits the ventral pons and ascends the clivus to reach the cavernous sinus. It is prone to injury with changes in intracranial pressure. Lesions of the clivus can also cause bilateral abducens palsy.

Conclusion Understanding the anatomic pathway of the ocular motor nerves can help focus the etiology and location of the lesion.

Commercial interest

• 1663

Supranuclear eye movement disorders

BORRUAT FX
Lausanne

Supranuclear disorders of eye movement result from a relative deafferentiation of oculomotor nuclei (III, IV, VI) in the presence of intact nuclei, cranial nerves and extraocular muscles. In supranuclear oculomotility disorders there is often a dissociation of eye movements (for example, gaze palsy with preserved vestibulo-ocular reflex, or saccadic palsy with preserved pursuit).This presentation will discuss the most important supranuclear disorders, including internuclear ophthalmoplegia, dorsal mesencephalic syndrome, skew deviation, and progressive supranuclear palsy.At the end of the session, participants should be able to recognize and provide a differential diagnosis for the aforementioned supranuclear disorders.

• 1671
Congenital pigmented lesions

BECHRAKIS NE
Department of Ophthalmology, Innsbruck Medical University, Innsbruck

A systematic description of congenital pigmented lesions is presented. These include congenital anomalies of the RPE such as hypertrophy, hyperplasia and hamartomas. The differential diagnosis of combined hamartoma of the retina and the RPE is presented, as well as congenital melanosis of the ocular fundus.

• 1672
Pathology of pigmented fundus lesions

COUPLAND SE
Pathology, Dept. of Molecular and Clinical Cancer Medicine, Liverpool

Purpose To describe the pathology of the most common pigmented fundus lesions.

Methods A review of the histomorphological, immunophenotypical and genotypical features of the most common pigmented fundus lesions.

Results Pigmented fundus lesions range in nature from benign to malignant lesions involving the retinal pigment epithelium and the melanocytes within the choroid as well as metastatic lesions to the posterior segment.

Conclusion Although most pigmented fundus lesions can be diagnosed clinically, in some cases histomorphological confirmation of the diagnosis is required. Further, the additional information that can be obtained from genetic examination of the tissue sample, is of predictive and prognostic value.

• 1673
Suspicious choroidal naevi

KIVELÄ T
HUCH Department of Ophthalmology, Helsinki

Purpose To summarize salient characetristics of suspicious uveal naevi and guidelines for their management.

Methods Review of literature and personal experience.

Results The differential diagnosis of uveal naevi and melanoma is based on clinical examination with the slit lamp and indirect ophthalmoscope together with ultrasonography of the eye. Large to medium-sized melanomas are reliably differentiated from naevi using these methods. The challenge lies in early detection of small melanomas which are more difficult to tell from presumed naevi. A useful mnemonic 'To Find Small Ocular Melanomas' reminds the general ophthalmologist to look for tumour Thickness of more than 2 mm, subretinal Fluid, visual Symptoms, Orange pigment and location of the tumour Margin at the optic disc. Optical coherence tomography and fundus autofluorescence imaging help in identifying subretinal fluid and orange pigment and in measuring the thickness of thin choroidal naevi and melanomas. Each of the risk characteristics roughly doubles the likelihood of growth so that the risk for growth is about 30 times higher when all five characteristics are present as compared to their absence. In addition, a low acoustic profile, the absence of a halo around the tumour and the absence of drusen over it increase the likelihood of growth. The trend is toward taking a biopsy of suspicious small choroidal tumours as an alternative to documenting growth before treating them as melanomas.

Conclusion Patients with a choroidal melanocytic tumour with at least one risk characteristic benefit from referral to an ocular oncologist. The rest of the patients can be made aware of their presumed naevus and that they should be observed periodically. The patients should be told to return immediately if they develop new visual symptoms.

• 1674
Malignant melanoma of the uvea: diagnosis, characterization and prognosis

MIDENA E
Padova

Purpose To summarize available data on uveal melanoma biology, diagnosis and clinical characterization.

Methods Herein, we review diagnostic criteria, clinical characterization and therapeutic implications of the emerging molecular biology in posterior uveal melanoma/high risk indeterminate choroidal pigmented lesion.

Results The diagnosis of uveal melanoma is based on clinical examination with indirect ophthalmoscope and ultrasonograpy. The use of mnemonic "to find small ocular melanoma" is useful in risk stratification of small indeterminate melanocytic choroidal lesions. The use of optical choerence tomograpy and autofluorescence also help in identifying sub-retinal fluid and orange pigment.In the cytogenetic era, tumor-sampling procedures are becoming the main prognostic tools for uveal melanoma patients.

Conclusion Ophthalmic oncology is moving in the same direction as all other oncologic subspecialties, starting to determine the patient's risk using sampling-based laboratory techniques. However, it is essential to start treating patients earlier (in the premalignant tumor stage) and to develop consistent, selective and effective adjuvant therapy

• 1675
Malignant melanoma of the uvea: radiotherapy techniques

DESJARDINS L
Paris

Purpose Malignant melanoma of the uvea is a relatively radioresistant tumor which can be treated with radiotherapy only with high dose. For this reason only radiotherapy techniques with precise location of the radiation doses are used

Methods Proton beam therapy has been used since 1975 by Gragoudas in Boston and the in Europe since 1983.Because of the Bragg pick, the use of an accelerated proton beam allows delivering homogenous high dose to the tumor while sparing the normal tissue around. Brachytherapy is also widely used. It consists to suture to the sclera against the tumor a radioactive plaque that can contain iodine 125 seeds or ruthenium. Iodine 125 is a low energy gamma emmeting isotope; the radiation is totally stopped by heavy metals like gold .The seeds need to be changed every two months because of its half life. Ruthenium 106 is a beta emmiting isotope. Its low penetration prevents its use for the bigger tumors. With brachytherapy the dose of 90 grays is usually delivered to the top of the tumor while the base receives more than 300grays.

Results Tumor control is excellent with proton beam (less than 5% recurrence at 5 years) and good with brachytherapy (less than 10% recurrence at 5 years) Globe preservation is possible in more than 90% of treated patients. The visual acuity depends of the size and location of the tumor. Mortality by metastasis is equal after conservative management by radiotherapy or enucleation.

Conclusion Various techniques of radiotherapy can achieve good local control and globe preservation in patients with uveal melanoma

• 1676
Malignant melanoma of the uvea: surgical techniques

DAMATO B
Ocular Oncology Service, Liverpool

Purpose To describe the surgical techniques in the management of uveal melanoma.

Methods The surgical techniques include: excision-, incision-, and aspiration-biopsy; various forms of exo-resection and endoresection; enucleation and exenteration. Local resection and enucleation can be primary or secondary.

Results Biopsy greatly enhances prognostication by allowing multivariate analysis of clinical, histological and genetic predictors of metastasis. Primary local resection is indicated in only a minority of patients, in whom radiotherapy is unlikely to be successful, because of tumour size or location. The role of neoadjuvant radiotherapy is controversial. Secondary local resection can salvage eyes with local tumour recurrence or the toxic tumour syndrome after radiotherapy. Enucleation may be necessary because the tumour is too extensive when the patient presents or because of complications after conservative forms of therapy.

Conclusion The results of biopsy and surgical treatment are highly surgeon-dependent and require appropriate skills if complications are to be avoided. Intensive efforts are required to ensure that skills are transferred between surgeons so that technical advances are not forgotten.

Oral presentations

• 2211

Dealing with cataracts in vitreoretinal surgery

TADAYONI R
Paris

Purpose Discussing techniques of combining cataract surgery with vitrectomy.

Conclusion To achieve a sustainable gain of vision in selected cases, combined surgery is performed by an increasing number of vitreoretinal surgeons. This combination needs adaptation of both cataract surgery and vitrectomy techniques.

• 2212

The iris-diaphragm in vitreoretinal surgery

BECHRAKIS NE
Department of Ophthalmology, Innsbruck Medical University, Innsbruck

Purpose of this lecture is the description of problems that can occur in vitreoretinal surgery from defects of the iris-diaphragm. These are associated with different intraocular tamponades that can cause severe corneal decompensation in case of endothelial contact. A variety of surgical procedures can address these issues, including surgery of the iris and implantation of artificial iris and lens-iris diaphragms.

• 2213

Anterior segment problems with vitreous substitutes

HEIMANN H
Liverpool

ABSTRACT NOT PROVIDED

• 2214

How to achieve optimal visualization in vitreoretinal surgery

BLATSIOS G
Innsbruck

Purpose of this presentation is not only to describe the various viewing systems, endoillumination possibilities and dyes, but also to give some useful tips on how to practically deal with anterior and posterior segment problems that may interfere with visualisation during vitreoretinal surgery.

• 2221
The first consultation

SPILEERS W
Leuven

Purpose Patients with "photophobia" need a full clinical ophthalmological work-up.

Methods Careful listening to the complaints and a clinical ophthalmological examination are the cornerstone of the decision making in the differential diagnosis.

Results Retinal disorders are indeed one of the possible causes of aversion to bright lights but many others have to be considered (refraction, lens, inflammation,...)

Conclusion When a patient does not like bright lights a well structured decision making tree of ophthalmological examinations is needed in order to proceed with the necessary technical investigations.

• 2222
Photophobia in inherited retinal disease

LEROY BP (1, 2)
(1) Dept of Ophthalmology, Ghent Univ Hosp, Ghent
(2) Ctr for Medical Genetics, Ghent Univ Hosp, Ghent

Purpose To describe the phenotypes and genotypes of photophobia due to inherited retinal disease.

Methods A case presentation format will be used to illustrate different genetically determined conditions leading to photophobia. Both clinical and electrophysiological phenotypes as well as genotypes will be discussed.

Results Phenotypes and genotypes of genetically determined diseases leading to photophobia are very different. An important distinction to be made is the one between stationary and progressive diseases. Indeed, such distinction is important as the visual outcome may differ considerably between different conditions.

Conclusion Genetically determined retinal diseases leading to photophobia are very diverse. Visual electrophysiology allows an important distinction between progressive and stationary conditions.

• 2223
Photophobia in neuro-ophthalmological conditions

KAWASAKI A
Lausanne

Purpose To understand the clinical presentation and possible mechanism of photophobia in neuro-ophthalmological conditions. migraine and meningitis and lesions along the anterior visual pathway.

Methods case studies, literature review

Results Photophobia is a symptom that commonly accompanies migraine and meningitis. It occurs occasionally with lesions along the anterior visual pathway and in particular with suprasellar mass lesions, even if there is no evidence of chiasmal dysfunction. Such patients complain of a variety of symptoms related to excessive light perception. These take the form of photopsias, glare, dazzle, light aversion and photooculodynia.

Conclusion Recent evidence and new physiologic concepts related to centrally-mediated light sensitivity and intolerance point to the thalamus as an integrating center for light and nociceptive signals. We will review these "photophobia circuits" and examine their application in clinical neuroophthalmology

Commercial interest

• 2224
The role of electrophysiology

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Purpose To demonstrate the role of electrophysiological assessment in the investigation and management of the patient with photophobia, or whose vision is worse under bright lighting conditions.

Methods The ISCEV standard techniques for ERG, PERGm, mfERG and EOG recording will be described, as will any necessary non-standard protocol additions.

Results Selected cases will be used to illustrate the value of the objective data provided by electrophysiology.

Conclusion The objective data provided by electrophysiological assessment is important to the assessment, diagnosis and management of this group of patients.

• 2231

Highly elastic epoxy cross-linked collagen hydrogels for corneal tissue engineering

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Purpose Our objective is to develop novel materials that support the regeneration of diseased or damaged corneas. Despite the promising clinical results that we previously reported on biosynthetic corneas, more robust and elastic materials are required to withstand the adverse host conditions faced for high risk transplantation in severely damaged or diseased corneas. This presentation will provide details on an epoxy cross-linked collagen-based scaffold with enhanced mechanical properties.

Methods We have developed a range of collagen-based materials as mimics of the cell-free corneal stromal extracellular matrix. In this study, cross-linked polymer networks of collagen hydrogels were prepared using a hybrid of 1,4-butanediol diglycidyl ether (BDDGE) and carbodiimides (e.g. EDC-NHS) as cross-linkers. Briefly, 10w/w% porcine collagen type I was mixed in a T-piece system at various compositions and pH, e.g. pH 5, pH 11, and incorporated with laminin adhesive peptides (YIGSR, and IKVAV). Promising material formulations were tested for their physiochemical properties (e.g. mechanical, optical, water uptake, FTIR, and thermal degradation) and physiological properties (e.g. interactions with corneal cells, and biodegradation).

Results The hybrid BDDGE hydrogels demonstrated improved mechanical properties and degree of cross-linking while maintaining their optical clarity and biocompatibility compared to controls (e.g. EDC/NHS-crosslinked hydrogels). Incorporation of laminin-derived cell-adhesive peptide (IKVAV) demonstrated significant increase in corneal cells (HCECs) proliferation compared to controls.

Conclusion The hybrid BDDGE-crosslinked collagen-based hydrogels have the potential for use as tissue-engineered corneal substitutes.

• 2232

Donor bone marrow derived dendritic cells promote corneal allograft survival in the rat

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Purpose Glucocorticoid treatment of ex-vivo generated donor bone marrow derived dendritic cells (BMDCs) will promote graft survival upon injection into corneal transplant recipients.

Methods BMDCs were propagated from Dark Agouti (DA) rat BM precursor cells and for glucocorticoid treated BMDCs, dexamethasone (Dexa) 10e-6M was added to the culture. BMDCs +/- Dexa phenotype, APC function and immunostimulatory capacity were examined. A fully allogeneic rat corneal transplantation model (DA to LEW) was used for in-vivo studies. BMDCs +/- Dexa were harvested and 1x10e6 cells injected intravenously into recipients 7 days prior to corneal transplantation. Graft survival and development of opacity, edema and neovascularisation were monitored. On the average day of rejection graft infiltrating cell populations were analysed.

Results Ex-vivo generated BMDCs have a semi-mature phenotype and can be treated with Dexa to maintain their immature phenotype (n=5 $p<0.05$). BMDCs are capable of activating allogeneic lymphocytes, efficiently presenting antigen and activating antigen specific T cells however, there is a reduction in the level of proliferation (n=4, $p<0.05$). When applied in-vivo BMDCs and Dexa BMDCs significantly prolong corneal allograft survival (MST> 30d, n=14 $p<0.0004$ and n=24 $p<0.0001$ resp.) compared to untreated allogeneic controls (MST 18d, n=11). A significant reduction in the total number of graft infiltrating cells was observed for both treated groups ($p<0.05$).

Conclusion Our results demonstrate a significant therapeutic effect of donor-derived BMDCs with and without glucocorticoid treatment to prolong corneal transplant survival which represents a novel therapeutic approach for the prevention of corneal allograft rejection.

• 2233

Concentration gradient of endogenous noradrenaline from periphery to centre in the rabbit cornea

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Purpose The source of endogenous catecholamines that activate corneal adrenoceptors is largely unknown. Since the cornea is a densely innervated tissue we hypothesized that the major source would be the neuronal release of noradrenaline (NA) from intrinsic sympathetic nerves rather than circulating or non-neuronal local production.

Methods Three concentric segments (central, intermediate, peripheral) were obtained by double trephination (9.5-7.25 mm) performed on corneas harvested from 3-4 month old rabbits, along with aqueous humor and blood samples. Endogenous catecholamines were quantified by HPLC-EC. Results are means±SEM. ANOVA was used for statistical analysis.

Results NA and adrenaline (AD) were identified in all corneal segments (n=15/16) at the following concentrations: 101.3±24.1 pmol/g for NA, 4.8±2.7 pmol/g for AD in the centre; 76.8±18.8 pmol/g for NA, 23.0±11.1 pmol/g for AD in the intermediate segment; 317.0±135.7 pmol/g for NA and11.1±6.1 pmol/g for AD in the periphery. Statistically significant ($P<0.05$) were the differences between: 1) NA concentrations in peripheral segments and those either in central or intermediate segments; 2) NA and AD concentrations in all segments. In the aqueous humor concentrations of NA were 77.0±9.8 nmol/L (n=6) and no AD was found. Plasma concentrations (n=4) were 28.0±2,5 µmol/L for NA, 36.2±8.5 µmol/L for AD.

Conclusion There is a concentration gradient for NA decreasing from the corneal periphery towards the centre. In contrast, no such gradient exists for AD. Moreover, NA is the most abundant of the two catecholamines in all segments, whereas in the plasma AD predominates. Taken together, these results suggest that corneal NA is mostly of neuronal origin.

• 2234

The fish scale-derived Biocornea as a scaffold for human corneal cells

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Purpose Collagen matrices are a promising alternative for corneal donor transplants. Existing collagen matrices are synthesized or derived from animal corneas. We investigated whether fish scale-derived collagen type I matrix could serve as a scaffold for in vitro corneal regeneration.

Methods Primary human keratocytes were cultured for 2 weeks onto uncoated and collagen type IV coated scaffolds. Additionally a cell line of human corneal epithelial cells (HCEC) were co-cultured with the scaffold. Cell morphology and tissue organization were assessed using fluorescence staining. Furthermore, epithelial morphogenesis, cell proliferation, cell infiltration and the effect of different protease treatments on scaffold permeability were analyzed as well.

Results Keratocytes and HCECs cultured onto the micro-patterned side covered the whole surface of the scaffold as well as keratocytes cultured onto the smooth side of the scaffold. No difference in cell attachment was observed between the uncoated and coated scaffolds. Cross sections showed no cellular infiltration into the scaffold. Dispase treatment separated the lamellae at the edges of the scaffold, but this did not induce cell penetration.

Conclusion The fish scale-derived scaffold is biocompatible with human corneal epithelial and stromal cells and could therefore be a promising non-expensive basis for corneal regeneration. Additional stromal-scaffold interaction and cell infiltration studies will be the focus of our research.

Commercial interest

• 2235

Cultivation and characterization of corneal limbal epithelial stem cells on lens capsule in animal material-free medium

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Purpose To develop simple, reproducible and animal-materials free method for cultivating and differentiating human limbal stem cells (LSCs) into corneal epithelium on human lens capsule (LC) for clinical transplantation.

Methods Limbal tissues (2x2x0,25 mm) were harvested from cadavers (44 males and 33 females, age 70,5+9,3 years) within 12 hours of biologic death. All tissue collection complied with the guidelines of the Helsinki Declaration and was approved by the Regional Ethical Committee. Cell viability was measured with the MTT and annexin-FITC/propidium iodide assays. Characterization of the growing cells was performed by RT-qPCR and immunfluorescence stainings accordingly.

Results Cell outgrowth at the edge of the explants was observed within 24 hours of cultivation and achieved viable outgrowth (>97% viability as measured by MTT assay and flow cytometry) within two weeks. The outgrowing cells were tested for positivity for markers of stemness (P63, ABCG2, CK19, ITGA9, VIM), proliferation (Ki-67), limbal epithelial cells (CK 8/18 and 14) and differentiated cornea epithelial cells (CK 3 and 12). Immunostaining revealed the non-hematopoietic, -endothelial and -mesenchymal stem cell phenotype, while the cell adhesion molecules, integrins and lectin-based surface carbohydrate profiling showed a specific pattern on the LESCs.

Conclusion We report a method for isolating and expanding cornea LESCs from cadavers or alternatively from autologous donors capable of producing viable cell outgrowth on LC for possible treatment of LESC deficiency.

• 2236 / T071

Identification of label-retaining endothelial cells in adult human corneas: a new clue for the existence of endothelial stem cells

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Purpose The lack of self-renewal capacity of human corneal endothelial cells (EC) in vivo was explained by cell cycle arrest in the G1-phase due to cell contact inhibition, TGF-beta signaling, and stress induced premature senescence. Nevertheless, their residual ability to divide in primary culture suggests the existence of progenitor cells, probably located at the endothelial periphery (Whikehart.MolVis2005; He.StemCells2012). Stem cells are slow-cycling cells characterized by their quiescent state in niches and their ability to retain for a long time markers of S-Phase like BrDU or EdU. Aim: to search for the presence of label-retaining EC in human corneas

Methods Label retaining EC were searched by 5-Ethynyl-2'-Deoxyuridine (Click-it EdU) incorporation during long-term culture: 30 days for organ cultured human corneas (n=10) or 15 days for in vitro primary cultured EC (n=5), both followed by a 30-day culture without EdU. Flat-mouted corneas and EC cultures were observed with an inverted fluorescent microscope

Results Label-retaining EC were observed in the peripheral area of all OC corneas, varying from 1 to 50. Numerous label-retaining EC were also present in all primary cultures, always attached to Descemet membrane fragments

Conclusion The presence of label-retaining EC constitutes a new clue for the existence of corneal endothelial stem cells in human. Their apparent scarcity is consistent with the inability of the human corneal endothelium to repair in vivo, but isolation and expansion of these endothelial stem cells or progenitors could allow development of bioengineered endothelium

• 2237 / T034

Coupling innovative imaging: in vivo multilaser confocal microscopy and ex vivo confocal Raman spectroscopy of cornea and skin in nephropathic cystinosis

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Purpose Nephropathic cystinosis is a rare, autosomal-recessive inherited disease, characterized by lysosomal accumulation of cystine crystals in almost all tissues. Aim: to describe an innovative in vivo confocal microscopy (IVCM) of crystals in the skin, the cornea and the conjunctiva as well as raman spectroscopy of the crystals in skin and cornea

Methods A 36 year-old women with advanced nephropatic cystinosis underwent penetrating keratoplasty for severe visual loss and chronic ulceration in her left eye. The only dermatology symptom was skin dryness. Cornea and skin was analysed with IVCM using the innovative multilaser (488, 658 and 785 nm) confocal microscope Vivascope 1500 and the handeld monolaser Vivascope 3000 (MAVIG GmbH). In order to obtain the chemical composition, ex vivo Raman spectroscopy (LabRAM ARAMIS,Horiba Jobin-Yvon,France) was performed on corneal button retrieved during keratoplasty and on a skin sample, both immediately frozen in liquid nitrogen without adjuvant

Results Multilaser and monolaser IVCM showed reflective crystals in the corneal epithelium, stroma, tarsal conjunctiva and forearm skin with the highest resolution obtained at 488nm. Ex vivo Raman spectra were obtained in skin and cornea

Conclusion Combination of IVCM with Raman spectroscopy may improve the diagnosis and follow-up for other metabolic diseases with skin and corneal thesaurismoses like amylosis, Wilson disease, Fabry disease or mucopolysaccharidosis

• 2241

Potential role of transporters in ocular pharmacokinetics

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Traditionally pharmacokinetics has been considered to be dominated by passive drug diffusion and metabolism. During the last decade pharmacokinetic research has shown that active drug transport by membrane transporter proteins is much more common than previously thought. The role of membrane transporters in ocular tissues is poorly known, but literature search on transporter interactions of ocular drugs reveals that there is high potential for such interactions, but expression of membrane transporters in the ocular tissues is not well understood. Drug concentrations relative to the affinity of the transporters is another factor that affects the importance of these interactions. Pharmacokinetic simulations reveal that the active transporters probably have important role in the access of systemic drugs to the eye (across blood retina barrier) and in the case of controlled release formulations. For drug absorption from the regular eye drops transporters seem to have relatively minor influence.

• 2242

New formulations for topical drug administration

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ABSTRACT NOT PROVIDED

• 2243

Intraocular administration of biodegradable microspheres to increase drug bioavailability and extend therapeutic effect

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Purpose Treatment of posterior segment diseases often requires repeated intravitreal injections to achieve and maintain steady state concentrations of the active substance in the target site. However, intraocular injections are associated to adverse effects and the risk of complications increases with the number of administrations. Biodegradable microspheres (MPs) are considered an alternative to multiple injections as they are able to release the encapsulated drug over weeks or months. Copolymers of lactic and glycolic acids (PLGA) are FDA approved biodegradable biomaterials commonly used to prepare MPs. They are biocompatible and degrade to metabolic products that are easily eliminated from the body. The main advantages of these systems is that they can be injected as a conventional suspension without surgical procedures. After intravitreal administration, PLGA microspheres suffer aggregation disappearing from the site of injection after delivering the drug. Microspheres can be loaded with different active substances (small molecules and biotechnological products) useful to treat vitreoretinal diseases. Administration of microparticles can be performed by periocular, intravitreal, sub- retinal, or other intraocular routes to treat posterior segment disorders.

Conclusion PLGA microspheres are emerging therapeutic tools for the treatment of posterior segment diseases in which steady state concentrations of the active substance is needed over an extended period of time. Acknowledgements: PANOPTES-Peptide-based Nanoparticles as Ocular Drug Delivery Vehicles- collaborative project (FP7-NMP-2009); Spanish Ministry of Economy MAT 2010-18242, UCM Research Group 920415 and RETICs (RD07/0062/2002)

• 2244

Mini-pump revisited for ocular drug delivery

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ABSTRACT NOT PROVIDED

• 2245

Suprachoroidal delivery: new directions and challenges

OLSEN T
Århus

ABSTRACT NOT PROVIDED

• 2246

Electroporation for ocular drug delivery

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ABSTRACT NOT PROVIDED

• 2251

Genetic basis of glaucomas

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Glaucoma is characterized by a progressive loss of retinal ganglion cells. The exact cause of the glaucoma is still unknown.The glaucoma is a multifactorial disease and affected by multiple genetic and environmental factors. Ethnic differences in the prevalence of glaucoma and positive family history support the inheritance of glaucoma. There is evidence showing that genetic factors may play an important role in the pathogenesis of the disease. Here we aim to emphasize the genetic basis of glaucoma.

• 2252

Vascular issues in glaucoma

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A literature review is done to analyze relevant data about the role of blood flow abnormalities in the pathogenesis of glaucomatous optic nerve damage.Elevated intraocular pressure that is incontestably the major risk factor for glaucomatous optic nerve damage alone cannot explain all glaucoma cases since despite low intraocular pressure some glaucoma cases continue to progress.The results of several studies suggest that ocular hemodynamic abnormalities also play a role in the pathogenesis of glaucomatous optic neuropathy.Another issue relevant to vascular factor is oxidative stress.Reduced blood flow may lead to hypoxia and consequently to accumulation of prooxidants leading to the optic nerve damage.The capillaries in the anterior optic nerve possess local autoregulatory mechanisms to maintain relatively a constant blood flow over a wide range of perfusion pressure.The role of endothelium generated vasoactive molecules in controlling vascular supply within the optic nerve head is important. The decreased perfusion in the anterior optic nerve and the failure of autoregulation in overcoming this decrease are the main mechanisms that compromise the blood supply to the optic nerve head. Intraocular pressure fluctuations and decreased ocular perfusion pressure may synergistically cause instability and decrease in blood flow. Although several methods exist to examine different aspects of the ocular blood flow in different vascular beds, there is no a standard method for blood flow measurements and the clinical role of this measurement in glaucoma is not still well determined. The data from future prospective, randomized and long-term clinical trials are required to well understand the role of ocular blood flow deficiencies in the development and progression of glaucoma.

• 2253

Damage integrity from eye to visual cortex

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Ever since the initial reports on the impacts of glaucoma on the optic nerve (ON), corpus geniculatum laterale (CGL) and visual cortex, its damage beyond the retinal ganglion cells into the brain substance became increasingly evident. In 2 consecutive studies, we aimed to evaluate the structural and functional extent of glaucomatous neurodegeneration in an attempt to develop techniques feasible for routine clinical application. Original diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI) techniques with 1,5T MRI system were applied in retrobulber imaging and evaluation. fMRI detects increased neuronal activity via changes in blood oxygenation, DTI is based on the movement principle of fluids in a plane connected to the nerve. ON damage and cortical hypofunction were imaged. Most importantly, optic coherence tomography (OCT), central visual field (CVF) findings show statistically significant positive and negative correlation with particular diffusion parameters of ON and CGL, respectively. Aside from the classical treatment methods based on management of the IOP, new strategies focusing on the area beyond the optic nerve head are needed to be developed. Better understanding of retrobulbar glaucomatous damage will enable us to develop more effective diagnostic and treatment strategies for glaucoma management, and possibly shed a light on the current unanswered questions about glaucoma.

• 2261
Use of bevacizumab (anti-VEGF treatment) in high-risk corneal grafts

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Purpose We evaluated the effect of bevacizumab treatment in a prospective 2 year follow-up study of 50 „high risk" eyes undergoing penetrating keratoplasty (PKP).

Methods Hihg-risk diseases were: 2 Stevens Johnson syndrome (SJS), 6 chemical burns, 9 post-herpetic, 16 other vascularized scars, 13 rejected grafts and 4 ulcers. PKP was performed in all 50 patients; combined with other procedures as follows: 12 "triple" procedures (PKP + cataract),11 PKP+ amniotic membrane transplantation (AMT),4 triple+AMT+ transplantation of limbal cells (LCAT). Subconjunctival injection of 25 mg/ml of bevacizumab was given to all patients at the end of surgery. Recipient corneal buttons were dissected into 3 corneal layers, stored in media for 24 hours at 37oC, and frozen till detection of VEGF quantity by immunoassay (ELISA). Corneal buttons from patients with non-inflammatory diseases served as controls.

Results Decrease of corneal neovascularization was observed in 88% of patients who received bevacizumab, and 86% of grafts remained clear. Mean best corrected visual acuity had statistically significant increase in all groups from 0.03 to 0.5, with the poorest visual outcome in SJS patients. Average postoperative astigmatism was -4,83 Dcyl. Average endothelial cell loss was 22.83% after one, and 31.97% after two years (similar in all groups). Secreted VEGF was significantly higher in high risk cases (2436.7 pg/ml) as compared to non-inflamed corneas (504.7 pg/ml).

Conclusion Combined "anti-inflammatory"approach of AMT, LCAT and bevacizumab may significantly improve corneal graft survival rate in „high-risk" eyes.

• 2262
Stem cell culture for limbal deficiency

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Purpose Cultured stem cell transplantation is a new promising technology for eye diseases associated with destruction, dysfunction, or genetic abnormalities of ocular stem cells. The first group of ocular diseases targeted is limbal stem cell deficiency. Various ocular disorders, including ocular burns, Stevens-Johnson syndrome, cicatricial ocular pemphigoid, severe infectious keratitis, contact lens-induced keratopathy, multiple surgical procedures involving the limbal region, aniridia, congenital erythrokerato-dermia, and keratitis associated with multiple endocrine deficiencies, may induce limbal deficiency.

Methods Various culture techniques have been developed that can be classified according to the type of stem cells (limbal epithelium or oral mucosal epithelium), the source of stem cells (autologous or allogeneic), the type of culture (explants or dissociated cells, feeders or no feeders), the carrier used to grow cells (amniotic membrane, fibrin, temperature-responsive plastic), and culture media. Eye banks are often involved in the preparation of these cell therapy products.

Results Prospective clinical trials have shown that transplantation of cultured epithelial stem cells improves the ocular surface condition of patients with limbal deficiency with a high success rate, especially when autologous limbal stem cells can be used as the source of cultured cells.

Conclusion However, many issues are still to be investigated. Among them, selection and screening of donor tissue, microbiological safety of stem cell production process, safety of transplantation of cells cultured with products or feeder cells from animal origin, choice of the best technology to be used for growing stem cells, evaluation of the cell therapy product before transplantation, definition of success after transplantation.

• 2263
Biomaterials for ocular surface reconstruction

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Purpose To provide an overview over the clinical need and recent developments regarding biomaterials for ocular surface reconstruction.

Methods Epithelial and stroma substitutes will be presented, as well as own data generated by electrospinning of a biodegradable elastomer.

Results Biofilms can be created and are sucessfully applied both on a research and on a clinical level.

Conclusion Biomaterials will become a reality in ophthalmosurgery.

• 2264
Pan-endothelial viability assessment with the triple HEC staining of organ cultured precut DSAEK vs full thickness corneas

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Purpose To assess the viable endothelial cell density (vECD) of posterior lamellar grafts, stored in organ culture, precut by eye bank technicians, and sent to a distant center.

Methods Paired corneas with an ECD >2200 cells/mm2 at the standard assessment with the SambaCornea analyser (TribVn, France), were stored in CorneaMax (Eurobio, France) and deswelled in CorneaJet (5% Dextran T500) for 6 to 24 hours prior to pre-cutting. They were randomly assigned as full-thickness grafts or as precut posterior transplants for DSAEK using a microkeratome with a 350µm head (Moria, France). Corneas were sent to a distant center where the vECD was assessed by using the triple Hoechst/Ethidium/Calcein (HEC) staining and fluorescent image analysis of the entire posterior surface: calculation of the area covered by living cells (H+/C+/E-) coupled with counting of nuclei in large areas allowed to determine the vECD, i.e. the useful cell pool (Pipparelli. IOVS 2011.52:6018). DSAEK and controls data were compared with non-parametric tests.

Results In both groups, the vECD was lower than the standard ECD determined by the eye bank (for 20±7% for full thickness grafts, 34±16% for DSAEK), because living cells never completely covered the entire posterior surface. vECD were respectively of 2006+/-349 vs 1661+/-464 (P=0.075).

Conclusion The HEC triple staining combined with image analysis provides a unique accurate assessment of the endothelial quality by giving the vECD. This laboratory technique allows a reliable assessment of the endothelial quality of tissues supplied to surgeons, precut or not. It can also be used to assess any methods liable to modify EC.

• 2265

European study on reliability assessment of endothelial cell count in eye banks: the Euro-Keratotest study

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Purpose In European eye banks, 15-20% of corneas are discarded for inappropriate ECD. Given the importance of a precise, robust and reproducible ECD, we organized an international survey of the quality of ECD determination

Methods The Euro-Keratotest study reproduced 2 surveys driven in 2003 and 2008 by our team in the 18 French eye banks (Transplantation2004), with substantial improvements: test slides (3rd generation keratotests) were fabricated with technologies employed in micro-optics, from images of real human corneas (Optics Letters2012). Twelve different mosaics with ECDs covering the usual range observed in eye banks, were created in a 8x8 mm quartz square. Keratotests, observable with transmitted light or specular microscopes, were sent simultaneously to all volunteer eye banks (n=100). Each technician had to determine ECD and morphometry of the 12 mosaics with his/her standard counting method. Data were collected on a specific website

Results A first analysis of 120 technicians of 38 eye banks will be presented. It allowed identification of inter and intra bank variability and of bias likely involved (inappropriate counting strategy or wrong microscope calibration) and susceptible to be improved

Conclusion Participation of the eye banks to this survey using 3rd generation keratotests improves our knowledge on the reliability of cell counting methods in eye banks, and help standardize graft quality assessment. Keratotests are also perfect tools for the initial formation and continuous training of eye banks technicians, as well as for the eye banks certification. Grant: Interregional Hospital Clinical Research Project 2011, Ministry of Health, DIRC Rhônes-Alpes

• 2266

Worldwide Eye Banking (WEB) project: international survey of demand and supply

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Purpose The whole eye banking (EB) process, from corneal retrieval to surgery, is improving. Paradoxically, corneal blindness worldwide is still increasing. Supply seems lagging far behind global demand but only partial data of the worldwide situation is available. We therefore launched an international survey on the balance of demand and supply, called the "Worldwide Eye Banking" (WEB)-project. Our goal is to identify suitable solutions in countries willing to improve their corneal supply

Methods Descriptive epidemiological worldwide transversal study. A questionnaire was designed and e-mailed to EB staff and ophthalmologists involved in corneal grafts using mailing lists from local and international ophthalmological societies or by face to face interview during international ophthalmology, eye research or EB congresses

Results Significant disparities were highlighted. Developed countries tended to satisfy corneal demand. EBs in the United-States use short term storage and are exporters, while Europeans use long-term organoculture and nearly satisfy local demand. Keratoplasty indications have 2 profiles: infections, mainly trachoma, for developing countries and keratoconus, endothelial dystrophy or iatrogenic edema in developed countries

Conclusion This demand/supply disparity, at this stage of the study (ongoing), is severe in most developing countries. Decreasing demand requires: 1) Trachoma fight in endemic zones, 2) Iatrogenic edema prevention. Increasing supply requires: 1) Corneal donation politic dynamism, 2) Local eye banking implantation in each country, 3) Optimizing storage technique for better efficiency (retrieved/delivered graft ratio), 4) Bioengineering of endothelial graft

• 2267

Light microscopy of the corneal pathologies that we meet in our daily practice as an eye banker

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Purpose Organ culture is the method of choice for the preservation of a human donor cornea for transplantation throughout Europe. This method is often closely connected with the assessment of the cornea using light microscopy. The corneal endothelium, its polymeghatism, pleomorphism, cornea guttata and other endothelial abnormalities as well as epithelial and stromal pathologies will be presented to show the usefulness of light microscopy in the evaluation of corneal pathologies.

Methods Photographs from light microscopy (both phase contrast and bright field) taken before and after corneal storage in organ culture will be compared and discussed in relation to changes in endothelial morphology and the swelling of the intercellular spaces. The individual corneal layers (the corneal epithelium, the stroma and the endothelium) of pathological corneas will be compared to those of control corneas.

Results Among corneal pathologies, cornea guttata, corneal dystrophies (Fuchs endothelial corneal dystrophy, posterior polymorphous corneal dystrophy) and crystalline keratopathy will be shown using pathological explants. Moreover, the corneal pathologies will be correlated with histological findings. Finally, bacterial and fungal contamination of the cornea during organ culture will be shown.

Conclusion Light microscopy is an essential part of qualitative and quantitative corneal assessment, which allows corneas with a variety of pathologies, mostly endothelial in origin, to be excluded from grafting.This work was supported by the project PRVOUK-P24LF13 of Charles University in Prague.

• 2268

A new and quantitative method to evaluate the overall quality of corneal tissues for clinical applications and research testing

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Purpose To demonstrate the validity of a new evaluation technique for measuring the overall quality of the cornea and check the efficacy of this quantitative approach in a comparative study of corneas preserved in CorneaCold® (new formulation) or Optisol-GS.

Methods 24 pairs of unsuitable corneas with intact epithelial layer and good morphology were collected. Right corneas were placed in CorneaCold® (Eurobio-France) and left corneas in Optisol-GS (Bausch&Lomb-USA) from the same donor and vice-versa for a 4 week comparative study. The study was divided into 2 phases, where phase 1 was open and phase 2 was blinded. Cells were stained with trypan blue and counted under an optical microscope to check the mortality and cell density. Difference between epithelial and endothelial layer was evaluated microscopically for thickness measurement. A transparency device was used for calculating the degree of transparency. All the above subjective parameters were converted to objective values for determining the overall quality of the cornea.

Results The conversion to objective values from subjective analysis helped to evaluate the quality of corneas at different time intervals of preservation in different media. Students t-test at week 2 (p=0.001) and week 4 (p=7.563E-09) showed statistically better results when corneas were preserved in CorneaCold® rather than in Optisol-GS.

Conclusion The overall quality evaluation of cornea presented here is efficient, consistent and easy. This new technique could be useful for comparative studies and to value corneas for eyebanks, biobanks and research or transplantation purposes. CorneaCold® is a promising corneal preservation medium for hypothermic storage with slightly longer preservation time.

Commercial interest

• 2269

Serum-free cornea culture with hydroxyethyl starch as a deswelling agent

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Purpose Varying states of hydration during organ culture and subsequent dehydration of corneas with Dextran prior to transplantation cause endothelial cell damage. Hydroxyethyl starch 130 (HES) has been suggested as a permanent dehydrating agent in serum-free cornea culture. This study compares corneas stored in a synthetic medium containing HES with corneas stored and dehydrated under standard conditions.

Methods Twenty pairs of human donor corneas were cultivated in MEM with antibiotics at 31°C for 16 days (groups A and B) or 28 days (groups C and D, n=10). Media contained 2%FCS in group A and C, and 7.5 % HES 130 plus 1mU/l human insulin in groups B and D. On day 15 or 27, corneas from group A and C were placed in dehydration medium (MEM + antibiotics + 2%FCS + 5% dextran 500). Endothelial cell density and morphology were investigated at the beginning and end of culture. Corneal thickness was assessed by pachymetry. Keratocyte viability was assessed by TUNEL and Annexin V staining.

Results Endothelial cell loss was higher in group A (278.5+/-184.2) vs. B (156.6+/-154; p=0.0293), and in group C (490+/-156.3) vs. D (301.8+/-189.6; p=0.0195), with similar morphology. Final corneal thickness was 882+119µm and 914+119µm in groups A and B, and 889+99µm and 957+87µm in groups C and D, resp. (n.s.). No significant differences were found in TUNEL and Annexin staining.

Conclusion The synthetic medium supplemented with HES 130 and insulin improves endothelial cell survival during cornea culture, without adverse effects ion keratocyte viability. It is thus feasible to store donor corneas in fully synthetic medium without the chemically undefined FCS and without the need for dehydration, resulting in increased safety and faster transplant availability.

• 2271

Novel interpretation of fundus autofluorescence (FAF) findings in choriocapillaritis

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Purpose To determine the significance of increased fundus autofluorescence (FAF488) in choriocapillaritis, comparing photobleaching process, SD-OCT and melanin-related fundus autofluorescence (FAF787) findings

Methods FAF488 signal depends on both the amount of bisretinoids in the RPE and the absorbion of light by photoreceptor pigments, macular pigment and RPE melanin. During the photobleaching process (absorbion of photons by photopigment in the outer photoreceptor segments), there is a reduction of the photopigment density and so an increase of the visualization of the autofluorescent signal

Results In MEWDS and MFC, the more striking FAF488 alteration is an increase of the autofluorescent signal and SD-OCT shows a disruption of IS/OS junction, probably sign of dismanting outer photoreceptor segments; there is not an increase of FAF787 and after the photobleaching process, the areas of increased FAF488 become isofluorescent. This could mean that the areas of hyperautofluorescence are due to a better visualization of the autofluorescent signal because there is a reduction of the visual pigments and not to an increase of the fluorophores. In the APMPPE group, during the convalescent stage, increased FAF488 and FAF787 are often seen in the center of chorioretinal scars, corresponding to accumulation of fuorophores debris and to hypertrophy/hyperplasia of RPE cells

Conclusion In MEWDS and MFC, photobleaching process, FAF787 and spectral-domain OCT findings may explain the increased FAF488 present in the acute phase of the diseases as a loss of the photopigments and not to an increase of fluorophores, because there is a limited pertubation of choriocapillaris circulation with a slight ischaemic insult to outer retina.

• 2272

Appraisal of choroiditis in birdshot retinochoroiditis is essential and only possible using indocyanine green angiography

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Purpose Birdshot retinochoroiditis (BRC) belongs to the group of stromal choroiditis entities including also VKH disease. In contrast to VKH where the origin of inflammation is limited to tha choroid, inflammation starts both in the choroid and the retina in BRC.Without indocyanine green angiography (ICGA), global appraisal of BRC is not possible as choroidal inflammation cannot be detected nor followed. The aim here was to analyze the practical contribution of ICGA to the management of BRC.

Methods Charts of patients with the diagnosis of BRC seen in the Centre for Ophthalmic Specialised Care (COS), Lausanne, Switzerland from 1995-2011 were reviewed. Standard fluorescein-ICGA work-up was performed at presentation and during follow-up. Diagnostic and monitoring contribution of ICGA was analyzed.

Results In a collective of 1268 patients seen from 1995-2011 at the COS, 25 patients (2.0%) were diagnosed as BRC. 19 had sufficient data to be included in the study. Mean age was 49 years, HLA-A29 positivity was 100% and follow-up was 112 months. IGA contribution was twofold; (1) Early diagnosis could not have been without ICGA in 3/19 patients a proportion that increased to 3/7 (43%) if only considering patients with early stage disease at entry. (2) ICGA further showed that choroidal disease responded well to therapy and stayed under control as long as therapy was continued.

Conclusion ICGA was found to be essential for early diagnosis of BRC, an element that is crucial as early therapy is crucial in the control of disease. ICGA further allowed to monitor choroidal disease showing a good response in contrast to retinal disease. Hence global appraisal is needed for BRC and is not possible without ICGA.

• 2273 / F101

Paediatric rheumatology clinic outcome at Leeds Teaching Hospitals, UK

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Purpose Present 1-year data of the combined ophthalmology and rheumatology pediatric uveitis clinic at Leeds Teaching Hospitals.

Methods Retrospective data collection

Results An estimated 230 patients with JIA were screened by ophthalmology in this time period.21 different paediatric patients with iritis were managed from June 2011 to May 2012 in the joint clinic.8(38%) patients were male and 13(62%) female with age at diagnosis ranged from 0.5 – 12 years. 11 patients (52%) were diagnosed with oligoarticular and 5(23%) with polyarticular JIA,3 patients were ANA +, 3(14%) did not have any joint involvement.9 patients(43%) presented with vision of 0.2logMar or worse, and 4 continued to have vision worse than 0.2 logMar while 17 patients (81%) improved or maintained stable vision of 0.1 or better.3 patients had intermediate uveitis,1 had panuveitis and 1 had papillitis with iritis.2 had eye complications of lens opacities and 1 patient had retinal detachment.17(81%) patients received systemic treatment, with 12 receiving methotrexate +/- mycophenolate mofetil and 5(29%) receiving anti-TNF α therapy (infliximab or adalimumab) in addition to methotrexate +/- mycophenolate mofetil. 13/16 patients with JIA (81%) had iritis associated with their joint flare-ups. 9 patients (50%) out of 18 with joint pathology received intra-articular steroid injections during this period and 6 received (28%) periocular steroid injection. A survey of the joint clinic by the patient and medical staff showed significantly high satisfaction rate.

Conclusion The joint clinic has numerous benefits and is the right approach to manage a condition where communication is crucial between team monitoring (ophthalmology) and managing (rheumatology) the condition

• 2274

Voclosporin: newer analyses of a randomized, controlled trial for noninfectious uveitis

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Purpose To provide an overview of the voclosporin clinical development program for noninfectious uveitis involving the posterior segment.

Methods Two trials, LX211-01 (active uveitis) and LX211-02 (clinically controlled, quiescent uveitis), were conducted for noninfectious uveitis involving the posterior segment. All trials were dose-ranging and double-masked.Study LX211-01 enrolled 218 patients with active, posterior segment uveitis. The co-primary efficacy endpoints were mean change from baseline in vitreous haze (VH) score after 16 and 24 weeks of therapy or at time of rescue, if earlier.Study LX211-02 enrolled 232 patients with clinically quiescent posterior segment uveitis. The primary endpoint for this study was the proportion of patients who experienced an inflammatory exacerbation.

Results In Study LX211-01, the voclosporin 0.4 mg/kg group BID demonstrated statistically significant differences from placebo in the co-primary endpoints, Week 16 and Week 24 (p=0.008 at 16 weeks, p=0.027 at 24 weeks). Analyses of important subpopulations, support the effect of voclosporin on severe uveitis.In Study LX211-02, voclosporin 0.4 mg/kg BID reduced the rate of recurrence of inflammatory exacerbation in patients with quiescent disease by up to 50% over a 26-week period.

Conclusion In Study LX211-01, clinically meaningful reduction in vitreous haze with strong statistical significance was observed. The response to treatment with voclosporin was early and sustained. In Study LX211-02, there was an up to 50% reduction vs. control in inflammatory exacerbation recurrence rate.Voclosporin safety is consistent with the class and is manageable with routine monitoring.

Commercial interest

• 2275

Long term efficacy and tolerability of anti-TNFα therapy in the treatment of non-infectious uveitis – a surveillance study

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Purpose To report the efficacy and tolerability of anti-TNFα agents in the management of non-infectious uveitis and scleritis in adult patients

Methods Forty adult patients treated for at least twelve months with anti-TNFα therapy for non-infectious uveitis or scleritis were identified using an online biologics registry. Data were collected regarding prednisolone doses, immunosuppressive agents, adverse effects and steroid rescues. The main outcome measures were 1. rates of reduction of daily prednisolone dose to 10mg, 5mg or less; 2. rates of reduction in concomitant immunosuppression 3. steroid rescues and 4.adverse events

Results In this patient cohort the use of anti-TNFα therapy enabled the daily prednisolone dose to be maintained at 10mg or less per day in 80% of patients. The rate of steroid rescue was reduced from 0.79 rescues per person per year (PPY) to 0.29PPY following the use of anti-TNFα therapy. In patients requiring more than 2 immunosuppressive agents at baseline, it was possible to reduce this to 1 or 0 in 80%

Conclusion This study supports the current use of anti-TNFα agents in the management of adult patients with non-infectious uveitis, whilst awaiting results of current on going randomized controlled trials. . Their use enables steroid sparing, a reduction in concurrent immunosuppressive agents and is associated with a lower risk of relapse. This is achieved with a low rate of adverse events.

• 2276

Final results of an investigator initiated, multicenter randomised controlled trial of the efficacy of Adalimumab in active uveitis refractoty to standard treatment (ADUR)

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Purpose TNF alpha inhibitors have revolutionized the care of autoimmune diseases, among them severe cases of non-infectious uveitis. Randomized clinical trials are lacking for this indication except for etanercept. We aimed to close this gap by initiating a randomized clinical trial testing Adalimumab (ADA) in severe forms of uveitis.

Methods Local and federal authorities approval has been obtained. Patients with active uveitis despite 0,1mg/kg/bodyweight of prednisone and already one immunosuppressive medication were eligible. Patients were randomized into either a therapy with ADA 40 mg s.c. every other week and high dose corticosteroids in a tapering regime or to increase the corticosteroids only. At three months main outcome parameters are assessed and efficacy determined. In case of treatment failure switch to the other arm was possible.

Results 25 patients were enrolled. The last patient will finish the trial in september 2012. 20 patients have been evaluated to date. The primary outcome criterion (Visual accuity improvement > 2 lines) was reached by 63.3% patients in the ADA group (mean improvement 0.29 logMar). In the control arm only 25% of patients improved > 2 lines. In parallel the control arm showed less reduction in inflammatory activity (reduction in activity score by a mean 2.89) as compared to the ADA group (mean reduction by 15.3 points).

Conclusion The results oft he trial show clear superiority of ADA over control in the treatment of severe uveitis forms in termy of visual accuity and inflammatory activty.

Commercial interest

• 2277 / F089

Tocilizumab for anterior uveitis and juvenile idopathic arthritis – a case report

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Purpose We report a case of Juvenile Idiopathic Arthritis (JIA) and Anterior Uveitis (AU) responding well to Tocilizumab, a new humanized monoclonal antibody against the IL-6 receptor, after having been refractory to classical immunosuppressive agents as well as to TNF-α inhibitors.

Methods The Patient was treated in our center from 2007-2012. Collected data included: visual acuity (VA), anterior chamber cells and –flare, flaremeter measurements, intraocular pressure (IOP), presence of macular edema (ME) and cataract, topical and systemic medications, number and site of affected joints, laboratory inflammation parameters.

Results Patient was born 1996, diagnosed with JIA 1998 and with AU 2005. Inflammation was initially controlled with methotrexate and corticosteroids, VA fluctuated between 20/40-20/15(OD) and 20/20(OS). In 2007 VA decreased to 20/200(OD) as ME developed. Additional systemic therapy included between 2008 and 2009: Ciclosporin, Adalimumab, Mycophenolate, Leflunomide, and Infliximab. Control of ocular and/or joint inflammation was always insufficient or short lived. Between 2008 and 2010 ME required multiple periocular Triamcinolone injections.IOP first rose in 2008 to 34mmHg(OD), requiring combined topical and systemic therapy and finally trabeculectomy in 2010. Cataract developed on both eyes.Tocilizumab therapy was started in 02/2010. Since then AU and joints are free from inflammation. Cataract-surgery and implantation of an artificial lens in OD was performed successfully in 2011. Systemic steroids could be reduced to 2 mg/d. IOP is <20mmHg; VA is stable at 20/32(OD) and 20/50(OS).

Conclusion Tocilizumab may be another treatment option for JIA-associated uveitis which is refractory to established immunosuppressants.

• 2411

How to detach vitreous in macular diseases

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ABSTRACT NOT PROVIDED

• 2412

How to stain ILM in macular surgery

HARITOGLOU C
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ABSTRACT NOT PROVIDED

• 2413

ILM peeling in macular surgery: side-effect

TADAYONI R
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Purpose Discussing data on side effects of ILM peeling.

Conclusion ILM peeling induces anatomical and functional alteration of the retina that should be weigh up against its benefits.

• 2414

ILM peeling in macular surgery: benefits

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Internal limiting membrane (ILM) peeling should be beneficial to improve the anatomic and functional outcomes in macular surgery. In macular hole surgery, it seems to be an additive tool to improve the closing rate especially in large macular hole. In epiretinal membrane surgery, it should be considered either to improve the functional outcome but also to decrease the recurrence of epiretinal membrane on the remaining ILM. However, the characteristics of the peeling (ie area, control with dye) should be given in all clinical trials to obtain more homogeneous surgical criteria.

• 2415

What to peel in macular surgery?

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ABSTRACT NOT PROVIDED

• 2421

The flicker ERG and retinal blood flow relationship in diabetic patients without retinopathy

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Purpose To evaluate the association between functional and hemodynamic alterations of the retina in diabetes mellitus (DM) without retinopathy (NDR).

Methods 15 patients (63±6.3 years) with DM type II (duration 6±3.5years) and NDR, and 40 age matched controls were examined. Color Doppler Imaging (CDI) was conducted to visualize blood flow in ophthalmic artery (OA), central retinal artery (CRA), medial and lateral posterior ciliary arteries brevis (PCAB). Photopic and scotopic flicker ERGs (p-FERG and s-FERG) were recorded at 8.3, 10, 12, 30 Hz flickering.

Results In NDR, the increase of the blood flow peak systolic velocity (V syst) and end diastolic velocity (Vdiast) was noted in AO. The most significant changes in blood flow were observed in CRA and PCAB. A reliable correlations were shown between Vdiast, the resistance index RI in CRA and insulin levels (r=0.64), serum C-peptide (r=0.60) and the index of insulin resistance IR (r=0.65); between Vdiast, RI in PCAB and insulin levels, the C-peptide level and IR (r=0.59, 0.56, 0.59, respectively). The amplitude of light and dark adapted FERG at 8.3-12 Hz declined in more than 60% eyes up to 69-80%. The p-FERGs at 24 and 30 Hz did not differ from the control; but we found a sharp increase in s-FERG (155.5±15.3 - 319.9±21.4% for 24 - 30 Hz respectively). Significant correlation was shown between the 10Hz-FERG amplitude (but not the 24Hz or 30Hz-FERG) and Vdiast in CRA and PCAB (r=0.51; r=0.50).

Conclusion There is a significant relationship between the retina hemodynamics and physiological effects of insulin, leading to metabolic disorders. Signs of blood flow deficiency in CRA and PCAB in NDR correlated with an early alteration in the photoreceptor function.

• 2422

Colour contrast sensitivity and electrophysiological abnormalities in patients undergoing long term desferrioxamine treatment

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Purpose To describe the spectrum of colour contrast sensitivity and electrophysiological abnormalities in patients undergoing long term desferrioxamine (DFO) treatment for systemic iron overload in blood transfusion-dependent anaemias.

Methods Thirty five patients on long term DFO treatment with abnormal colour contrast sensitivity and/or abnormal retinal electrophysiology examined in the Electrophysiology Department at Moorfields Eye Hospital were included in this study. They underwent visual acuity testing, colour contrast sensitivity and International-standard electrophysiological evaluation including pattern and full-field electroretinography (PERG and FFERG). In most patients follow up investigation also included recording of ocular symptoms, fundus morphology and DFO treatment (dose and route of administration).

Results Most patients manifested colour contrast threshold elevation, mainly along the tritan axis and also pattern ERG abnormalities as an indication of macular dysfunction. Full-field ERG abnormalities, when present, were consistent with generalised photoreceptor dysfunction involving rods only, cones only, or both rods and cones. In some patients these abnormalities were partly reversible following cessation or reduction of DFO treatment.

Conclusion When DFO retinal toxicity occurs, it can present with a wide range of electrophysiological abnormalities, including macular and/or generalised retinal dysfunction. Early colour vision abnormalities usually involve the S-cone-driven pathway. Colour contrast sensitivity and electrophysiological evaluation may be used to detect DFO retinal toxicity and monitor recovery, providing an essential aid to the management of the patient.

• 2423

Genotype-phenotype correlations in Stargardt disease/ABCA4-related retinopathy

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Purpose To investigate genotype-phenotype correlations in patients with Stargardt Disease (STGD) / ABCA4-related retinopathy

Methods 195 patients diagnosed with STGD and harbouring ABCA4 variants were recruited. A detailed clinical history and examination were undertaken. Pattern and full-field ERGs (PERG; ERG) were used to classify 175 patients into three groups (Lois et al. 1999); dysfunction confined to the macula; macular and cone ERG abnormality; and macular and both cone and rod abnormality. Patients were also grouped by genotype: G1 - two null variants (N=9); G2 - at least one null variant with or without missense variants (67); G 3 - at least two missense variants (50); G 4 - one missense variant (69).

Results All G1 patients had a group 3 ERG. 26/58 G2 were in ERG group 1; 26/58 in Group 3. 24/47 G3 patients were ERG group 1; 7/47 group 2; and 16/47 in ERG group 3. 31/61 G4 patients were in ERG group 1; 5 in group 2; and 25/61 in group 3. Significant clinical differences were also observed between the genotypes.

Conclusion Patients with two null ABCA4 variants had the most severe phenotype. In comparison, patients with two or more missense variants had a more variable phenotype and included many with normal full-field ERGs. This large survey confirms previous suggestions based on smaller cohorts and individual families.

• 2424

Recovery of the ERG from very low SNR recordings using a robust frequency domain approach: an Internet open source implementation

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Purpose To present a statistically robust method of estimating the transient electroretinogram (ERG) in extremely poor recordings (very low SNR) contaminated by continuous noise (electrode noise, EMG, exogenous electrical interference) and discontinuous noise (eye-movements and blinks).The transient ERG (ERG) is estimated by ensemble averaging with standard errors and p value, derived by either Magnitude Square Coherence or Bootstrap Resampling. However, both techniques are susceptible to noise. A robust estimator noise is required.

Methods A series of ERG's was recorded in normal subjects, containing numbers of prescribed eye movements and blinks. AR models were derived using the Burg algorithm over a range of explicit SNR's. The ERG record was recovered as its Fourier Series representation over 9 harmonics. p values were derived for all estimates. An Excel implementation is presented which accesses remote Internet resources using MatSOAP©.

Results The robust estimator was validated in Monte Carlo realisations of the AR model with expected high levels of performance for amplitudes and p values. In estimations in the raw data sets, high levels of statistical agreement were achieved for each subject across no-noise:noise series. The recovery by ensemble averaging performed poorly.

Conclusion The robust estimation in the ERG as presented here is novel and offers an important advance in clinical ERG measurement. The complexity is hidden from the User by providing a familiar Excel© spreadsheet interface.

• 2425

Mechanisms & recovery of vitamin A deficiency

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Purpose To illustrate different mechanisms which lead to vitamin A deficiency and result in retinal dysfunction. To show how a diagnosis can be made, and how, and to which degree, in such cases, retinal function can be recovered.

Methods A case presentation format will be used to illustrate different mechanisms of retinal dysfunctions due to vitamin A deficiency. Patient history taking, clinical and electrophysiological phenotypes and therapeutic approaches will be addressed.

Results Mechanisms of vitamin A deficiency are very different, but all have fat malabsorption in common. Often, other concomitant vitamin deficiencies exist. With vitamin A repletion therapy, either partial or complete restoration of retinal function can be attained.

Conclusion Causes of vitamin A deficiency are very diverse. Thorough history taking, in combination with an extensive clinical examination and psychophysical and electrophysiological tests, most often allows making a more specific diagnosis of an underlying malabsorption. Vitamin A repletion therapy is effective in such cases.

• 2431

An update on the vision simulator

CHATEAU N
Orsay

ABSTRACT NOT PROVIDED

• 2432

Spherical aberration and binocularity

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Purpose To evaluate the effect of different combinations of spherical (SA4) and secondary spherical (SA6) aberration on each eye on binocular subjective quality of vision.

Methods A numerical eye model was used to generate images (ie three 0.4 logMAR high contrast letters) viewed through a 4.7mm pupil diameter and degraded by various spherical aberrations (SA4-0.4µm, SA4+0.4µm, SA4-0.4µm and SA6+0.2µm, SA4+0.4µm and SA6-0.2µm). Binocular vision was simulated using a 3D-NVIDIA video system projecting different image on each eye. Through-focus quality of vision was evaluated using a grading scale (ITU-R 500 recommendation) by three subjects under monocular and binocular condition for each tested conditions (ie various combination of the five aberration profiles).

Results Binocular through-focus curve followed the best monocular curve. Binocular inhibition was obtained if subjective image quality was too different between the two eyes. We rarely measured binocular summation in term of subjective quality of vision. Ocular dominance seemed to affect the level of inhibition: binocular inhibition was limited when the dominant eye saw the best image. Area under the binocular curve (ie a way to evaluate subjective depth-of-focus) measured for a fair or higher image quality was increased with all combinations compared to naked eye because of the summation of the two best monocular curves. The greatest increase was obtained with reverse profile of SA4 and SA6 between each eye (ie SA4-0.4µm and SA6+0.2µm on one eye and SA4+0.4µm and SA6-0.2µm on the other eye).

Conclusion The use of different spherical aberration on each eye leads to a better binocular through-focus curve especially with combination of opposite sign of SA4 and SA6. However there is no binocular summation of vision quality.

• 2433

Shack-Hartmann aberrometry vs OQAS : the quarrel of the ancients and the moderns ?

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The Optical Quality Analysis System (OQAS) has the advantage over Hartmann-Shack aberrometers of being capable of measuring both wavefront aberrations and scatter. In patients with eyes with mild scatter, both techniques give similar results. However in eyes severe amount of scatter, Hartmann-Shack aberrometry may overestimate the quality of vision. On the other hand, the OQAS suffers from a certain level of background noise, generated by the choroid. During this presentation we will determine the current indications for those two techniques.

• 2434

Should you decide to perform cataract surgery on your patients, based only on straylight?

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Purpose A widely accepted validation criterion for cataract surgery is the likelihood that the surgery will be beneficial to the patient. Yet important variation exists between individual ophthalmologists in what constitute criteria for cataract surgery, and optometrists vary widely in their referral criteria. As a consequence huge differences in the amount of cataracts being treated exists between different centres. Some degree of standardisation is wanted. Visual acuity is considered, but predictability of surgical outcome is often difficult because visual acuity is confounded by the retinal condition. Straylight on the other hand is independent of retinal condition, and constitutes a complementary measure of quality of vision, complementary to visual acuity, corresponding to complaints such as glare, hazy vision, face recognition problems.

Methods A population of 217 patients for cataract surgery was studied. Before and after cataract extraction best corrected distance visual acuity (CDVA), and straylight using the C-Quant from Oculus were recorded for all patients. Subjective complaints were documented before and after surgery by the 39-item National Eye Institute Visual Function Questionnaire (NEI VFQ-39) and a home made straylight questionnaire. Data are compared to a 5000 eye database from an earlier study.

Results Before and after cataract extraction, questionnaires show straylight to have almost the same influence on subjective quality of vision as CDVA, as show by correlation analysis. Straylight improvement upon surgery is strongly correlated with preop straylight level.

Conclusion When straylight is added to pre-operative considerations of cataract extraction post-operative improvement is better predictable.

Commercial interest

• 2435

Impact of higher-order aberrations on accommodation in phakic presbyopic patients

PISELLA PJ
Tours

ABSTRACT NOT PROVIDED

• 2436

Quality of vision and 3D

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Purpose Multiple functional disturbances related to disorder of the stereoscopic vision have been revealed by the development during these last few years of 3D on all kinds of screens. In order to understand and potentially predict the occurrence of this new symptoms, a platform for detection and qualification has been designed at 3-D Fovea Observatory - Brest (France)

Methods - This platform includes: • 3D 107 cm plasma screen• 3D active pair of glasses equipped with a LCD opturator specifically developed for the study (high blocker level > 1/1000 and contrast sensitivity C1 : 350-400), • oculometer able to follow the visual strategy, • computer for the tests diffusion and collection of data- We developed a first kit of 4 tests focused on the detection of capacities for 3D tolerance. The evaluated parameters are : stereo-acuity, simultaneous perception, total fusion and hyper stereopsis.

Results Outcome issued from these 4 tests can be expressed in different ways according to the competence level of the user. A simple colored scale for the general population and quantification for the ophthalmologist and the orthoptist. Mean time required for performing this first series of exams is 403 seconds +/- 93. An evaluation in a risky population for abnormal binocular vision is ongoing.

Conclusion preliminary results seem encouraging and should allow an extrapolation to the quality of relief perception on a movie in 3D. The interest of this platform lies on its simplicity of use, its ability to predict the tolerance to 3D exposure and to offer new tools for a modern and dynamic evaluation of binocular vision.

• 2441

Scleritis: general concepts

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Inflammation of the sclera may be a very serious condition, not only because it can produce structural damage to the globe and eventually result in blindness, but also because it may be a manifestation of a life-threatening systemic disease. It is predominantly a disease of the middle aged and elderly, probably reflecting the age group of the commonly associated systemic diseases. Females are more likely to be affected, and no geographical or racial differences have been detected, either in incidence or prevalence. There is also no evidence of any genetic predisposition. The disease may start in one eye only but becomes bilateral in one third of the patients, the second eye becoming involved from three months to six years after the first. It is typically a very painful condition, but painless scleritis can occur. Clinical features of anterior and posterior scleritis will be discussed.

• 2442

Imaging and scleritis

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ABSTRACT NOT PROVIDED

• 2443

Infectious scleritis

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Scleritis can occur as a result of an immunological response in systemic infectious diseases such as tuberculosis, leprosy, syphilis and lyme disease. These diseases are becoming more common and, as under-treatment in many countries leads to incomplete elimination of the underlying infection, scleritis is becoming more common. Scleritis can also result from an immunological reponse to a systemic infection by bacteria, viruses , parasites or fungi. More rarely the sclera can be infected directly through the introduction of the organism into the sclera by trauma or from the spread of infection from adjacent sources. This is much more likely to happen if the tissue has been previously irradiated or surgically treated particularly after pterygium surgery. Infectious scleritis is less common than immunologically induced scleritis , diagnosis is difficult so treatment is often delayed and frequently incorrectly treated with steroids with sometimes disastrous consequences. Therefore in all patients with scleritis it is important to ask oneself: Could this be infective?

• 2444

Scleritis and systemic diseases

LEE R
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ABSTRACT NOT PROVIDED

• 2445
Conditions mimicking scleritis

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Scleritis is an inflammatory process due to a huge number of inflammatory systemic etiologies and treated with corticosteroids or immunosuppressive drugs. Pseudoscleritis are represented by tumoral diseases that looks like scleritis but with a painless clinical presentation, and unresponsive to corticosteroids. Theses tumoral pathologies that may simulate scleritis are usually tumors of the conjunctiva (carcinoma, achromic melanoma, sarcoma, Malt lymphoma…) however some atypical presentation of intraocular tumors can mimic anterior or posterior scleritis. The tumoral origin of ocular pathologies must not be delayed because it increases the risk of metastasis and death. One a tumor is suspected patient should be referred to an onco ophthalmologist for diagnosis and management. In this paper, the different tumoral pathologies and their management will be described.

• 2446
PUK from diagnosis to treatment

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Purpose To describe the treatment strategy in the management of peripheral ulcerative keratitis (PUK).

Methods The current literature is reviewed and the experience of a tertiary referral centre is reported.

Results Peripheral ulcerative keratitis (PUK) is rare but severe sight-threatening disease affecting the peripheral cornea. The causes of PUK are multiple and insidious. Infectious diseases, both secondary to systemic rather than purely local diseases, and non-infectious diseases can be identified as a cause of PUK. Non-infectious systemic diseases, which can induce deposition of immune complexes in the cornea and, hence, lead to corneal ulcers, include peripheral vasculitides and inflammatory diseases of collagen, such as Rheumathoid arthritis, Wegener Granulomatosis and Systemic Lupus Erythematosus. Mooren's ulcer is one of the most characteristic PUKs: often unilateral and self-limiting in the elderly, sometimes bilateral and relentless in young patients, may cause severe visual impairment following extensive corneal destruction. Immunosuppressive therapy has been demonstrated effective in improving the prognosis of progressive cases, although a certain number of patients remain refractory to treatment. Resolution of refractory cases of Mooren's ulcer with new systemic biologic agents, such as campath-1H and anti-tumor necrosis factor (TNF)-α, has been reported.

Conclusion PUK can be a severe disease, leading to significant visual impairment. Although no guideline is provided, the current medical literature can give the basis for a successful treatment strategy. The detection of the infectious trigger can lead to the correct, specific therapy. Non-infectious diseases are basically treated with the combination of steroids with immunesuppresives and, when necessary, biologics.

• 2451

Is spectral domain optical coherence tomography useful in improving the contour line with the Heidelberg Retina Tomograph?

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Purpose To compare the measurements of the optic disc in glaucoma patients and glaucoma suspects with spectral domain optical coherence tomography (SD-OCT) and confocal scanning laser ophthalmoscopy (HRT) before and after adjustment of the contour line with the help of the OCT.

Methods In 109 consecutive patients (109 eyes), optic disc parameters were compared prospectively between the 2 devices before and after adjustment of the optic disc area (ODA) on the HRT3 with ODA obtained with the Cirrus SD-OCT as a reference. Intraclass correlation coefficients (ICC) and the 95% limits of agreement (LoA) with Bland-Altman plots were used to compare the agreement of the pre and post-adjustment measurements with the OCT and the HRT.

Results The ICC for the optic disc area (ODA) was better after adjustment of the contour line on the HRT3 with the help of ODA obtained with the OCT, 0.785 and 0.985, respectively. However the ICC for the rim area (RA) was still moderate after the adjustment, 0.543 and 0.627 respectively. Other parameters C/D ratio, cup area and cup volume were almost unchanged. The 95% limits of agreement (LoA) with Bland-Altman analysis were narrowed after the adjustment of the ODA, from -0.52 to + 0.71 mm2 to -0.12 to + 0.15 mm2. However the LoA remained wide for the RA even after correction of the contour line on the HRT with the help of the OCT, -0.32 to + 0.74 mm2 vs -0.23 to +0.61 mm2.

Conclusion SD-OCT is an additional valuable tool in improving the placement of the contour line on the HRT. However the parameters of the optic disc measured by the 2 methods are not interchangeable.

• 2452

The relationship between standard automated perimetry and retinal ganglion cell–inner plexiform layer thickness measured by the cirrus spectral domain optical coherence tomograph

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Purpose To evaluate the strength and pattern of the relationship between the ganglion cell–inner plexiform layer (GCIPL) thickness measured with Cirrus high-definition (HD)-OCT and visual field (VF) assessed by standard automated perimetry (SAP).

Methods Ninety-three eyes of 49 glaucoma patients were enrolled. In all patients, parameters of both GCIPL and the peripapillary retinal nerve fiber laye(pRNFL) thickness were measured by Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA). Mean sensitivity(MS) was recorded on the decibel (dB) and 1/L scales. The relationship between function and structure (GCIPL, pRNFL) was sought.

Results Correlations were seen between GCIPL sectors and RNFL sectors patients with glaucoma. (r = 0.38–0.792). Average GCIPL thickness and MD correlated most strongly of a strength similar to that demonstrated between average pRNFL thickness and MD. The highest correlations were observed between superior VF cluster (in dB scale) and inferior GCIPL thickness(R2=0.49) or inferior RNFL thickness (R2 = 0.51). Correlations were slightly greater with dB scale than 1/L scale.

Conclusion There was a moderate association between the GCIPL thickness and SAP. Cirrus HD-OCT measurements of the GCIPL relate well with functional loss in patients with glaucomatous optic neuropathy.

• 2453

Choroidal thickness in glaucoma patients and glaucoma suspects measured by spectral domain optical coherence tomography

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Purpose The aim of our study was to evaluate and compare retro-foveolar choroidal thickness (RFCT) of healthy subjects, individuals with intraocular hypertension, patients with primary open-angle glaucoma (POAG), patients with normal tension glaucoma (NTG) and patients with primary angle-closure glaucoma (PACG) by spectral domain optical coherence tomography (SD-OCT).

Methods Sixty-five healthy eyes, 30 eyes with intraocular hypertension, 90 eyes with POAG, 30 eyes with NTG and 20 eyes with PACG were included in this cross-sectional study. RFCT, foveolar retinal thickness and average retinal nerve fiber layer thickness (RNFL) were measured by SD-OCT (Spectralis HRA-OCT, Heidelberg Engineering). Choroidal area was measured centered on the fovea, extending 2500 µm in temporal and nasal directions with Image J software. Parapapillary atrophy (PPA) was noted with optic nerve digital stereophotography. Humphrey 24-2 visual field was also performed and spherical equivalent (SE) was measured with an automatic refractometer.

Results In univariate analysis, significant correlations were observed between RFCT and age, choroidal area, PPA ($p<0.001$), SE, intraocular pressure, topical prostaglandin analogs ($p<0.030$), POAG, PACG ($p<0.001$) and NTG ($p=0.006$). In multivariate analysis, RFCT was correlated with age, choroidal area, PPA and PACG ($p<0.001$). Average RFCT was statistically thicker in PACG patients compared to healthy subjects (341 ± 95 µm versus 235 ± 56 µm, $p<0.001$).

Conclusion This preliminary study showed that RFCT measured by SD-OCT was significantly thicker in PACG compared to healthy subjects.

• 2454

Reproducibility and repeatability of retinal nerve fiber layer parameters measured by scanning laser polarimetry with enhanced corneal compensation in glaucomatous eyes

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Purpose To determine the reproducibility and repeatability of retinal nerve fiber layer parameters measured using scanning laser polarimetry (SLP) with enhanced corneal compensation (GDx-ECC) in glaucoma patients.

Methods Fifty-four consecutive glaucomatous subjects were prospectively selected. All participants underwent a comprehensive eye exam and at least a reliable standard automated perimetry (Humphrey, 24-2 SITA Standard). Only one eye per patient was randomly included in the statistical analysis. Three scans were acquired during the same visit using the GDxPRO (Carl Zeiss Meditec, Dublin, CA). Two additional scans were obtained within a 2-month period. Intraclass correlation coefficient (ICC), coefficient of variation (COV), and test-retest variability were calculated for all SLP parameters.

Results Mean age was 58.27 ± 8.9 years ($p=0.09$) and mean deviation of standard automated perimetry was -7.04 ± 7.0 dB. ICCs were higher than 0.91 for all SLP parameters. The nerve fiber indicator (NFI) showed the highest ICC in the intra-test sequence (0.982; 95% confidence interval: 0.972-0.989; $p<0.001$). The TSNIT average showed the lowest COVs (4.40% and 4.71% in the intra- and inter-test, respectively). Test-retest variability for the NFI ranged from 10.6 to 12.8.

Conclusion The GDx-ECC had an excellent intravisit and intervisit reproducibility in glaucoma patients. SLP is an imaging technology that may be useful in monitoring glaucoma progression.

Commercial interest

• 2455 / F023
Defects in macular-retinal layer analysis of glaucoma patients compared to normative database

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Purpose High-resolution optical coherence tomography (HR-OCT) enables a quantitative analysis of the configuration of retinal layers. The aim of this study was to analyze the topographic distribution of pathologic thinning of specific macular retinal layers of glaucoma patients.

Methods Macular 3D-scans were recorded with HR-OCT (Cirrus®, Carl Zeiss Meditec). Retinal layers, especially the retinal nerve fiber layer (RNFL) and the retinal ganglion cell plus inner plexiform layer (RGIPL), were automatically segmented with a custom made software (Matlab R2009b®, The Mathworks Inc.). A normative database for the thickness of the RNFL, the RGIPL and the retina was created using healthy subjects (n=84) taking into account for the effects of age. 18 glaucoma patients were compared to the 95% confidence interval of the normative database using the thickness values of RNFL, RGIPL and retina within 65 segments.

Results On average the glaucoma patients showed for RNFL, RGIPL and retina 29.8, 49.4 and 53.9 pathologic segments within the macula. The minimum number of pathologic segments per patient was 5, 24 and 29. The average thickness values for healthy subjects were 32.95 µm (RNFL), 79.02 µm (GCIPL) and 321.46 µm (retina), for glaucoma patients 24.85 µm, 57.46 µm and 281.30 µm, respectively.

Conclusion In our study quantitative analysis of retinal layer thickness based on macular HR-OCT showed a decrease of RNFL, RGIPL and retinal thickness in glaucoma patients. Within our sample all patients had several pathologic segments for all of the analyzed retinal layers. In most of the cases those segments were clustered. Further studies including larger numbers of patients to confirm our findings are advisable.

• 2456 / F024
Manual placement of SD-OCT peripapillary circle scan: possible influence on RNFLT classification and profile shape

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Purpose Automatic classification of peripapillary retinal nerve fiber layer thickness (RNFLT) with Spectral Domain OCT (SD-OCT) using a circle scan centered at the optic nerve head (ONH) is a standard test in glaucoma diagnosis. Possible influences of manual center selection on the double-hump (DH) shape of RNFLT profile and classification have been evaluated.

Methods SD-OCT (Spectralis , Heidelberg Engineering GmbH, Germany) standard circle scans were performed on 17 healthy eyes. Based on the infrared (IR) reflectance image, the center (C) of the circle scan was manually aligned to the ONH center and then shifted half way to the rim and on the rim at 3, 6, 9 and 12 o'clock position. Angle (AHP) and thickness (THP) of the highest peak in the superior and inferior RNFLT profile were calculated. Changes in RNFLT classification were analyzed.

Results Horizontal shift of C significantly affects the AHP. Temporal shift moves the DH together, nasal shift diverges it. Temporal or nasal shift results in higher changes of superior than inferior RNFLT profile. Vertical shift induces a significant difference between THP and AHP. Superior shift increases inferior THP, decreases superior THP and moves the DH slightly to the left. Inferior shift does the opposite. The first temporal shift changed normal RNFLT classification in 15 of 119 sectors: 10 borderline (BL), 5 outside normal limits (ONL). Shifting C further on the temporal rim changed 33 sectors: 9 to BL, 24 to ONL.

Conclusion Extreme decentration of the circle scan center (C) can significantly affect position and height of the RNFLT profile double hump (DH). If the RNFLT DH profile does not match the typical normal shape, decentration of C should be considered as a possible reason.

Commercial interest

• 2457 / F028
Clinical trial for the evaluation of neuroprotective effects of palmitoylethanolamide: Visual Field and Pattern-ERG

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Purpose To study the effects of palmitoylethanolamide (PEA), a fatty acid ethanolamide, on IOP, visual field and pattern-ERG in glaucoma patients.

Methods 36 glaucoma (POAG) patients treated topically with timolol 0.5% were randomly assigned to either orally PEA 300 mg/die 2 times daily (Group A) or placebo (Group B). The patients had at least 5 VF tests using the Humphrey Visual Field Analyzer (Threshold 30-2) for more than a 2-year period before PEA treatment. At baseline and after 6, 12, 18, 24 months of treatments we evaluated in both groups the change of progression rate of visual field using mean deviation (MD), and pattern standard deviation (PSD). Comparison of means was performed with the paired t-test. The involvement of retinal ganglion cells (RGCs) were investigated using pattern electroretinograms (PERG) recorded twice a year in 36 glaucoma patients over at least 2 years.

Results Significative IOP reduction was observed in the Group A, PEA treated patients (16.94 ± 3.96 vs. 13.8 ± 3.24 mm Hg; $P < 0.001$).A statistically significant difference in the MD was found between the two groups (PEA treated, -2.9 dB±2.93; Placebo treated, -8.55 dB±6.51 P=0.001). Furthermore, the change in PSD reached statistical significance: PEA 2.63 dB ±1.47; Placebo 6.59 dB ±6.51 P=0.002. PERG amplitude decreased significantly ($P<0.01$) in patients treated with placebo compared with PEA. PEA tablets continued to be safe and well-tolerated, with no drug-related adverse events.

Conclusion These findings show substantial clinical benefits of PEA treatment in POAG patients:reduction of IOP as well as significative improvement in visual field and PERG.

• 2458 / F035
Case from hell in narrow angle glaucoma patient

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Purpose To present the complicated case of a young man with Bechterew uveitis and secondary glaucoma, who underwent glaucoma implant surgery.

Methods From the age of 8 years he presented with multiple attacks of anterior uveitis of his right eye. Each attack was treated with high dose of corticosteroids, leading to pressure rise. Quickly tampering the amount of steroids lead to reactivation of his uveitis. From 2011 on, he developed intraocular pressures up to 40 mmHg, treated with local drops and acetazolamide.

Results A tube implantation (Baerveldt 350) was performed with good eye pressure for the first 6 postoperative weeks continuing under maximal therapy (due to the Vicryl ligature).After these 6 weeks he developed multiple attacks of hypotony, for what an anterior chamber filling was performed each time with different types of viscoelasticum. After 3 attempts a bleb revision was performed, leading again to a massive intraocular pressure rise. Mainwhile the uveitis remained fairly inactive.

Conclusion Patients with juvenile rheumatoid arthritis often have a very difficult intraocular pressure regulation. Their response to a Baerveldt implantation is really unpredictable. It is either too high or too low.

• 2461

Bilateral progressive coats-type exudative retinopathy in Usher syndrome type IIIA from c.528T>G Clarin 1 (CLRN1) mutation

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Purpose To describe bilateral, progressive, Coats-type exudative retinopathy in a boy with Usher syndrome type IIIA.

Methods An interventional case report from a tertiary referral center.

Results A 9-year-old boy with a hearing loss of medium severity diagnosed 4 y earlier developed nyctalopia and began to stumble on objects, leading to suspicion of a visual field defect. His visual acuity (VA) was 20/50 OD and 20/40 OS with no significant refractive error. The RPE was distinctly flecked. Dilated retinal vessels with a confluent accumulation of subretinal lipid were seen temporally, OD, and two similar smaller lesions without obvious vascular pathology, OS. The vitreous showed diffuse cellular or lipoid deposits. The ERG was almost isoelectric and Goldmann visual fields were constricted. Two months later, vision had deteriorated to 20/100 and exudates extended to the macula, OD. He underwent bilateral peripheral cryocoagulation. Genetic testing uncovered the predominant Finnish c.528T>G homozygous mutation of CLRN1 (clarin-1). During the next 8 months, exudates slowly regressed with vision improvement to 20/40, OD, but the telangiectasias appeared leading to extension of exudation to the macular area, OS. Twenty months after a second cryocoagulation, OS, the exudates remain regressed bilaterally with 20/40 vision, OD, and 20/30 vision, OS.

Conclusion Bilateral Coats-like exudative retinopathy is well known from diverse types of retinitis pigmentosa and from Usher syndrome type II unrelated to CLRN1. It has not been reported in Usher syndrome type IIIA, which predominates in Finland, highlighting the possibility that other genes may may contribute to Coats' type retinitis pigmentosa.

• 2462

The effect of a Gas6 c.834+7G>a polymorphism and the interaction of known risk factors on AMD pathogenesis in Hungarian patients

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Purpose We performed a case-control study to search for genetic interactions and for differences in dry and wet age-related macular degeneration (AMD) pathogenesis.

Methods We enrolled 213 patients with exudative, 67 patients with dry AMD and 106 age and ethnically matched controls. Altogether 12 polymorphisms in Apolipoprotein E, complement factor H, complement factor I, complement component 3, blood coagulation factor XIII, HTRA1, LOC387715, Gas6 and MerTK genes were tested.

Results No association was found between either the exudative or the dry form and the genetic backround in the case of Apolipoprotein E, complement factor I, FXIII and MerTK polymorphisms. Gas6 c.834+7G>A polymorphism was found to be significantly protective irrespective of other genotypes, reducing the odds of wet type AMD by a half (OR=0.50, 95%CI: 0.26-0.97, p=0.04). Multiple regression models revealed a genetic interaction in the dry AMD subgroup. In the absence of a C3 risk allele, mutated alleles of both CFH and HTRA1 behaved as strongly significant risk factors (OR=7.96, 95%CI: 2.39=26.50, p=0.0007, and OR=36.02, 95%CI: 3.30-393.02, p=0.0033, respectively), but reduced to neutrality otherwise. The risk allele of C3 was observed to carry a significant risk in the simultaneous absence of homozygous CFH and HTRA1 polymorphisms only, in which case it was associated with a near-five-fold relative increase in the odds of dry type AMD(OR=4.93, 95%CI: 1.98-12.25, p=0.0006)

Conclusion Our results shed light on the protective role of Gas6 c.834+7G>A polymorphism in exudative AMD development. In addition, novel genetic interactions were revealed in dry AMD pathogenesis.

• 2463

Ocular morbidity Brazilian study: causes of visual impairment

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Purpose To determined the causes of visual impairment among patients seeking ophthalmic treatment, in secondary and tertiary level outpatients clinics, in Brazil.

Methods The authors and the Collaborating Groups recorded the main complaints and diagnoses of all the new cases attended at 29 services that maintain Courses of Specialization in Ophthalmology accredited by the Brazilian Council of Ophthalmology (CBO) during a typical week for each one of them.

Results Twenty-nine centers from ten states in the five regions of the country participated, with a total 3,997 new cases registered and included in the study. Median patient age was 49 years and 42.9% were males. The most frequent complaint (50.1%) was gradual/chronic reduction of visual acuity. The frequency of visual deficiency (low vision and blindness) was 20,3%, and the main causes were Cataract (34.7%), Diseases of the retina (18.0%), Glaucoma (8.0%), Diseases of the Cornea (7.3%), Diseases of the Conjunctiva (5.3%) and non-corrected Refractive Errors (4.9%). The bilateral blindness rate, among the 3,997 participants, was 3.10% and the main determinants were Cataract(36.3%), Diseases of the Retina (25.0%) and Glaucoma (6.5%).

Conclusion As expected, the frequency of visual impairment in patients seeking eye care was higher than in general population, of regions with similar level of development. The study provided indicators for the establishment of ocular health actions and for the prevention of blindness in Brazil.

• 2464

A mutation in peroxidasin causes microphalmia and anterior segment dysgenesis in mice

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Purpose The purpose of this study was to analyze the phenotype of ENU induced Pxdn-/- eyes in mice(KTA48 mutants) and investigate the molecular mechanisms of peroxidasin in eye development and disease.

Methods The eyes of the mutants were analyzed by morphologically and histologically. The molecular expression was measured by immunofluorescence, in situ hybridization and real time PCR.

Results The genome-wide linkage analysis mapped the KTA48 mutation on chromosome 12; positional candidate gene analysis detected a mutation in the Pxdn gene (encoding peroxidasin) co-segregating with the mutation. The Pxdn-mRNA of the KTA48 mutants contains a T->A mutation at pos. 3816 (T3816A) creating a new Alw26I restriction site; the mutation converts the Cys at codon 1272 into a stop codon (Cys1272X).Whole mount immunostaining showed that peroxidasin is mainly expressed in the eye at E9.5. Immunostaining study showed peroxidasin is mainly express in the eye lids, developing cornea, lens, inner retina at embryonic stages. At E15.5, the phenotype of the homozygous mutant is most obvious but varies little, with its different tissues (especially anterior segment) severely impaired. At P11 Pxdn-/- mice showed further anomalies in addition to the phenotype in embryonic eyes, including congenital corneal opacity, congenital cataract and congenital glaucoma. Real-time PCR showed the expression of Pax6 is dramatically increased at E15.5 Pxdn-/- eyes compared to wild-type eyes, which was confirmed by immunofluorescence and in-situ hybridization.

Conclusion Our findings demonstrate a requirement for peroxidasin in normal eye development, which may be through regulating Pax6 expression.

• 2465 / T015
Activity and epidemiology of a recently-opened ophthalmic emergency center in an University Hospital

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Purpose To investigate characteristics of ophthalmic emergencies in a new unit of emergency care in an University hospital in order to improve the management of patients.

Methods Prospective monocentric cross-sectional study of ophtalmic emergencies over a 2-month period. All patients presenting themselves have been included. Patients characteristics, waiting-time, pathology, and the reality of the emergency were analysed.

Results 1506 patients were examined (average 24 per day). Mean age was 47 years and 60% were male. The median of waiting time was 30 minutes and 24% of patients were registered during the on-call time. The main reasons for consultation were pain (37%), red eye (32%), vision loss (24%). The main diagnoses were ocular trauma (29%), ocular inflammation and infection (24%), normal examination and refractive error (13%). We have estimated that 38% of our patients did not need an ophthalmic specialized emergency examination or treatment.Numerus and various daily ophtalmic emergencies require relevant diagnosis and treatment. Better information of the population and prevention of trauma and infection could help to decrease the number and the severity of ophtalmic emergencies. An improvement of the general and emergency practitioners knowledges in regards to ophthalmic pathologies could allow them to diagnose and treat begnin cases.

Conclusion There is a real need for a permanent ophthalmic emergency department. However patient education and an improvement of care network could allow us to focus on cases that require specialized cares.

• 2466 / T013
Polymorphism of endothelial nitric oxide synthase T786C in patients with normal tension glaucoma and primary open angle glaucoma

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Purpose Comparison of allelic variant frequency of eNOS gene T786C in patients with normal tension glaucoma and primary open angle glaucoma.

Methods The studied group constituted 97 patients with NTG and 49 patients with POAG. DNA was isolated from peripheral blood and T786C polymorphism was studied by RT-PCR method.

Results In NTG patients TT genotype was present in 36% patients, TC in 52.6% and CC in 11.3%. In POAG patients genotype TT was detected in 42.9% persons, TC in 48.9% and CC in 8.2%. The difference in allelic frequency was not statistically significant (p=0.75). In women with NTG the allelic frequency was similar to men (respectively, in women: TT-35.9%, TC-48.4%, CC-15.6% and men TT-36.4%, TC-60.6%, CC-3%; p=0.92). In group of women with POAG the allelic frequency was also similar to men (in women: TT-41.2%, TC-50%, CC-8.8% and men: TT-46.7%, TC-46.7% a CC-6.7%; p=0.09). Comparing the difference in genotype frequencies between both glaucoma types no significant difference was detected in women (p=0.9) and men (p=0.7). The CC genotype was most frequently present in NTG women (15.6%), comparing to NTG men (3%) and POAG women (8.8%).

Conclusion The frequency of particular genotypes of T786C polymorphism of eNOS gene did not significantly differ in patients with NTG and POAG, yet the mutated allelic form is most frequent in NTG women.

• 2467 / T010
Diabetic retinopathy in Greek Caucasian type 2 diabetic patients, relationship with polymorphism in the plasminogen activator inhibitor 1 and 2 genes

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Purpose Diabetic retinopathy is a sight thratening chronic complication of diabetes and the leading cause of acquired blindness in adults.Population and family studies showed that pathogenesis of diabetic retinopathy depends upon the interaction of several environmental and genetic factors.Plasminogen activator inhibitor 1 and 2 is the major inhibitor of fibrinolysis and gene polymorphism has been related to hypofibrinolysis.

Methods A case control study was carried out.Assesment of diabetic retinopathy was performed by ophthalmoscopy and fluoroangiography when indicated.The comparison of the groups of patients was performed according to the presence or absence of diabetic retinopathy.In each patient the genotype of pai-1 and pai-2 was determined using PCR and RFLP techniques.

Results 246 controls & 352 cases observed

SERPINB2Statistical significance of the observed linkage disequilibrium:

rs2070682	rs1050813	rs2227690	rs2227692	
rs2227667	1.55e-15	3.55e-15	1.11e-16	2.22e-16
rs2070682	-	2.22e-16	1.78e-15	0
rs1050813	-	-	2.04e-12	2.17e-7
rs2227690	-	-	-	3.02e-8

Global result:
Fisher's p value is 0.573984
Pearson's p value is 0.573939
SERPINE1
Statistical significance of the observed linkage disequilibrium:

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rs2227667	1.55e-15	3.55e-15	1.11e-16	2.22e-16
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rs1050813	-	-	2.04e-12	2.17e-7
rs2227690	-	-	-	3.02e-8

Global result:
Fisher's p value is 0.573984
Pearson's p value is 0.573939

Conclusion Based on the primary analysis derived some important relationship between gene polymorphism and diabetic retinopathy that even last the bonferroni correction.

• 2471
The Lid Wiper – a specialized structure at the inner eyelid margin for distribution of the tear film

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Purpose The lid wiper is an epithelial structure at the inner eyelid border that distributes the thin precorneal tear film during the up-phase of the blink. Clinically it is the first area of the ocular surface that shows epithelial alterations in dry eye disease.

Methods A literature review on the posterior lid margin and lid wiper is discussed together with own data and considerations of the relevance of the lid wiper region in ocular surface physiology and pathology.

Results The posterior side of the inner lid border has an epithelium of conjunctival morphology with goblet cells. It forms an elevation of about 100µm (10-12 cell layers) thickness immediately at the crest of the inner border with a slope towards the subtarsal fold. The lid wiper hence forms a distinct epithelial lip that is the only region of the upper lid in contact with the globe as verified by functional tests. It extends along the upper and lower eyelid margins, has a width of typically about 1mm, narrower in the middle and wider to the temporal and nasal sides. The lid wiper of the upper lid appears as a suitable device to distribute the thin precorneal tear film during the blink as supported by the finding that in conditions with increased friction, such as dry eye disease and contact lens wear, the lid wiper is the first zone of the ocular surface that shows a pathological vital staining indicating epithelial destruction.

Conclusion The lid wiper is of underestimated importance for tear film distribution and ocular surface integrity as well as a sensitive early indicator of dry eye disease. Integration and scoring of lid wiper epitheliopathy in dry eye diagnosis and therapy schemes could be a valuable addition to clinical practice. Support DFG KN317/11

• 2472
Non invasive tear film break-up time and blinking

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Purpose The break-up time of the tear film for evaluation of dry eyes is performed with fluorescein in blue light of the slit lamp. Errors may occure by the observer and has to be repeated for accurat results.The BUT can also be seen with a Keratograph 4 (KG-BUT). In this pilot-study we want to evaluate the measurements with KG-BUT in patients with dry eyes. The Fluorescein-BUT (FL-BUT) and the KG-BUT was compared and we observed the correlation of both kinds of BUT with the Lid-opening-time LOT. So we wanted to find out, if the KG-BUT is more accurate compared to the FL-BUT.

Methods 17 eyes of 10 patients were observed. The keratograph 4 of Oculus was used for measurements, five times for each eye. Than the measurement of the LOT was done in ten blink-intervalls. At last the FL-BUT was measured at the slit lamp, three time repeated. The BUT was performed single blinded by two different observers.We compared the mean time of each patient of KG-BUT with Fl-BUT and both with the LOT .For statistic analysis the Pearson correlation was used.

Results The Fl-BUT was 4,2 sec average, (0,7-8sec for single patients, stdev 1,8) the KG-BUT 5,6 sec average (1,2-14,5sec; stdev 4,13). The LOT was 3,6 sec average (1,75 -6,3sec; stdev 1,8). There was no significant correlation between Fl-BUT and KG-BUT (R: -20),no correlation between LOT and KG BUT (R:8). There was a positive correlation between Fl-BUT and LOT (R: 50).

Conclusion This pilot study point at a relation of Fl-BUT with the lid opening time LOT. The clinic observation seemes to be more accurate than the measurement with the Keratograph. But as the KG-BUT is independent from the observer and without contact further observations have to be performed additionally.

• 2473
Lubricin: translating an idea into a cure

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Purpose We hypothesize that lubricin, a boundary lubricant, is transcribed, translated and expressed by the ocular surface and serves to protect the cornea and conjunctiva against significant shear forces generated during an eyelid blink. We also hypothesize that lubricin deficiency increases shear stress and promotes corneal damage. Our objective was to test these hypotheses.

Methods Human tissues and cells were processed for molecular, immunochemical and/or biomechanical procedures. Techniques included the use of real-time PCR, microarrays, sequencing, immunohistochemistry and friction analyses. Methods also involved the corneal evaluation of wildtype and lubricin knockout (KO) mice.

Results Our results show that lubricin is produced by human corneal and conjunctival epithelial cells. Lubricin absence in KO mice is associated with a significant increase in corneal fluorescein staining. Our findings also demonstrate that lubricin functions as a very effective friction-lowering boundary lubricant at the human cornea-eyelid interface.

Conclusion Our data indicate that lubricin acts as a natural boundary lubricant to reduce shear stress at the ocular surface. We thank S Richards, S Liu, A Sahin, R Rahimi Darabad and W Kam (Boston) and S Morrison (Calgary) for their help with these studies. This research was supported by NIH grant R01EY05612, the Margaret S. Sinon Scholar in Ocular Surface Research fund, the Canadian Natural Sciences and Engineering Research Council & the Centre for Bioengineering Research and Education at the University of Calgary.

Commercial interest

• 2474
The lid margin and Demodex

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Purpose Demodex infestation can be associated with blepharitis. To date, the pathogenic potential of these mites in Meibomian Gland Dysfunction (MGD) remains unclear. The purpose of this study was to determine the relationship between the prevalence of Demodex in eyelashes and changes of the anterior and posterior lid margin.

Methods Between October 2011 and March 2012, 229 consecutive patients with ocular discomfort from the dry eye unit of the Ophthalmological Department, Medical University Graz, Austria, were investigated for the presence of Demodex mites on sampled eyelashes. Lid margins were evaluated according to scales, vascularisation, Marx line, expressibility and quality of meibomian gland secretion.

Results Demodex spp. were found in 40.2% of patients with ocular discomfort. The presence of Demodex mites was significantly associated to blepharitis. No difference in Demodex occurrence was found between the sexes.Compared to the non-infested, patients with Demodex mites had significantly more scales formed as sleeves, a higher Marx line score and a lower quality of the meibomian gland secretion. No significant association was observed with vascularisation of the lid margins and expressibility of meibomian glands. Within the infested patients the mean Demodex count per patient was 3.28 ± 2.89 and Demodex count was found to increase with increasing age.

Conclusion Demodex mites are associated with changes of the anterior and posterior lid margin and therefore may play a pathogenic role in blepharitis and MGD.

• 2475

Meibography follow up studies in dry eye patients

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Purpose Meibomian-Gland-Dysfunction (MGD) is one of the main causes for the development of a hyperevaporative dry eye. Non-contact Meibography can achieve a non-invasive investigation of the meibomian glands inside the tarsal plates of the eyelids. The purpose of this study was to evaluate non-contact Meibography as a tool for follow-up studies in dry eye patients.

Methods We examined 50 patients suffering from dry eye disease of the dry eye unit of the Ophthalmological Department of the Medical University of Graz.Subjective dry eye symptoms and objective signs of dry eye were evaluated. Non-contact Meibography was performed by a Heidelberg Retina Angiograph 1, featuring two infrared diode lasers. Partial or complete loss of the meibomian glands was scored according to meiboscore of Arita and colleagues.After one year non-contact Meibography was reassessed. Changes in the meiboscore were evaluated.

Results The mean age of the study population was 57.9 ± 14.1 years and 64.7 % were women. There was no statistically significant change in the mean meiboscore.

Conclusion Non-contact Meibography is a valuable tool in the diagnosis of MGD. Morphological changes and a possible drop out of Meibomian glands can easily be assessed. The ideal follow-up interval to detect changes in the meiboscore has yet to be determined.

• 2521

Clinical results on the efficacy of Thealoz vs autologous serum in moderate to severe dry eye

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Purpose To study the clinical effect and morphologic aspects of the cornea in using corneal confocal microscopy in patients affected by moderate to severe dry eye and treated with either autologous serum or Thealoz.

Methods Twenty two patients were included and randomized in 3 groups: 7 patients (4 affected by Sjoegren Syndrome -SS) were switched from autologous serum eye drop treatment to Thealoz 6-8 times a day (group 1); 7 patients (4 SS) maintained their treatment by autologous serum 6-8 times a day (group 2); 8 new patients (3 SS) were treated by Thealoz 6-8 times a day (group 3).The OSDI questionnaire, tear film evaluation by BUT, fluoresceine and lissamine green staining, Schirmer test and corneal confocal microscopy were performed at the beginning of the study (T0) after 4 (T1) and 8 weeks (T2). ConfoScan CS4 (Nidek, Gamagori, Japan) images of the central cornea were obtained with a 40x non-contact lens and Z-ring device. The epithelial cell, endothelial cell and keratocyte densities of the central cornea, the characteristics of the sub-basal long nerve fibers and of the sub-basal nerve plexus were studied.

Results In group1, 4 of the 7 patients maintained unmodified their clinical benefit and corneal morphology after switching from autologous serum to Thealoz. Two severe SS patients needed to return to the autologous serum treatment because of worsening of the OSDI at T1 without a significant change in the other parameters. However, in remaining 5 patients, the OSDI questionnaire improved at T2 compared to T1. In group 2, all patients maintained a stable clinical and morphological ocular surface condition over the 8 weeks study period. Group 3, at T2, showed an objective improvement of ocular surface morphology and reported a significant subjective relief of symptoms (OSDI) compared to T0 and T1. All patients showed improvement of confocal microscopy parameters after treatment with Thealoz.

Conclusion Thealoz was effective and well tolerated in patients with moderate to severe dry eye. Severe SS patients may need an additional treatment, however even switching from autologous serum, most of the patients maintain a stable clinical condition.

• 2522

A new matrix therapy agent in the treatment of corneal ulcers resistant to conventional treatments

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Purpose To report the cases of a series of patients suffering from corneal ulcers resistant to conventional therapies and treated with a new ophthalmologic solution based on ReGeneraTing Agent technology (RGTA, Cacicol®).

Methods Twenty four patients with corneal ulcer, most often chronic, were included in this opened series. Eleven patients had a neurotrophic ulcer (5 post-infectious keratitis, 3 chemical burns, 1 Lyell syndrome, 2 others) with corneal anesthesia and persisting despite a 15-day treatment with only unpreserved artificial tears. Other patients (n=12) had a chronic corneal ulcer of various etiologies (including 2 chemical burns, one associated with neurotrophic keratitis, one Moreen ulcer), and one patient had a severe confluent keratitis. These 13 patients were previously treated with classical lachrymal substitutes, some of them also with topical cyclosporine, corticoids, and/or A vitamin ocular ointment. A total of 11 patients had already received one or several amniotic membrane grafts, without success. All Patients were treated with Cacicol® at a dose regimen of one drop daily every 2 or 3 days for one to 3 months depending on healing.

Results Complete healing was observed for 16 patients, including 7 out of the 11 patients with neurotrophic ulcer, i.e. a cure rate of 67%. However, a large variation has been noted in the time period recovery of corneal surface integrity going from few days to few weeks. An analysis of potential factors that could influence the healing process will be provided. For other patients, 5 failures and 3 improvements without complete healing were reported.

Conclusion Cacicol® appears as a new interesting healing eye drops in the context of severe corneal ulcers resistant to conventional therapies. Its efficacy remains to be proven in randomized double-blind studies.

• 2523

Ocular surface in surgery

DUA H
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ABSTRACT NOT PROVIDED

• 2611

Optical coherence tomography: signal signature on neuronal ageing and blood-retinal barrier status

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Purpose We aim to identify the features that allow the discrimination between healthy controls and diabetic patients with optical coherence tomography (OCT) data from the human retina.

Methods Prior studies from our research group showed the association between the status of the blood-retinal barrier and the consequent changes on the optical characteristics of the retina. Following the same rationale, we have demonstrated the possibility to discriminate healthy controls and diabetic patients by age group and healthy controls from diabetic subjects even though no visible changes could be identified, using a spectral domain OCT, Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA), to gather the refractive index data in between the inner limiting membrane and the retinal pigment epithelium, and the support vector machine (SVM) for the automatic classification.In the work herewith presented, we applied a backward elimination process aiming to reduce the number of features used while simultaneously increase the classification performance.

Results In this work we were able to reduce the number of features used in the SVM algorithm from the initial 46 features down to 10, while simultaneously increase the accuracy up to 97%. Moreover, the different feature set used for the different classifications suggest the presence of specific signatures within OCT data distribution.

Conclusion These findings also suggest the possibility to use this noninvasive imaging modality to assess the neuronal condition and blood-retinal barrier status.

• 2612

High-resolution spectral domain optical coherence tomography findings in reticular pattern dystrohy

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Purpose To analyze specific outer retinal and retinal pigment epithelium (RPE) features in reticular pattern dystrophy using spectral-domain optical coherence tomography (SD-OCT).

Methods Consecutive patients with reticular pattern dystrophy underwent a complete ophthalmologic examination, including assessment of best-corrected visual acuity (BCVA), fundus biomicroscopy, and SD-OCT (Spectralis SD-OCT, Heidelberg Engineering). Outer retinal and RPE macular features, as evaluated by SD-OCT (scan passing through the fovea) were analyzed by 3 authors (JZ, NM and GQ).

Results 24 eyes of 13 patients (5 males, 8 women, mean age 71.4) were included. Mean visual acuity was measured at 0.30 (logMAR). The RPE layer in the foveal area appeared normal in 41.7% of scans, while small RPE elevations and RPE bumps were detected in 33.3% and 20.8% of scans, respectively. Inner segment/outer segment (IS/OS) junction appeared disrupted in 50% of scans, and absent in 58.3% of scans. SD-OCT showed a slight IS/OS elevation in 54.2% of scans. The external limiting membrane (ELM), appeared disrupted in 50% of scans, absent in 37.5% of scans, and elevated in 66.7% of scans. Hypereflective subretinal material accumulation or hyporeflective subretinal lesions, were detected in 33.3% and in 12.5% of scans, respectively. SD-OCT showed hyporeflective retinal pseudocysts in 16.7% of scans.

Conclusion In this series of reticular pattern dystrophy, SD-OCT showed disruption of RPE layer and RPE bumps. Outer retinal changes included absence and disruption of both IS/OS junction and ELM. Hypereflective subretinal material accumulation or hyporeflective subretinal lesions, and hyporeflective retinal pseudocysts were also noticed.

• 2613

Assessment of the spectralis spectral domain oct segmentation software in a retrospective cohort study of exudative amd patients

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Purpose To assess the ability of the Spectralis optical coherence tomography (OCT) segmentation software to identify the inner limiting membrane and the Bruch's membrane in exudative AMD patients.

Methods Thirty-eight eyes of 38 naive exudative AMD patients were retrospectively included. They all had a complete ophthalmologic examination including Spectralis OCT at baseline, at month-1 and at month-2. Reliability of the segmentation software was was defined as good if both inner limiting membrane and Bruch's membrane were correctly drawn.

Results A total of 38 patients charts were reviewed (114 scans). The inner limiting membrane was correctly drawn in 114/114 SD-OCT scans (100 %). Conversely, the Bruch's membrane was correctly drawn in 59/114 scans (51.8 %). The software was less reliable in locating the Bruch's membrane in case of pigment epithelium detachment (PED) than without PED (42.5% vs 73.5 % respectively, p =0.049).

Conclusion Segmentation of inner limiting membrane was constantly trustworthy but Bruch's membrane segmentation was poorly reliable using the automatic SD-OCT Spectralis segmentation software. Based on this software, evaluation of retinal thickness may be incorrect, particularly in case of PED.

• 2614

Natural evolution of idiopathic lamellar macular holes (LMH) and macular pseudoholes (MPH)

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Purpose To analyze the natural evolution of idiopathic Lamellar Macular Holes (LMH) and Macular Pseudoholes (MPH), in the long-term, based on Optical Coherence Tomography (OCT) configuration and in Best Corrected Visual Acuity (BCVA) evolution.

Methods We prospectively analyzed 68 eyes (41 right eyes and 27 left eyes) of 61 patients (40 female and 21 male), which were diagnosed as having a MPH or a LMH on OCT examination. The following variables were assessed: BCVA, lens status, and hole size (Diameter -D, Residual foveal Thickness –RT, and Perifoveal Thickness -PT)(software Caliper of Cirrus OCT), at baseline and final examination. Eyes with significant cataract underwent phacoemulsification.

Results The mean follow-up period was 34.33 ± 15.02 (12-78) months. Mean BCVA (logMAR notation) in the total group at baseline was 0.40 ± 0.25 and at final was 0.36 ± 0.13 (p=0,082). PAM showed slightly better BCVA than LMH (p<0.05). BCVA improved in those eyes who underwent cataract surgery and remained unchanged in the rest of the eyes.No statistically significant differences regarding D, RT and PT were observed during the follow-up period (p=0,125).

Conclusion Most of idiopathic LMH and MPH do not progress anatomically and do not contribute to a significant diminution of visual acuity during the follow-up period. We must take into account that the diminishment in visual acuity in most LMH and MPH can be due to the presence of an opacified crystalline and not to the lamellar hole itself.

• 2615
Coats disease: fluorescein angiography guided management

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Purpose To study the anatomical and visual outcome of patients (pts) with Coats disease treated with laser or cryotherapy on the basis of fluorescein angiography (FA) findings.

Methods 28 children, mean age at diagnosis 6 ys, have been included. They all underwent examination under anaesthesia, fluorescein angiography (FA) with RetCam and laser treatment or cryotherapy. Changes in best corrected visual acuity (VA) pre and post treatment were recorded. Retinal imaging was repeated when possible.

Results 6 pts were classified as Stage 2a, 17 as Stage 2b, 4 as stage 3Ai, one as Stage 3b. In the 25 patients who had FA, 15 had telangectatic vessels for less than 6 clock hours, mainly in the temporal periphery, and in 10 they involved more than 6 clock hours. FA showed areas of capillary bed closure starting from the area of the telangectasia up to 360 degree in the retinal periphery. 21 patients were treated with laser photocoagulation, 2 with cryotherapy and 4 with cryotherapy and laser to the telangectatic vessels and peripheral ischaemic areas.After treatment, 22 pts showed reduced exudation or no change, 6 pts had an increase in exudation and required further laser or cryo therapy. 9 pts with stage 2b showed improvement or stabilization of VA, in 4 VA deteriorated. All pts with stage 2a maintained good VA.

Conclusion FA provides useful information about the distribution of telangectasia and of ischaemic areas in Coats disease. Laser treatment to the telangectatic vessels and ischaemic area is effective in improving the anatomical outcome and preserve vision. FA is helpful in guiding treatment and reduces the number of treatments necessary.

• 2616 / S099
Influence of cataract in reproducibility of Optical Coherence Tomography measurements

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Purpose To evaluate the effect of lens opacities in quality of images and reproducibility of retinal nerve fiber layer (RNFL) thickness measurements using Spectralis Optical Coherence Tomography (OCT).

Methods Fifty eyes of 50 subjects (25 men and 25 women; aged from 62 to 88 years) underwent three 360° circular scans centred on the optic disc by the same experienced examiner using the "RNFL Fast" Glaucoma Application and the "RNFL-N Fast" Axonal Application of Spectralis OCT instrument one month before and one month after cataract surgery. Comparison between the two visits and changes in reproducibility (using intra-class correlation coefficients and coefficients of variation) were analyzed. The quality of images was also compared between both visits.

Results RNFL and RNFL-N differences were detected between both visits for average thickness, temporal and nasal quadrants ($p<0.05$) using Glaucoma Application and for inferior and nasal quadrants ($p<0.05$) with Axonal Application. RNFL average thickness was 99.6 µm in pre-surgery visit and 102.4 µm in post-surgery visit using Glaucoma Application; and 94.3 and 94.7 µm, respectively, with Axonal Application. Reproducibility shows better values in post-surgery evaluation (mean coefficient of variation of 5.55% in pre-surgery visit vs 4.32% in post-surgery). Intra-class correlation coefficients were higher than 0.834 in all visits and parameters, so reliability of Spectralis measurements was high with both Spectralis OCT applications. The quality of images was better in post-surgery evaluations.

Conclusion The measurements of RNFL thickness and the reproducibility of Spectralis OCT are affected by lens opacity.

• 2617 / S100
Subfoveal choriodal thickness: the Beijing Eye Study

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Purpose To study subfoveal choroidal thickness (SFCT) in adult Chinese subjects

Methods The population-based Beijing Eye Study 2011 included 3468 individuals. Spectral-domain optical coherence tomography (SD-OCT) with enhanced depth imaging was used for measurement of SFCT.

Results Mean SFCT was 253.8 ± 107.4µm (range: 8µm to 854µm). In multivariate analysis, SFCT increased with younger age ($P<0.001$), shorter axial length ($P<0.001$), male gender ($P<0.001$), deeper anterior chamber depth ($P<0.001$), thicker lens ($P<0.001$), flatter cornea ($P<0.001$) and better best corrected visual acuity ($P=0.001$). In multivariate analysis, SFCT was not significantly associated with blood pressure, ocular perfusion pressure, intraocular pressure, cigarette smoking, alcohol consumption, serum concentrations of lipids and glucose, diabetes mellitus and arterial hypertension. In the myopic refractive error range of more than -1 diopters, SFCT decreased by 15µm (95%confidence interval (CI): 11.9, 18.5) for every increase in myopic refractive error of one diopter, or by 32µm (95%CI: 37.1, 26.0) for every increase in axial length of one millimeter. For each year increase in age, the SFCT decreased by 4.1µm (95%CI: 4.6, 3.7) (multivariate analysis).

Conclusion SFCT with a mean of 254±107µm in elderly subjects with a mean age of 65 years decreased with age (4µm per year of age) and myopia (15 µm per diopter of myopia). It was additionally associated with male gender and the ocular biometric parameters of a deeper anterior chamber and thicker lens. The association between SFCT and best corrected visual acuity strongly points towards a functional aspect of SFCT

• 2621

European Vision Award 2012: From chickens to humans - learning about the puzzles of myopia

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After it was found that the growing vertebrate eye uses the focus of the retinal image to fine-tune its axial length to the focal length of the optics, it seemed as if the solution of the problem of myopia was in close reach. While a lot was learned about the fascinating details of biological mechanisms coordinating eye growth by vision from animal experiments, it is still a puzzle why eyes of children start to deviate from the correct path and become too long. Currently, a major challenge is to find out which details of visual experience in kids may have a similar effect as wearing a negative lens or a diffuser - since these are the two treatments that induce axial myopia in animal models. The talk will also review some current attempts to slow down the progression of myopia once it had already started.

• 2631

Meganuclease targeting HSV-1 limits viral endothelitis in vivo

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Purpose The aim of this study is to assess the antiviral property of a meganuclease targeting HSV-1 in the prevention of HSV endothelitis in a newly develloped rabbit in vivo model.

Methods NZW received intracamerular injection of recombinant adeno-associated virus equipped with a constitutive expression cassette containing either the meganuclease gene or a non-coding sequence. After treatment with intravitreal triamcinolone acetonide, HSV-1 F(1) virus recombinant for LacZ reporter was injected in the inner chamber of the eye,for an analysis 2 days later. Corneal edema, keratic precipitates and the number of contamination plaques were evaluated.

Results In 4 tests with 24 experimental or control corneas, the meganuclease-treated groups systematically showed a decrease in their average number of contamination plaques while compared to controls (from 15 to 71%). Presence of protein and inflammatory cells in the aqueous humor or at the endothelium surface, as well as the extension of focal edema, was also limited by the endonuclease.

Conclusion Meganuclease gene therapy targeting HSV-1 DNA restricts degradation of the endothelium initiated by HSV-1 injection.

• 2632

Cis-urocanic acid inhibits conjunctivitis and blepharitis in rat model of acute eye irritation

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Purpose In vitro studies have shown anti-inflammatory and cytoprotective effects of cis-urocanic acid (cis-UCA) in human ocular epithelial cells exposed to UV-B irradiation. In this study, we aimed to investigate the efficacy of topical cis-UCA against compound 48/80 induced eye irritation in a rat model.

Methods Adult Wistar rats in groups of six animals were treated with 1000 µg/ml compound 48/80 in both eyes. Cis-UCA 0.5% solution, corticosteroid dexamethasone 1 mg/ml (Oftan® Dexa), antihistamine ketotifen 0.25 mg/ml (Zaditen), or PBS was applied in both eyes at time points 0.5, 6, and 12 h after application of compound 48/80. Clinical signs of ocular inflammation were evaluated by scoring from photographs by ophthalmologist 1, 6, 12, and 24 h after the last drug application.

Results Cis-UCA solution attenuated conjunctival hyperemia in compound 48/80 irritated eyes equally well compared to dexamethasone and ketotifen. At time points 12 and 24 h, the mean decrease in severity score was 50% and 40%, respectively, for the cis-UCA group. Redness of the eyelid margin was prevented best by ketotifen at 1-h time point, whereas cis-UCA and dexamethasone almost completely abolished lid redness at 6, 12, and 24 h.

Conclusion These results suggest that cis-UCA has an anti-inflammatory effect in acute eye irritation, which is comparable to corticosteroid dexamethasone and antihistamine ketotifen.

• 2633

Scleritis, clinical features, etiological diagnosis and treatment : a review of 32 cases

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Purpose To evaluate the various clinical presentations, etiological diagnosis and prognosis of patients with scleritis at a tertiary care eye center.

Methods Retrospective, monocentric and analytical study on a series of 32 patients with scleritis seen in the departments of Ophthalmology and Internal Medicine at Croix-Rousse University Hospital, Lyon, France from 2004 through 2011.

Results The mean age of patients with scleritis was 46.8 years (range 22-77years). Nineteen of the patients were women and 13 were men. Twenty-six patients (81%) had anterior scleritis (15 nodular, 8 diffuse and 3 necrotizing), six (19%) had posterior scleritis. Unilateral inflammation was present in 24 patients (75%). Twelve of the 32 patients (37.5%) had a systemic disease : Wegener's granulomatosis (n = 3),Behçet's disease (n = 2), unspecified inflammatory arthritis (n = 2), psoriatic arthritis (n = 1),ankylosing spondylitis (n = 1), sarcoidosis (n = 1), Cogan's syndrome (n = 1), ulcerative colitis (n = 1). Six patients (18.8%) were suspected of having infectious disease with herpes : clinical context and positive treatment response with oral valacyclovir. Systemic agents and topical agents were required in 28 patients (87.5%). The first line therapy was mainly oral non steroidal anti-inflammatory drugs in 15 patients (47%) and oral corticosteroids in 8 (25%). Immunosuppressive drugs were required in 6 patients, 4 with systemic disease. The mean follow-up was 16.3 months.

Conclusion The number of systemic disease in our series is similarto the main series in the literature. Treatment with valacyclovir might be effective in patients with suspected herpes simplex scleritis.

• 2634

In vivo confocal microscopic examination of corneal Langerhans cell density, distribution and evaluation of dry eye in rheumatoid arthritis

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Purpose To examine the density and the distribution of corneal Langerhans cells (LCs) and to compare the results with dry-eye related parameters in rheumatoid arthritis (RA).

Methods 52 RA patients (mean age: 58 [49-66]) with various degree of disease activity and 24 healthy subjects (mean age: 61 [52.5-67]) were enrolled. Central and peripheral LC number and morphology were assessed with in vivo confocal laser corneal microscopy. In addition, lid parallel conjunctival folds (LIPCOF), tear break up time (TBUT), Schirmer's-test (ST), and ocular surface disease index (OSDI) were also evaluated. .

Results The prevalence of central and peripheral LCs and the central LC morphology values (LCM) were higher in RA compared to controls (median [interquartile range]: 42.50 [22.95-93.50] vs 10.00 [0.00-42.33] cell/mm2, 98.00 [62.00-154.5] vs 59.50 [45.25-94.75] cell/mm2, and 2.00 [1.00-2.00] vs 1.00 [0.25-1.00], respectively, $p<0.05$ for all). Within the RA group, LC prevalence and morphology were not affected by disease activity. However, patients on anti-TNF or corticosteroid therapy exhibited LCM and central and peripheral LC density comparable to controls. TBUT values were lower and OSDI scores were higher in RA than in controls (9.00 [7.00-12.00] vs 12.00[9.00-14.00] seconds and 20.00 [10.93-38.21] vs 9.75 [4.93-16.28], respectively, $p<0.05$ for all). ST results were comparable in RA and controls.

Conclusion Dendritic cell accumulation and maturation in the corneal center suggest the involvement of the cornea in RA, even in patients in inactive stage and without ocular symptoms.

• 2635

The effects of autologous serum eye drops in the treatment of ocular surface diseases : a retrospective study

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Purpose To evaluate the efficiency of autologous serum eyedrops in the treatment of severe dry eye (DE) and persistent epithelial defects (PED).

Methods Ninety-seven patients with PED or DE, unresponsive to conventional treatment, were studied. Functional symptoms and slit-lamp findings were recorded.

Results The mean LogMAR visual acuity significantly improved from 1.81 (20/1291) +/- 9 lines before to 1.69 (20/980) +/- 6 lines after treatment (p = 0.01). Visual acuity increased by 2 lines or more in 29 out of 97 eyes (30%) and it decreased by 2 lines or more in 15 eyes (15%). Resolution of 3 subjective symptoms was noticed in 14 out of 97 eyes (14%), resolution of 2 in 22 (23%), resolution of 1 in 29 (30%), and no subjective improvement was found in 32 eyes (33%). Among 75 eyes with PED, ulcer healing was observed in 31 (41%) at 1 month and 61 (81%) at 3 months. In multivariate analysis only presence of limbal deficiency significantly influenced the healing time. The average time from treatment onset to ulcer healing was 213 days in eyes with limbal deficiency and 59 days in eyes with no limbal deficiency (p<0.0001). Among 22 eyes with DE, improvement of subjective symptoms was observed in 8 (36%) at 1 month and 12 (55%) at 3 months. At the end of follow-up improvement of subjective symptoms was observed in 20 (91%) eyes.

Conclusion Cicatrisation of PED and improvement of DE symptoms were observed in most eyes under autologous serum.

• 2636 / T067

Severe corticoresistant Mooren Ulcers: management with Rituximab and peripheral lamellar graft

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Purpose Mooren's ulcer is a rapidly progressive, painful, ulcerative keratitis which affects the peripheral cornea. We report 6 severe cases of Mooren Ulcers (4 patients) with corticoresistance favourably responding to Rituximab infusions.

Methods Retrospective Case series

Results Despite systemic intensive steroid (4/4 patients), and Cyclophosphamide (2/4 patients) therapy, the 6 cases of Mooren's ulcers progressively spread circumferentially and centrally. Perforation occurred in 4/6 affected eyes, treatment included conjunctival resection and peripheral corneal graft. Rituximab biotherapy was associated with the stabilisation and the healing of the corneal lesions. Systemic steroid therapy was tapered then stopped in all patients within 2-4 months following rituximab therapy.

Conclusion Rituximab, an anti-CD20 monoclonal antibody, has been successfully used off-label for treatment of Severe corticoresistant Mooren's Ulcer.

• 2637 / T033

Comparison of viral vectors for gene transfer to corneal endothelial cells

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Purpose Thanks to its anatomical location at the posterior surface of the cornea and its monolayer structure, the corneal endothelium is an ideal target for gene therapy approaches. Lentiviral vectors have been shown by our group to be suitable vectors for the transfer of genes into corneal endothelial cells (EC). Aiming for an alternative to these HIV-based vectors, it was the goal of this study to determine the suitability of non-pathogenic adeno-associated viral vectors (AAV) for gene transfer to EC.

Methods Comparison of protein expression after EC transduction using a lentiviral vector or AAV 2/2 with GFP in murine EC (Balb/C) and in human EC (cell line and primary cells)by flow cytometry.

Results Following transduction of EC using lentiviral vector, kinetics of the protein expression are considerably different compared to gene transfer using AAV. In contrast to AAV with protein expression showing a plateau after two to three weeks, lentiviral transfer results in a very rapid of reporter protein. Moreover, we detected significant differences in transduction rates between human and murine EC lines as well as betweeen human EC lines and human corneas (plateau at 70% versus 50% GFP-positive cells with AAV, versus 90-95% with lentivirus).

Conclusion DNA transfer using AAV vectors seems to be an appropriate alternative to lentiviral vectors for gene transfer to EC. Relating to the cultivation of human donor corneas in eye banks over weeks, translation of AAV from bench to bedside, e.g. to reduce apoptosis in corneas, seems to be a promising approach for future gene transfer into donor corneas.

• 2641

Ocular toxoplasmosis: patient age and other risk factors for a severe course of disease

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Purpose Atypical disease courses of ocular toxoplasmosis (OT) have been reported in elderly patients. The aim of this study was to determine whether patient age is correlated with relevant clinical parameters.

Methods A retrospective clinical study and statistical analysis was conducted on patients (n=180) with active OT.

Results The age of first disease manifestation showed a clear unimodal distribution with a median incidence peak at age 26 while recurrences did not follow an age specific pattern (median= 35 years). First manifestation of OT or recurrence occurring after the age of 35 are associated with larger lesion size (2-3 PD; contingency coefficient [CC]=0.304; p=0.047; n=60) and (CC=0.32; p=0.009) respectively. Additionally, older patients displayed uveitis anterior (63.2%; p=0.055; n=56) and vitreous involvement (89.5%; p=0.054; n=78) more frequently. Complications during OT (secondary IOP, macula and peripapillary edema, ablatio) did not correlate with patient age, but were attributable to localisation of lesions (central= 29.2% vs. peripheral=9%; p=0.039). Recurrences were present in 70% of patients (47.9%:1-3 episodes vs. 21.8%:4-7 episodes), whereas bi-ocular OT always predisposes for recurrences. Standard therapy consisted of clindamycin. Large OT lesions more frequently required systemic steroid treatment (72.9% in 2-3 PD cases vs. 48.3% in 1 PD cases; CC=0.271; p=0.007; n=124).

Conclusion Patient age was significantly correlated with lesion size and inflammatory involvement of the anterior part of the eye. Localisation of lesions is a predictor for complications.

• 2642

Etiologic diversity in patients presenting with atypical and severe anterior uveitis

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Purpose To analyze the etiological distribution of long-lasting and severe anterior uveitis based on the analysis of the aqueous humor.

Methods Retrospective study of patients presenting with atypical and severe anterior uveitis and managed in a tertiary referral centre, between January 2008 and December 2009. Patients with panuveitis, intermediate and posterior uveitis and typical B27-associated uveitis or herpes zoster ophthalmicus were excluded. Patients were divided into three groups : atypical viral uveitis (group 1), typical herpetic uveitis (group 2), Fuchs uveitis (group 3). An anterior chamber paracentesis was performed in all cases.

Results The medical files of 153 patients were analysed. The mean age was 49 years (range 8-83 Years), the M/F sex ratio was 84/69. Uveitis was unilateral in 86.5% of cases. Group 1 included 42 patients with sarcoidosis (13 cases), tuberculosis (7 cases), endophthalmitis (6 cases), spondylarthropathy (10 cases), syphilis (2 cases), neoplasia (2 cases) and multiple sclerosis (2 cases). Group 2 included 83 cases. A viral agent was definitely identified in 33 cases (39.8%). The distribution of herpes viruses was the following : CMV (19 cases), HSV-1 (8 cases) and VZV (6 cases). The yield of anterior chamber paracentesis is increased by repetition of the procedure (up to 77.4% for CMV). The PCR-negative patients in Group 2 responded well to a specific antiviral treatment. None of the patients with Fuchs uveitis (Group 3) had a positive PCR for CMV.

Conclusion Most cases of atypical anterior uveitis, especially when unilateral, are viral-induced. Molecular tools applied to ocular fluids may confirm a viral infection in atypical cases of anterior uveitis, leading to a specific antiviral therapy.

• 2643

Positive interferon-gamma release assay (IGRA) test in a case of non-tuberculous mycobacterium associated uveitis

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Purpose It is not always known that Interferon-gamma release assay (IGRA) tests can also react with some non-tuberculous atypical strains of mycobacteria (NTM). The aim of this work was to review the cross-reactivity of IGRA tests and its consequences in a case of with a positive IGRA test associated with of a non-tuberculous mycobacterium (M. kansasii).

Methods Report of a 66 year old male uveitis patient with cystoid macular oedema and occult bilateral indocyanine green angiography-detected choroiditis resistant to inflammation suppressive therapy. A QuantiFERON®-TB Gold test was positive indicating exposure to the Mycobacterium tuberculosis complex. Before starting antibiotic treatment cultures from bronchial aspirates was performed yielding the agent Mycobacterium kansasii. A review of cross-reactivity of IGRA tests with non-tuberculous atypical mycobacteria was performed.

Results Drug-sensitivity of Mycobacterium kansasii was found to be equal to Mycobacterium tuberculosis although a longer duration of therapy is recommended. The patient was treated with anti-tuberculous drugs for 18 months. Uveitis responded to treatment within three months. A review showed that there are at least 7 NTM strains that cross-react with IGRA tests some of which do not respond to classical anti-tuberculous therapy.

Conclusion A positive IGRA test is a support for diagnosing tuberculous uveitis. However, these tests cross-react with NTM atypical strains, some of which do not respond to classical anti-tubercultuberculous therapy with deleterious consequences if an adequate therapy is not given.

• 2644

Evaluation of a complete-kill assay for anti-acanthamoeba solutions

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Purpose Acanthamoeba keratitis is a sight debilitating disease that requires effective topical drug therapy to eradicate the pathogenic agent.

Methods An assay was created to determine whether 0.02% poly(hexamethylene biguanide) hydrochloride (PHMB), 0.02% chlorhexidinedigluconate (CHL), 0.1% c-desomedine (DESO), and 1.0% c-voriconazole (VOR) were effective in completely killing 15 different isolates of acanthamoeba at time points 24, 48, and 72 hours in comparison to a saline control. Each 0.5 ml volume of solution was inoculated with 0.1 ml of acanthamoeba cysts at a concentration of 1-5 x 106 /ml determined with a hemacytometer and allowed to incubate at 30o C. At the time points listed, aliquots from each treatment group were inoculated onto non-nutrient agar overlaid with Enterobacter aerogenes. The plates were microscopically examined for growth at time points 1 and 2 weeks. At 2 weeks, all plates were sub-cultured onto fresh medium. At 7 days, growth in sub-culture at each time point was graded 1 for growth and zero for no growth. The time points were combined for each drug with a possible grade from 0 to 3. The grades were non-parametrically (Mann Whitney) compared to determine any significance in positive growth between the drugs.

Results Complete–kill was determined more frequently with PHMB and DESO (p=1.0) than CHL (p=0.04). PHMB, DESO, and CHL demonstrated more complete-kill than VOR (p=0.01) which was more effective than the saline control (p=0.0003).

Conclusion The complete-kill assay appears to provide separation in the effectiveness of different anti-amoebic drug solutions, and may provide an alternative evaluation of possible new anti-infectives in the treatment of acanthamoeba keratitis.

• 2645

16S RNA PCR in the diagnosis of bacterial keratitis and endophthalmitis

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Purpose Classical bacterial culture often fails to detect the infecting agent in bacterial keratitis and endophthalmitis. Our study was designed to evaluate the contribution of 16S RNA amplification using polymerase chain reaction (PCR) and nested PCR, when compared to culture, in the diagnosis of bacterial keratitis and endophthalmitis.

Methods In this prospective study, we included 63 patients (24 bacterial keratitis and 39 endophthalmitis). For every patient, two samples were taken: one for bacterial culture, the other for PCR. PCR and nested PCR 16S rRNA were performed using universal primers (8/27-1510 for PCR and 91E-13BS for nested PCR) and the amplicons were thereafter sequenced.

Results Culture offers a sensibility of 25%; associated to first PCR (8/27-1510), this rate increase to 31,7%, and with nested PCR (91E-13BS), we had 34,9% of identifications. We have to note that the rate of positive PCR were much better, but the sequencing rate was 59,5% only.For bacterial keratitis, culture was positive in 25% and PCR in 8%. For aqueous humor samples, culture was positive in 32%, PCR in 25% and nested PCR in 20,6%. Sequencing was possible in 76,5% for humor aqueous samples.. For vitreous samples, the culture alone was positive in 9%, PCR in 36,3%, and nested PCR in 36,3%.

Conclusion 16S rRNA PCR is a rapid alternative to culture, sensitive and reproductible.. PCR associated to culture increases the number of positive samples. PCR was found necessary for the microbiological diagnosis in 10% of all cases (PCR+, cultures-).

• 2646 / F086

Miltefosine and polyhexamethylene biguanide, a new drug combination for the treatment of Acanthamoeba keratitis. Results from in-vivo toxicological and efficacy studies

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Purpose Miltefosine (MLT) and combinations of Miltefosine and polyhexamethylene biguanide (PHMB), chlorhexidine (CHX), and propamidine isethionate (PI), respectively, have been tested in a rat efficacy model for treatment of Acanthamoeba keratitis. In a second step, the most promising treatment regimens from efficacy studies have been tested for local tolerance in a fully GLP-compliant toxicological study in pigmented rabbits.

Methods The cornea of rats were infected with Acanthamoeba hatchetti. Cornea infections were graded microscopically. Nine groups were treated with varous treatment regimens for 28 days (8 times per day during the first week, and 3 times per day for the last three weeks). Efficacy of treatment was examined by determination of the degree of infection and culturing of excised eyes after the end of the treatment period. On day 28 the eyes were inspected under the microscope, re-graded and were then compered with the grades before starting the therapy.

Results Best treatment results were obtained from PHMB-MLT group. The ratio of fully recovered eyes was 28.4%. The highets therapeutic activity was yielded by the combination MLT-PHMB (86%), followed by MLT, CHX, or PI (72%) and the combination MLT–PI (70%. The fully GLP-compliant study in pigmented rabbits (28 days, 8 treatments per day) showed excellent local tolerance.

Conclusion Thus the combination of Miltefosine and PHMB can be seen as a highly effective and save option for treatment of AK.

• 2647 / F092

Time profile of viral DNA in aqueous humor of patients treated for VZV acute retinal necrosis using quantitative real-time PCR

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Purpose To evaluate the kinetics of varicella zoster virus (VZV) load using quantitative PCR (qPCR) in patients treated for acute retinal necrosis (ARN). Design: Cohort study, evaluation of diagnostic test or technology.

Methods Six patients (52±13 years) with ARN syndrome were consecutively studied. Aqueous humor (AH) was sampled from all eyes for qPCR evaluation. The patients were treated with intravenous aciclovir and intravitreal injections of antiviral drugs. The mean follow-up was 17.6±16.4 months.

Results Two main portions of the viral load curves were observed for each patient: a plateau phase (27.8±24.9 days) followed by a decrease in the number of viral genome copies. The mean baseline viral load was 3.4×107±4.45×107copies/ml (6×106 to 1.2×108). The viral load decreased following a logarithmic model, with a 50% reduction obtained in 3±0.7 days. There was a significant viral load (> 102 copies/ml) at 50 days after the onset of treatment, despite antiviral drugs.

Conclusion qPCR use demonstrated reproducible VZV DNA kinetics with a two-phase evolution: plateau followed by logarithmic decrease. These data suggest that high-dosage antiviral therapy during the conventional 10 days duration is insufficient in most patients. This patient's series responded with a similar decrease in viral load once initiated, this may be used to predict the progression of future patients. The correlation of the viral load threshold with clinical improvement needs to be more clearly defined.

• 2651
Aquaporins in glaucoma eyes

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Purpose Glaucoma is a neurodegenerative disorder with loss of retinal ganglion cells and axons. Elevated intraocular pressure is a significant risk factor in the development of glaucoma. Aqueous humour secretion is in part maintained by the aquaporins (AQPs) and AQPs also regulate fluid homeostasis in the retina. We investigate the expression of AQP1, -3, -4, -5, -7 and -9 in human glaucoma eyes compared to control normal eyes.

Methods Immunohistochemistry for AQP1, -3, -4, -5, -7 and -9 was performed on human paraffin embedded eyes. Nine glaucoma eyes were examined comprising three eyes diagnosed with simplex glaucoma, three eyes with neovascular glaucoma and three eyes with chronic angle closure glaucoma. The six control eyes had normal intraocular pressure without glaucoma. From each immunohistochemical slide representative fields (x20 objective) within the eye were captured. Using Photoshop software optical densities were generated and indices of staining intensity were calculated.

Results Immunostaining showed labeling of AQP7 in the Müller cell endfeet with an increased intensity in glaucoma eyes (p=0,02). AQP9 labeling of the retinal ganglion cells showed decreased intensity per cell (p=0,005). In the optic nerve there were no difference in AQP1, AQP4 and AQP9 labeling in the optic nerve astrocytes between normal and glaucoma eyes

Conclusion This is the first study investigating the AQPs in human glaucoma eyes. We found a reduced expression of AQP9 in retinal ganglion cells in glaucoma eyes. Glaucoma also induced increased AQP7 expression in the Müller cell endfeet. These results suggest that changes in retinal AQP expression are associated with the development of glaucoma

• 2652
Ocular perfusion pressure – a risk factor for open-angle glaucoma or a statistical artifact?

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Purpose Epidemiological studies have reported ocular perfusion pressure (OPP) as a risk factor for open-angle glaucoma (OAG). OPP is essentially the difference between blood pressure and intraocular pressure (IOP). IOP is thus part of OPP. As IOP itself is a strong OAG risk factor, the crucial question is whether the linear adjustment for IOP as commonly used in statistical models is sufficient to remove all confounding by IOP - a prerequisite to consider OPP an independent risk factor if significant after adjustment for IOP. This question was addressed in our study.

Methods We performed Cox regression on longitudinal data from the Rotterdam Study comprising 103 incident OAG cases and 3779 controls. All models were adjusted for age, gender and IOP. First, we entered diastolic OPP (DOPP) in the model as tertiles. Next, we entered systolic OPP (SOPP). Subsequently, we replaced the blood pressure values in DOPP and SOPP by normally distributed random numbers. Based on the diastolic and systolic blood pressure distributions in our data, we used standard deviation (SD) values of 10 and 20 mmHg. For both SD values, the analyses were repeated 10 times.

Results The hazard ratio (HR) for the lowest tertile of DOPP was 1.11 (95% confidence interval 0.68-1.83) and of SOPP 1.21 (0.74-1.98). The median (range) HR of the lowest tertile of the resampled DOPPs (diastolic blood pressure replaced by noise with a SD of 10 mmHg) was 1.27 (1.03-1.97) and of the resampled SOPPs (systolic blood pressure replaced by noise with a SD of 20 mmHg) 0.99 (0.72-1.35).

Conclusion Residual confounding by IOP can reveal a significant spurious association between a low DOPP and incident OAG with HRs similar to those reported in the literature.

• 2653
Analysis of eye hydrodynamics on the basis of tests with a mechanical load applied

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Purpose To use the results of tonography and other measurements on the mechanically loaded eye for obtaining information about its hydraulic system.

Methods We carried out tests of two types: standard 4 min tonography using a digital indentation tonograph Glautest-60 and discrete IOP measurements for up to 20 min after the load was removed. The experimental data were processed on the basis of our model of the eyeball as an elastic water-filled shell, which makes it possible to correctly estimate the individual elastic properties. The entire pressure vs. time tonography curve was used.

Results We introduce two parameters measurable from tonography: the IOP stabilization time and the limiting pressure in the loaded eye (the standard processing method yields one parameter). This and comparison with other data, including those available from literature, enabled us to test different hypotheses that specify the model and make it possible to calculate the hydraulic characteristics, e.g., the outflow facility coefficient. It is shown that the set of assumptions commonly used in processing the tonography data is inconsistent with the facts. The most intriguing are the apparent increase in the output (episcleral vein) pressure and the presence in the system of two characteristic times. Possible mechanisms to which these observations can be attributed are the pressure dependence of the outflow resistance and the capacitance of the outflow system.

Conclusion Under mechanical actions, in the hydraulic system of the eye substantial changes occur. The correct interpretation of these, strongly individual, changes may be important for diagnostics. Tonography may be a useful tool but the method of processing its data needs modification.

• 2654
Evaluation of retrobulbar hemodynamics and aqueous humor levels of Endothelin-1 in exfoliation syndrome, exfoliative glaucoma and primary open-angle glaucoma

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Purpose To compare mean Endothelin-1 (ET-1) concentration in aqueous humor and retrobulbar hemodynamics in patients with exfoliation syndrome (XFS), exfoliative glaucoma (XFG), primary open-angle glaucoma (POAG), and normal controls, and to evaluate the role of these index in the management of glaucoma.

Methods Aqueous Humour samples were collected from 20 subjects with POAG, 18 with XFG, 20 with XFS and 19 with senile cataract (CONTROL). Pre-surgery Color Doppler Imaging (CDI) in Ophthalmic Artery (OA), Posterior Ciliary Arteries (PCA) and Central Retinal Artery (CRA) were performed. Samples were frozen at -70oC and were analyzed with ELISA method.

Results ET-1 level in aqueous samples of XFS, POAG, and XFG groups were statistically higher than that in CONTROL group (p1=0,008, p2=0,005, p3=0,020). However, there was no significant difference between aqueous ET-1 levels of the three glaucoma groups (p< 0,900). Mean EDV of Ophthalmic Artery in subjects with XFG was significantly lower (p<0.05) than the other groups (XFS, POAG, Control). The mean PSV of the Ophthalmic Artery, yet, it was not statistically different between subjects with XFG, POAG and XFS, it was significantly lower (p<0.05) when comparing XFG and control groups. Resistivity index (RI) of OA in subjects with XFG was significantly higher compared with POAG and XFS patients (p<0.05).

Conclusion This study confirms a lower hemodynamics in patients with XFG, a statistically higher levels of ET-1 in glaucoma subjects, and no significant difference between levels of ET-1 in glaucoma groups, which may in the future, indicate a useful parameter as a result of glaucoma damage and not as cause

• 2655

SPARCS: a new method of evaluating contrast sensitivity in patients with glaucoma

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Purpose To evaluate a new contrast sensitivity instrument as a diagnostic test for glaucoma.

Methods Glaucoma patients, glaucoma suspects, and controls were prospectively evaluated using the Spaeth-Richman Contrast Sensitivity (SPARCS) method. Testing was performed monocularly in a standardized testing environment. Contrast thresholds for the central, superonasal, superotemporal, inferonasal, and inferotemporal areas of vision were determined. The contrast sensitivity scores for each area of vision and the cumulative scores were then compared to subjects' visual field and the amount of optic nerve damage, measured by the Disc Damage Likelihood Scale (DDLS) and the vertical cup to disc ratio. The results were analyzed with Spearman coefficients for continuous variables and the Kruskal-Wallis test for categorical variables.

Results One hundred and eighteen patients with glaucoma, 18 glaucoma suspects, and 125 controls completed the study. The mean SPARCS scores were 63.0 for patients with glaucoma, 71.9 for glaucoma suspects, and 77.1 for controls ($p < 0.01$). SPARCS had strong correlations with patients' visual field ($r = 0.76$, $p < 0.01$), DDLS ($r = -0.73$, $p < 0.01$), and vertical cup to disc ($r = -0.64$, $p < 0.01$).

Conclusion SPARCS was able to discriminate well between patients with glaucoma, glaucoma suspects, and controls. SPARCS had strong relationships with the degree of visual field and optic nerve damage. SPARCS may become a standard technique to assess visual ability in glaucoma patients.

Commercial interest

• 2656

Evaluation of the flicker defined form test versus matrix, in normal and glaucoma eyes

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Purpose To evaluate a new perimetric test, the Flicker Defined Form (FDF), and to analyze its capacity to detect visual field defect, comparatively to Matrix, in normal subjects and patients treated for primary angle glaucoma (POAG).

Methods Clinical comparative trial including 65 eyes of 35 subjects who performed: clinical examination, measurement of the retinal nerve fiber layer thickness by scanning laser polarimetry GDx-Pro, standard automated perimetry (SAP) Humphrey SITA 24.2 test, and Matrix 24.2 test; each subject performed SAP, Matrix and FDF two times, and only the second test was used in the study. Subjects were classified in 2 groups. Control group:35 normal eyes, mean age 40,5 years, without any abnormality in GDx-Pro or SAP. POAG group: 30 eyes, mean age 69,1 years, treated for POAG, and presenting glaucomatous abnormalities in GDx and SAP: 23 early POAG, 4 moderate and 3 advanced.

Results Control group: 37% (13/35 eyes) present defects revealed by FDF, and 6% (2/35) by Matrix. FDF defects are significantly more frequent than Matrix defects (Pearson Chi 2 test: $p < 0,01$); in 8 cases of these 13, defects are extended more than 1 quadrant. POAG group: 87% (26/30 eyes) present defects revealed by FDF, and 90% (27/30) by Matrix; there is no significant difference between the 2 tests (Pearson Chi 2 test: $p > 0,9$). All moderate and advanced POAG eyes present defects in the both tests. Eyes without defect (FDF or Matrix) are 7 early POAG with mild SAP defects.

Conclusion In POAG patients, FDF test and Matrix seem to present high sensibilities: 87% and 90%. Inversely, FDF test specificity is very low, 63%, comparatively to Matrix, 94%, probably in relation with a learning effect.

• 2661
Who wants it?

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Purpose Until recently, genetic testing in retinal dystrophy has been limited to a small proportion of families. Next Generation Sequencing is now being developed within clinical laboratories to deliver genetic testing to a much greater number of families. Retinal dystrophy is a very heterogenous condition affecting 1 in 3,000 people, but with new NGS technology, we now estimate that mutations can be identified in around 60-70% of families.

Results Understanding the clinical utility and applicability of testing in the care and management of families will be very important. Research suggests that patients want genetic testing in order to confirm the inheritance pattern in the family, identify those at risk and to give hope of future gene-based therapies in the future.

Conclusion We report on our experience in the genetic eye clinic since the introduction of NGS testing, the impact on families and some of the complexities including the identification of de-novo dominant mutations in sporadic cases as well as unexpected syndrome diagnoses.

• 2662
Delivering it: retinitis pigmentosa

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Purpose Current technologies for delivering genetesting through conventioinal Sanger sequencing are labour-intensive and expensive. Over recent years, high-throughput DNA sequencing techniques (next generation sequencing; NGS) have been successfully implemented in a research context. This presentation discusses the use of using in a clinical service context.

Methods We have applied NGS of 105 genes to patients known to be affected by inherited forms of blindness. This is delivered in the setting of a UK National Health Service accredited diagnostic molecular genetics laboratory. Thepresentation will discuss the ability of an NGS protocol to identify likely disease-causing genetic variants.

Results Conventional testing is applicable to theminority of patients with inherited retinal disease andidentifies mutations in fewer than one in four of thosepatients tested. The current NGS assay is directed at all patients with such disorders and identifies disease-causingmutations in 50-55% a dramatic increase.

Conclusion An NGS approach delivers a step change in the diagnosis of inherited retnial disease and provides precise diagnostic information and extends the possibility of targeted treatments including gene therapy. Importantly it is likely that this approach will develop rapidly in the near future.

• 2663
Delivering it: Stargardt disease

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Purpose To investigate the use of Sanger and Next Generation Sequencing (NGS) in patients with Stargardt Disease and other ABCA4 retinopathies

Methods Comparison of NGS with traditional Sanger sequencing in patients with possible ABCA4 retinopathies and the development of a clinical diagnostics service for inherited retinal degeneration using NGS.

Results When ABCA4 was tested using Sanger sequencing, the mutation detection rate in patients with a clinical diagnosis of STGD disease was ~80%. In patients with other phenotypes compatible with ABCA4 mutations (eg. end-stage chorioretinal atrophy, Bulls eye maculopathy or Pattern dystrophy) the detection rate was lower but still significant. Evaluation of NGS using ABCA4 as a test system showed that this technology, particularly the Illumina platform, was highly reliable in detecting the mutations found using Sanger sequencing. When NGS was used in a group of patients with Retinitis Pigmentosa or Cone-Rod Dystrophy, ~ 6% were found to have ABCA4 mutations, illustrating the heterogeneous phenotype of ABCA4 retinopathies and the difficulties in making a clinical diagnosis.

Conclusion Sequencing is the most efficient method of detecting mutations in STGD and will replace screening technologies. Genetic testing in STGD allows clinicians to improve their clinical pattern recognition, facilitate genetic counselling and identify patients for clinical trials. NGS compared to Sanger sequencing has the added advantage that numerous other genes can be sequenced at the same time and is reliable and cost effective, thereby providing an invaluable diagnostic tool. Genetic testing using NGS for genes involved in retinal degeneration is now available as a service through the Oxford laboratory (www.ouh.nhs.uk/geneticslab).

• 2664
Using it: NGS in the inherited retinal degeneration clinic

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Purpose To describe the clinical application of Next Generation Sequencing (NGS) in a retinal dystrophy clinic

Methods The use of NGS in a clinic setting is discussed using case histories from our research using NGS in IRD to illustrate the potential and complexities of NGS testing for the clinician.

Results Inherited retinal degeneration (IRD) is a common cause of visual impairment (prevalence ~1/3500). There is considerable phenotype and genotype heterogeneity, making a specific diagnosis very difficult without molecular testing. With the introduction of NGS huge amounts of genetic information are generated which highlight the importance of careful clinical phenotyping in the proband and family members with follow up segregation studies and functional analysis in many cases.

Conclusion From our experience in the clinical setting it is evident that NGS has a useful role in diagnosis. In our NGS study our mutation detection rate suggests that many patients are likely to have mutations in novel genes and it is clear that resources are needed to carry out careful family studies and appropriate functional analysis.

• 2671
Investigation of intra-cellular metabolism by time-resolved autofluorescence

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Purpose Changes in metabolism are first signs of pathological processes. The extra-cellular metabolism can be estimated by parameters of microcirculation. The fluorescence of endogenous fluorophores characterizes the intracellular metabolism. Besides of NADH and FAD which act as electron transporter in the respiratory chain, several other fluorophores like lipofuscin and advanced glycation end products, or collagen and elastin form the autofluorescence of the fundus.

Methods The influence of single fluorophores can be determined combining measurements of fluorescence decay after pulse excitation with spectral measurements. Based on fluorescence and lifetime measurements on isolated fluorophores and separated anatomical structures of porcine eyes, a laser scanner ophthalmoscope was modified for Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO). The eye-ground of human eyes is excited at 448 nm (70 ps FWHM, 80 MHz) and the fluorescence is detected in 2 spectral channels (490-560 nm and 560-700 nm) in TCSPC in 1024 time channels.

Results A certain relation was found between exponents of triple-exponential fit and anatomical structures. The lifetime tau 1 (about 70 ps) corresponds to the fluorescence in retinal pigment epithelium. The lifetime tau 2 (about 400 ps) originates from layers in the neuronal retina (receptors, bi-polares, ganglion cells). The lifetime tau 3 (about 3ns) is determined by connective tissue in the nerve fiber layer and to a certain degree by the fluorescence of the crystalline lens, too.

Conclusion The changes of tau 2 in the short wavelength spectral range which were found in the neuronal retina for diabetic patients having no signs of diabetic retinopathy,are interpretable as a loss of free NADH and a shift to protein-bound NADH.

Commercial interest

• 2672
Retinal oximetry technology

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Purpose Disturbances in retinal oxygenation are believed to be involved in several eye diseases, among them retinal vessel occlusions, diabetic retinopathy and possibly glaucoma and age-related macular degeneration. The technology to reliably and non-invasively measure retinal oxygenation is emerging after decades of development.

Methods Non-invasive retinal oximetry utilises the fact that the colour of blood changes as oxygen saturation changes. The most reliable measurements can be obtained from the larger retinal vessels, while measurements of retinal capillaries need further development. Several instruments have been built for non-invasive oximetry. They measure light absorbance of retinal blood vessels at two or more wavelengths and use the result to calculate retinal vessel oxygen saturation.

Results Several research groups have shown that their instruments are sensitive to changes in retinal vessel oxygen saturation and that the measurements are reproducible. Oximetry has successfully been used to detect differences in retinal oxygenation in many diseases as well as responses to treatment or provocation tests. Accurate calibration is, however, difficult.

Conclusion The current retinal oximetry technology can reliably be used to measure changes in retinal vessel oxygen saturation in the same eye with time. Oximetry can also easily measure differences in means between groups. Further development is needed to increase the accuracy of single measurements.

Commercial interest

• 2673
New developments in optical coherence tomography

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Purpose Optical coherence tomography (OCT) has become a standard tool in imaging the retina, the optic nerve head and the anterior segment of the eye. In the recent years much effort was directed towards improving the acquisition speed and the resolution of the technique. In addition, functional extensions of the technique were presented.

Methods Ultrahigh-speed swept sources can be used to improve A-scan rate in OCT, a technique also called optical frequency domain imaging. Increasing the bandwidth can improve longitudinal resolution in OCT and longer wavelengths in the near infrared improve penetration depth. Adaptive optics OCT improves transversal resolution. Functional extensions include measurement of blood flow and oxygenation.

Results High-speed imaging allows for three-dimensional imaging of the posterior and anterior segment of the eye. Using adaptive optics volumetric cellular resolution imaging becomes possible. 1050 nm OCT allows for visualization of the sclera and therefore measurement of choroidal thickness. Functional OCT provides insight into retinal metabolism.

Conclusion Improvements and extensions of OCT have been reported that will find its way into clinical routine. This is expected to result in improved understanding of retinal and optic nerve head disease.

• 2681

Expression of Lubricin mRNA and protein in human ocular surface tissues

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Purpose Friction is an inherent potential source of wounding for ocular surface tissues during the blink and bulbus movements and is identified as a major contributor to ocular surface disease of the dry eye type. The expression of lubricin, a boundary lubricant in articulating joints that protects against frictional forces, cell adhesion and protein deposition, was investigated at the ocular surface.

Methods Human corneal, conjunctival and control cartilage tissues were fixed with 4% paraformaldehyde, embedded in paraffin, sectioned serially, exposed to antigen retrieval buffers, and stained for lubricin by immunohistochemistry (IHC) with a rabbit polyclonal anti-human lubricin antibody. Several negative and positive controls were performed. Respective fresh tissues were analysed by reverse transcriptase polymerase chain reaction (RT-PCR) in order to verify the presence of the mRNA.

Results The mRNA for lubricin was found in human corneal and conjunctival cell lines and in complete ocular surface tissues similar to cartilage. The mRNA is translated and expressed into lubricin protein and protein staining was observed along the complete corneal and conjunctival epithelial surface, most strongly expressed in the corneal epithelium . The specificity of staining was verified in several positive and negative controls including use of irrelevant antibodies and preincubation of the anti-lubricin antibody with a pure peptide, which had served to generate the antibody.

Conclusion These findings verify that lubricin is synthesized and expressed by epithelial cells of the human cornea and conjunctiva and conceivably serves protective functions against frictional forces at the human ocular surface similar to the joint.

• 2682

Aquaporin-1 expression in membranes from proliferative vitreoretinopathy and in epiretinal membranes

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Purpose Aquaporin-1 (AQP1) is involved in cell migration and proliferation. This study aims to investigate AQP1 expression in membranes from proliferative vitreoretinopathy (PVR) and epiretinal membranes (ERM)

Methods 20 Membranes PVR and ERM were collected following eye surgery from 20 eyes from 20 patients. AQP1 mRNA and protein expression were determined by RT-qPCR and immunofluorescence in both PVR and ERM

Results AQP1 mRNA and protein were expressed in both PVR and ERM as shown by both RT-qPCR and immunofluorescence. Moreover, AQP1 protein expression was heterogeneous among and between PVR and ERM, and was highly colocalized with alpha-smooth muscle actin (SMA or Acta2) and slightly colocalized with glial fibrillary acidic protein (GFAP).

Conclusion AQP1 mRNA and protein were expressed in membranes from PVR and in ERM. Due to the absence of SMA and GFAP colocalization, it is likely that AQP1 is expressed by at least two distinct cells types. AQP1 might play a role in cell migration and proliferation occurring during the formation of PVR and ERM, and could represent a new therapeutic target

• 2683

Expression of lysophosphatidic acid, autotaxin and acylglycerol kinase

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Purpose To measure the levels of LPA and LPA-producing enzymes, autotaxin (ATX) and acylglycerol kinase (AGK) in the vitreous fluid from patients with proliferative diabetic retinopathy (PDR) and to correlate their levels with clinical disease activity and the level of vascular endothelial growth factor (VEGF). In addition, we examined the expression of ATX, AGK and VEGFR-2 in the retinas of diabetic rats.

Methods Vitreous samples from 42 PDR and 35 nondiabetic patients were studied by enzyme-linked immunosorbent assay. Vitreous samples and retinas of rats were examined by Western blot analysis.

Results VEGF, LPA and AGK levels in vitreous samples from PDR patients were significantly higher than those in control patients without diabetes ($p<0.001$ for all comparisons). ATX levels in PDR with active neovascularization and inactive PDR were significantly lower than those in nondiabetic patients ($p=0.045$). Mean VEGF and AGK levels in PDR with active neovascularization were significantly higher than those in inactive PDR and nondiabetic patients ($p<0.001$ for both comparisons). A significant correlation was observed between levels of VEGF and levels of AGK in PDR patients ($r=0.954$, $p<0.001$). Western blot analysis revealed a significant increase in the expression of AGK and VEGFR-2 in vitreous samples and the retinas of diabetic rats compared to nondiabetic controls, whereas ATX was significantly downregulated.

Conclusion ATX-AGK-LPA signaling axis might be an important player in the development and progression of diabetic retinopathy.

• 2684

Retinal pathways involved in the control of eye growth and myopia

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Purpose To integrate information from studies on gene expression in animal mpdels and from genetic studies on human myopia to define the pathways which are involved in the development of myopia

Methods A literature search of studies on gene expression in animal models of myopia and human genetic studies was carried out using the Medline database

Results Human genetic studies identify two clusters of mutations which are involved in human high myopia. One involves genes which affect photoreceptor and ON-bipolar cell function in the outer retina. These mutations are associated with congenital stationary night blindness. A second cluster involves genes involved in extracellular matrix structure and function, which may be important in the sclera, which changes markedly during the development of myopia. ON-bipolar cells play a major role in the control of dopamine release in the retina. Other evidence supports a role for dopamine in the control of eye growth, which suggests a plausible pathway linking the genes involved in the outer retina to control of eye growth. However, the down-stream effects of changes in dpoamine release are not well-characterised studies. However, animal studies have suggested that changes in the expression of the early intermediate gene ZENK and changes in glucagon release within the retina may play a role

Conclusion Huamn genetic studies and studies of changes in gene expression in animal models of myopia provide a consistent but still incomplete picture of the pathways involved in the control of eye growth. Further studies on these pathways are of particular importance given that they implicate retinal dopamine release , which links them to the epidemiological evidence that bright light- induced dopamine release can prevent the development of myopia in humans

• 2685

Retinal ganglion cell differentiation and protection using neuronally differentiated human dental pulp stem cells

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Purpose To investigate whether the neuronally differentiated human dental pulp stem cells (NDhDPSCs) can differentiate into retinal ganglion cells (RGCs) and whether the NDhDPSCs can protect primary mouse RGCs against oxidative stress injury.

Methods Human dental pulp stem cells were harvested and neuronally differentiated using various conditioned media. By immunohistochemistry, western immunoblots, and real-time RT-PCR, their cellular characteristics were evaluated and the best culture condition was determined for differentiation into RGC/glia-like NDhDPSCs. Regarding glial-like NDhDPSCs, they were cocultured with primary mouse RGCs under oxidative stress injury.

Results In specialized conditioned media, human dental pulp stem cells were differentiated into RGC/glia-like NDhDPSCs. They expressed RGC/glia-specfic markers as well as neuronal stem cell markers. When the glia-like NDhDPSCs were indirectly cocultured with primary mouse RGCs, they protect the RGCs against oxidative stress injury as determined by TUNEL assay.

Conclusion The human dental pulp stem cells may differentiate into RGC-like NDhDPSCs in a suitable culture condition. And the glia-like NDhDPSCs can protect primary mouse RGCs against oxidative stress injury in vitro.

• 2686 / T019

Intermembranaceous spaces of human optic nerve intracanal part

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Purpose Purpose of research - to reveal laws of structure and distribution of intermembranaceous spaces of optic nerve intracanal part.

Methods 43 bone blocks including optic canal with located in them membranes (dura, arachnoidea, pia), ophthalmic artery of people aged from 26 weeks of prenatal development till 75 years were histologically studied. The structure of optic nerve membranes and intermembranaceous spaces in the cranial, transitive and orbital compartments of optic canal were established. The received data were compared to optic canal MRI results of 27 patients (54 optic canals) aged from 2 months till 75 years on the "VISTA" MP-tomograph 1 T intensity of magnetic field.

Results Wide, uniform, continuous intermembranaceous spaces are characteristic for optic canal cranial compartment, medially and laterally of optic nerve they are more expressed. In optic canal orbital compartment subdural space is the narrowest, non-uniform on MRI and bone blocks research. The subarahnoidal space is most expressed in cranial compartment of canal laterally of optic nerve above of it, and on MRI medially of nerve it is absent or narrow, non-uniform, faltering crack (the similar data is received on histologic research). In transitive optic canal compartment there are separate fragments of subarahnoidal space or its absence in different directions from optic nerve (according to histologic research - above of nerve). In orbital compartment this space in the most cases is closed above and below of optic nerve (by results of research of bone blocks - on all circle of optic nerve).

Conclusion The laws of intermembranaceous space structure and their distributions in optic canal were revealed. MRI was effective method in study of intermembranaceous spaces of optic nerve intracanal part.

• 2711

Foveal changes during ocular movements in normal eyes. A prospective study.Kinetics of posterior pole during ocular movements in various diseases:a videomorphing technique

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Purpose To reveal the structural changes of the fovea and the posterior pole during ocular movements (OM) and specifically from the temporal gaze to nasal gaze. Videomorphing is proposed to study the kinetics of posterior pole during OM in various diseases.

Methods A prospective controlled study.The right normal eye of healthy individuals was enrolled. SD OCT cube scans were used. The central fovea thickness (CFT) was chosen as the primary measurement.The measurements were obtained at the primary positions and at the temporal and nasal gaze.Four CFT values were recorded:the CFTtemp at the temporal gaze with a vertex1 distance ,the CFTnasal at the nasal gaze with a vertex2 distance,the CFT1 at the vertex1 and the straightforward position and the CFT2 at the vertex2 and the straightforward position.The absolute difference between the CFT temp-CFT nasal was compared with the absolute difference between CFT1-CFT2 at the straightforward position of every patient . Paired t-test was used. Videomorphing of the OCT images with the same method was used to animate the posterior pole deformation during horizontal OM in healthy individuals,in patients with dry and wet AMD,with CSC and with high myopia.

Results 20 patients were included.The |CFT1-CFT2| ranged from 1μm to 4μm with mean value 1.6μm. |CFTtemp-CFTnasal| ranged from 1μm to 10μm with mean 5.8μm. (p= 0.0013). Videomorping revealed oscillation of the posterior pole during OM with specific characteristics for every disease.

Conclusion CFT showed significant fluctuation during ocular movements. Animation of posterior pole deformation during OM show different characteristics between normal eyes , AMD , CSC and high myopic eyes.

• 2712

3D blood vessels segmentation from optical coherence tomography

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Purpose To compute the 3D retinal vascular network, from standard high-definition optical coherence tomography (HD-OCT) data.

Methods Abnormal retinal vascular patterns were shown to be related to retinal and cardiac diseases. Studies have been performed using 2D fundus images. However, the obtained measurements may suffer from missing depth information for improved quantitative accuracy.In this work we resorted to Cirrus HD-OCT data (Carl Zeiss Meditec, Inc., Dublin, CA, USA) to scan the human macula. Our approach to obtain vessel positioning (depth-wise) takes advantage of the 2D automatic vessel segmentation of an OCT fundus image.To locate vessels in depth, we compare A-scans where in the fundus image no vessels were detected to neighbor A-scans containing vessels. Hence, we are able to identify the location of particular landmarks that characterize the presence of a vessel, such as, the hyper-reflectivity and the shadowing effect (due to the light absorption by blood).

Results Our algorithm is able to locate both above-mentioned vessel markers (hyper-reflective region and shadow). Preliminary data shows promising results. Both markers present good robustness and coherence, as demonstrated by the smoothness of vessels across different B-scans and the possibility to discriminate between different depth paths of crossing vessels.

Conclusion The findings suggest the possibility to compute the 3D vascular network, noninvasively, using a standard high-definition OCT. Additionally, accounting for vessel depth will lead to improved measurements of retinal vascular network properties and therefore to possible better correlations between its shape, location, and disease status.

• 2713

Vascular network of the human macula from OCT

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Purpose To compute the vascular network of the human macula from spectral-domain optical coherence tomography (OCT) to an extent similar to that of color fundus photography (CFP).

Methods Macular cube protocol scans of 512x128x1024 and 200x200x1024 voxels of 20 eyes from 13 type 2 diabetic patients and 10 eyes from 10 healthy volunteers were collected from the Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA) database. Additionally, CFPs and fluorescein angiograms (FAs) from the patients' eyes were gathered from the imaging database.Three distinct fundus references were computed from the OCT volumes after proper preprocessing. An additional OCT fundus image (OCTref) is computed as the principal component of these 3 OCT fundus references. The visible vascular network was manually segmented on CFP, FA and OCTref for comparison.Finally, a support vector machine (SVM) pattern classification algorithm was used to classify each pixel of the OCTref image into the vessel or non-vessel classes from a set of 14 features computed from the OCT fundus references.

Results Over 67% (67.8(7.2)%, average(SD)) of the vascular network manually segmented from the FA was manually segmented from the CFP, while this percentage raises to 69.2(8.9)% for OCT. In this way, the OCTref allows to compute an extended vascular network as compared to the CFP (102.8(14.4)%). When comparing the automatic versus the manual vascular segmentation, a specificity of 99.4(0.2)% and a sensitivity of 83.9(4.0)% were obtained. Overall, the accuracy of the automatic classification is of 98.0(0.4)%.

Conclusion The proposed algorithm allows for the segmentation of the vascular network from OCT scans of the ocular fundus to a level similar to that of color fundus photography.

• 2714

Observation of fundus using a novel high-speed and high resolution optical coherent tomography: a preliminary report

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Purpose to evaluate capability of femto-second white laser in observing the fundus when applying it to optical coherent tomography (OCT) as a light source.

Methods We have successfully developed 8 fs cw mode0locked Titanium Sapphire (TiS) laser which had broad band with ranging from 650 nm down to 950 nm. Using this laser, over 200 nm bandwidth portion ranging from 750 nm down to 950 nm pulse was created.. Acquistion time of one OCT image is o.o2 second and vertical resolution in the air is 2 μm in the air. Horizontal resolution is less than1 μm. High-speed acquisition time allows us to observe time sequential OCT images like an OCT movie for one second using a computer soft ware. Fundus examination using this OCT system was performed in eyes of healthy volunteers and patients with age-related macular degeneration (AMD) under approval of IRB. Effect of indocyanine green (ICG) in OCT images was also evaluated in the AMD patients when who has a routine ICG examination at clinic.

Results Pulsative movement of choroidal vasculature and retinal vessels at the optic disc head could be observed in motion OCT images. Single scan OCT image of healthy macula delineated four distinctive lines in stead of three when observed with a conventional SD-OCT, particularly in images scanned through extra fovea. Furthermore, as structure of the optic nerve head was clearly illustrated, so a manner of optic nerve how getting through the lamina cribrosa was well appreciated.

Conclusion Femto-second laser OCT is a promising tool to explore a new dimension of clinical ophthalmology particularly in examining AMD as well as glaucoma patients.

Commercial interest

• 2715
Follow-up study of MEWDS using adaptive optics retinal imaging

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Purpose To study the effects of pathological damage in cone photoreceptor outer segments (OS) on the visibility of cones in adaptive optics (AO) images.

Methods Four patients with multiple evanescent white dot syndrome (MEWDS) underwent multimodal retinal imaging using optical coherence tomography (OCT), scanning laser ophthalmoscopy (SLO). AO images were acquired with a field of 4 x 4 deg at eccentricities ranging from 0 to 8 deg from fovea using an infrared flood-illumination AO camera (rtx1, Imagine Eyes, France). Cone phoreceptor density was measured and analyzed in comparison to the findings from the other imaging modalities. The procedure was repeated at a follow-up visit after one month. One patient had 3 additional follow-up examinations over a 10-month time.

Results OCT images showed irregularities and disruptions in the OS tip line. Local thinning of the OS layer was observed in several areas of the macula. AO images revealed marked decreases in the density of detectable cones in the exact same regions. The measured cone density was superior to 30000 cells per mm2 in the areas of normal OS length and dropped to less than 10000 cells per mm2 in the regions of shortened OS. The locations of cone mosaic defects in the AO images also corresponded with hypo-fluorescent areas observed in the late phase of ICG angiography. During clinical recovery, the progressive return of the IS/OS and the OS tip lines to a normal layered structure in OCT images was correlated to an increase in cone density in AO images.

Conclusion AO imaging facilitates detection and monitoring of damage and recovery of the photoreceptor OS during MEWDS. The visibility of cones in AO images seems to be strongly dependent on OS structure and length.

• 2716 / S098
Assessment of different methods for inter-individual registration of OCT topography for statistical analysis

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Purpose Assessment of OCT topography is subjective. A statistical method of analysis would be helpful to aid interpretation. This requires the generation of accurate normative topography which in turn requires accurate alignment of normal OCTs. This study assesses 9 methods of alignment.

Methods Normal topography maps were exported from a spectral domain OCT system. Code was written to perform image registration using different methods: User selection of foveal centre, cross-correlation to a difference of two Gaussian macula template, finding of the thinnest central point and automatic fovea-finding using Gaussian convolution and centroiding for the red, green and blue channels of the image respectively.

Results Data from 127 left and 110 right eyes were analysed. Mean and total standard deviation across the central 400x400 pixels of the aligned maps were calculated. The lowest standard deviation was achieved by the cross-correlation method (38.9 microns), followed by the blue channel centroiding method (40.4 microns), the thinnest central point (40.5 microns) and the user-selected foveal centre (40.6 microns). Convolution with a Gaussian to identify the fovea produced the worst results with mean SD of 49.9-64.8 microns.

Conclusion Cross-correlation with a difference of two Gaussian macula template appears superior for inter-individual topography registration in OCT in comparison with fovea-finding methods. Blue centroid and thinnest point were the best other methods. The cross-correlation technique will lead to the most accurate normal maps for statistical comparison with data from pathological OCT topography.

• 2717 / S097
Atrophic areas and/with neovascular AMD. Characteristics, evolution of atrophic lesions associated to neovascular AMD treated by series of 3 Ranibizumab IVT protocol, 4 years follow-up

GONZALEZ C
FUTUROPHTA, Toulouse

Purpose To evaluate atrophic areas characteristics, at the first time, their change, evolution and correlation or no with and during the follow-up of neovascular AMD treatment by series of 3 Ranibizumab IVT

Methods 102 eyes of 91 patients, 28 men, 63 women, with retrofoveolar neovascularisation complicating AMD. Atrophic areas were evaluated by autofluorescence imaging Spectralis (in particular with region finder software), OCT (notably choriocapillary depth), FA, ICG. We evaluate the size, characteristics, topography of the lesions, their growth way. The areas themselves, their edge and rim were considered and evaluated. Each element was studied, compared cut to cut and time to time to itself and to each other data, every 2 months. The impact of AMD and / or this treatment protocol on the evolution of atrophic areas is also valuate.

Results VA improved in 85% cases, stabilized in 15%. AF imaging and their region finder analyze were the main elements of the atrophic lesions' study. The surface of the atrophic area grows by 17%, the edge changes in 20%. Speed growth was in average 1,15mm2/ year. At OCT, thickness of photoreceptor, pigment epithelium layer diminished about 25% and 35% at the area's edge. Choriocapillary depth values, FA and ICG data were mainly significative in the large atrophic areas and less than AF indications. This protocol has a little impact on the evolution of atrophic areas, apparently less than monthly IVT, and the same as AMD by itself.

Conclusion The study of atrophic process and its progression is a main question in the AMD follow –up, the evaluation of the protocol treatments and their safety too.

• 2721

Therapeutic targets in glaucoma

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Glaucoma leads to irreversible blindness and is characterized by changes in the optic disc and the visual field. The elevated intraocular pressure is considered the most important factor responsible for the glaucomatous optic neuropathy. There are multiple factors involved in the development of retinal ganglion cell death. The goal of glaucoma treatment is to preserve the visual field of patients and prevent the loss of visual function that is associated with the disease (European Guidelines). We should focus at least on three separate targets of glaucoma treatment (Brubaker RF. Survey of Ophthalmology 2003: Three targets for glaucoma management): Intraocular pressure (IOP), outflow facility, and the retinal ganglion cell (RGC).Elevated IOP is still the primary risk factor for the development and progression of glaucoma, and many studies have shown that IOP reduction can limit the progression of glaucoma and slow the loss of visual function. IOP lowering can be beneficial for normal-tension as well as high-tension glaucoma patients, and it may also prevent or delay the onset of visual field loss and optic disk damage in individuals with ocular hypertension.The second target of glaucoma treatment is outflow facility. In a healthy eye, aqueous production (flow) equals aqueous outflow through the trabecular and uveoscleral outflow pathways. Any imbalance between flow and outflow results in a change in IOP, yet even a transient elevation of IOP may cause significant glaucomatous damage.The third target of glaucoma treatment is the RGC itself. RGC death in glaucoma might have many causes, including vascular insufficiency, blockage of axonal transport, diffusion of toxic agents into the nerve cell, or initiation of apoptosis. Treatment that aims to directly protect the RGC from every possible insult might be the ultimate treatment for glaucoma because a strategy of neuroprotection could preserve the visual function of patients regardless of the etiology of their glaucoma.

• 2722

Trends in anterior segment surgery: what is coming?

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CS nº 7, Alicante

Anterior segment surgery has experienced a huge development in the last 25 years. Presently, in spite of this accelerated development, new technologies have emerged that have impacted considerably the surgery of the crystalline lens, the cornea and its pathologies. Corneal blindness, corneal debilitating diseases (corneal ectatic disease), corneal opacities, post infectious or traumatic problems and complication of cataract surgery has increased the rate of performance of corneal surgery, with corneal blindness still being a worldwide problem. Concerning the crystalline lens, cataract surgery is the most widely performed surgical procedure in the human being, and every step forward in this surgery affects millions of people around the world every year. Corneal surgery has been opened to a new stage of development thanks to the introduction of femtosecond laser technology, corneal crosslinking procedures, better knowledge of corneal biomechanics, improvements in corneal transplantation, development of corneal regenerating techniques, new antiinflammatory and immunological medication and a better knowledge about the ocular surface biological behaviour.Crystalline lens and cataract surgery have experienced a major recent impact with the introduction of femtosecond lasers for cataract surgery, and the so-called premium IOLs. Jointly, they represent a large step forward in the outcomes that are expected for cataract surgery, in which not only vision research is expected but also the spectacle independent condition for far and for near. Different models of accommodative lenses, multifocal lenses and other technologies have approached this refractive purpose. In this presentation the actual trends based on evidence based knowledge about the immediate evolution of corneal and crystalline lens surgery, the recent developments in the knowledge of the corneal diopter in normal and diseased conditions and the implementation that cataract surgery and IOL technology is undergoing today will be explained. The concept of eye modelling with modern customization of all these procedures through a global modern eye based on recent knowledge will be also outlined.

• 2723

Femtosecond laser and microkeratome preparation of ultrathin (UT) DSAEK grafts

MURTA J
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An important limitation of DSAEK is that some eyes do not achieve good visual acuity despite a clear cornea and minimal residual astigmatism. The thickness of the stromal lamella may influence the final visual acuity and better results may be achieved with thinner grafts.We describe a new technique that combines a femtosecond laser with a microkeratome to obtain consistently thin grafts, with no loss of corneas. This clinical study involves ultrathin DSAEK tissue preparation used in 28 patients with endothelial dysfunction. The first cut was performed with an Intralase FS60 laser and the second cut with a Moria CBm 300-µm microkeratome. The thickness of the first cut was modified for each cornea to obtain a final graft thickness of 120 µm. Post-op central graft thickness was performed with corneal laser tomography (Spectralis). Associated visual results, disk thickness and endothelial cell loss before and after surgery were evaluated. Final graft thickness was 88.3+27.6 µm, 77.2+26.6 µm and 74.3+27.5 µm at one week, one and three months post-op, respectively. No loss of corneas due to irregular cuts or perforation during preparation. The mean BSCVA was 0.41, 0.52, and 0.72(0.39, 0.28 and 0.14 LogMAR) after one week, one and three months post-op, respectively. Precut and post-op (3 months) ECDs averaged 2553 cells/mm2 and 1882 cells/mm2, respectively, representing 26.3% endothelial cell loss after 3 months of the surgery. Femtosecond laser and microkeratome can be used sequentially to prepare custom ultrathin DSAEK grafts with no loss of corneas. This procedure minimizes the variability inherent to microkeratomes and allows very quick recovery of visual acuity after posterior lamellar keratoplasty.

• 2724

Perspectives for new treatments at Alcon - part 1

RICH C
Head, Clinical Trial Management –Pharmaceuticals, Alcon, Fort Worth

This presentation will give the audience an overview of how we identify a wide variety of potential products to develop and how we condense this list down to the final candidates that will establish our pipeline strategy for each year. This process is conducted across the 3 main franchises of Alcon: Pharmaceuticals, Surgical and Vision Care. This presentation will review products in development in the areas of Glaucoma, Anterior Segment and the Ocular Surface.In the area of Glaucoma we currently have several products that will be reviewed. This includes potential new chemical entities with novel mechanisms of action and combination products that have the IOP lowering power greater than a beta-blocker without the risk of a beta-blocker. In the area of anterior segment we have several exciting programs in development to meet the unmet medical need around cataract surgery healing and post-operative infection. In the area of the ocular surface we have several projects in development for improved treatment in allergy (both nasal and ocular) and dry eye. In addition, as an extension of this area, we have projects for the treatment of acute otitis externa and antibacterial use during the peri-operative placement of tympanostomy tubes.

• 2725
The STRONG study

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University Medical Center, Mainz

Neovascular glaucoma (NVG) is a very aggressive, rare type of glaucoma but contributes disproportionately to blindness from all eye diseases. NVG is also the second most common cause for the removal of the eye-ball across all eye diseases, usually for intractable pain. The major cause of NVG is Ischaemic Central Retinal Vein Occlusion (CRVO) leading to neovascularisation and obstruction of aqueous humour outflow and increased intraocular pressure. Today's therapeutic approaches are insufficient and include destruction of the retina by coagulation, or off-label anti-VEGF injection into the eye. Clearly, there is a need for better treatments. Aganirsen is an antisense oligonucleotid that can interrupt the production of Vascular Endothelial growth factor, which plays a major role in the pathogenesis of NVG and is developed by GENE SIGNAL. A Phase II/III randomised, double-masked, 3-group, placebo-controlled trial (STRONG) is proposed to assess Aganirsen's efficacy in reducing the rate of anterior and posterior segment neovascularisation and NVG development after CRVO. Aganirsen is manufactured by AMATSI, another SME. Involving 333 subjects at 35 sites, the study is operationalized via a disease specific network (EVICR.net). The study aims at assessing a new therapeutic approach for NVG for which conditional authorization will be sought at the end of the project. STRONG also delivers new insights into the natural course of the disease and its risk factors analysing one of the largest patient cohorts ever. Also, it allows for a novel classification of NVG, yields image analysis tools, and proposes biomarkers able to differentiate between high- and low-risk patients and drug responders.

• 2726
Gullstrand (ECR-CCRS-2010-01)

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Purpose To present the current status of the Project Gullstrand study, aimed at measuring a large amount of biometric and visual function data in multiple centers Europe-wide.

Results At the time of writing (29/5/2012) 630 subjects have been measured in 12 participating sites located in 6 countries. One site has already finished recruiting. In order to give all other sites, some of which started recruiting only a few weeks ago, the chance to reach the targeted number of 200 subjects per site, the recruitment period has been extended to 31 December 2012. Given the current progress rates in the different sites it is very likely that the recruitment targets will be met at this time.

Conclusion The study is progressing well and is expected to reach its recruitment target by the end of the recruitment period.

• 2731
Compressive lesions

KAWASAKI A
Lausanne

Purpose To learn about compressive lesions which can mimic optic neuritis

Methods Case presentations

Results Idiopathic demyelinating optic neuritis is an acute unilateral optic neuropathy associated with pain. Compressive lesions are typically distinguished by chronic, progressive visual loss that is painless. Sometimes, a compressive lesion will manifest itself acutely and can be mistaken for optic neuritis.Focal inflammatory mass at the orbital apex (orbital pseudotumor) , lesions of the optic canal , expanding ophthalmc artery aneurysm, and infarction of an undiagnosed pituitary tumor (apoplexy) are examples of a compressive mass lesion that can present as an acute painful optic neruopathy. The clinical features of these entities will be discussed along with pearls for. suspecting the correct diagnosis.

Conclusion Careful history and examination can reveal important clues for distinguishing compressive lesion from optic neuritis

Commercial interest

• 2732
Inflammatory optic neuropathies

BORRUAT FX
Lausanne

Acute inflammatory optic neuropathy result frequently from a demyelinating disorder, multiple sclerosis being often the underlying pathology. However, the possibility of other causes of inflammatory optic neuropathies should be entertained when the clinical presentation is atypical (for example, massive disc swelling, painless visual loss, bilateral simultaneous optic neuropathy or, relentless progression of visual loss).This presentation will discuss the clinical presentations and differential diagnosis of typical optic neuritis, including Devic's syndrome (neuromyelitis optica), neuroretinitis, sarcoidosis, acute idiopathic blind spot enlargement, optic perineuritis, Leber's hereditary optic neuropathy.At the end of the session, participants should be able to recognize the typical and atypical features of optic neuritis.

• 2733
Optic neuropathy in Devic's disease: a diagnostic challenge

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Neuromyelitis optica (Devic's disease) is a severe inflammatory condition of the central nervous system, affecting the optic nerves and the spinal cord, that is distinct from multiple sclerosis by its pathophysiology and treatment. Serum antibody to aquaporin-4 (AQP-4 Ab) is a specific although inconstant biomarker of the condition. It helps also to identify among patients with isolated optic neuritis (ON) those who are at risk to convert to Devic's disease. AQP4 Ab assessment is becoming routinely ordered in atypical ON.We present here our personal experience of the clinical phenotypes of isolated atypical ON that were associated to positivity for AQP-4 Ab. Six cases were included. There were 4 females and two males, ranging in age from 24 to 68 (mean: 37.6). Follow up duration varied from 6 months to 9 years. Only one patient showed the prototypical monophasic bilateral simultaneous and non regressive visual loss. In the five other cases, presentation was less suggestive and covered a whole range of phenotypes of atypical ON. Thus, they presented with chronic-relapsing bilateral ON (3 cases), monophasic acute and remitting unilateral ON (1 case) and monophasic progressive unilateral ON (1 case). The prototypical ON case experienced later on several attacks of myelitis. The five other cases remained monosymptomatic to date but were considered as having a high risk for developing myelitis and were kept on immunosuppressive treatments. In conclusion, the clinical spectrum of AQP4-Ab- associated ON is larger than expected. AQP4-Ab assay has to be performed in any case of severe or relapsing ON. Diagnosis has therapeutic implications. Long term treatment with immune suppressive agents may both improve or stabilize vision and prevent occurrence of myelitis.

• 2734
Retinopathies

BOSCHI A
Brussels

Purpose How recognize acquired and hereditary retinal disorders in patient with acute visual loss mimicking an optic neuritis.

Methods Presentation of clinical cases

Results Optic neuritis can be mimicked by other optic neuropathies, and by anterior segment, choroidal as well as retinal diseases.This is particularly challenging when retinal disorders involved the macula or the peripapillary area, like central serous retinopathy, hereditary retinal disorders, and white dots syndrome. A complete neuro-ophthalmological examination and a detailed history are mandatory to differentiate optic nerve dysfunction from retinal disorders. Fluorescein angiography, OCT and electrophysiological testing might be relevant for the differential diagnosis particularly in case where the fundus appearance is completely normal.

Conclusion Through the presentation of various clinical case the different clinical clue that are helpful to differentiate the acquired and hereditary retinal diseases from optic neuritis will be argue.

• 2741

Graft rejection in keratoplasty - what are the benefits of systemic immune modulation?

GRUENERT A
Düsseldorf

Purpose Graft rejection is one of the major causes of corneal transplant failure after keratoplasty, especially in case of an ocular or systemic inflammatory disease. To reduce the patient's immune reaction against the corneal allograft, topical or systemic immunosuppression is a clinical necessity. This talk provides an overview of the benefits of systemic immunosuppression and of its indications.

Methods The advantages and disadvantages of the use of systemic immunomodulatory drugs in the prevention of corneal allograft rejection after keratoplasty will be analyzed and demonstrated.

Results Various systemic immunomodulatory drugs are available to prevent or to reduce the risk of corneal allograft rejection. The use of systemic immunosuppressive drugs may be limited by side effects.

Conclusion Systemic immunosuppression prolongs corneal allograft survival and reduces the risk of graft rejections. While the use of systemic immunosuppressive drugs is beneficial in the perioperative stage, the long-term-use is restricted to high-risk settings.

• 2742

Graft rejection in keratoplasty - is there a place for topical immune modulation?

PLEYER U
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Topical corticosteroids, although effective in the treatment of ocular immune-mediated diseases, are well known for their ocular side-effects. Not surprisingly, a variety of alternative immunomodulatory agents have been tested for topical use including cyclosporin A (CsA), mycophenolate mofetil (MMF), tacrolimus (FK506), rapamycin (sirolimus) and leflunomide. Local application bears the possibility to avoid the severe side-effects of systemic therapy. The effect of topical therapy is naturally restricted to local immune response mechanisms, such as antigen presentation by Langerhans and dendritic cells. Moreover, many immunomodulatory agents (e.g. CsA) are lipophilic and thus have low water solubility and penetrate insufficiently intra-ocularly, often being stored in the lipophilic corneal epithelial barrier. Therefore, the therapeutical success is limited for intra-ocular immune-mediated diseases like anterior uveitis. However, a multitude of strategies have been introduced to circumvent these problems including complexing substances such as cyclodextrins (CDs) and liposomes. In the prevention and treatment of transplant rejection after keratoplasty, many attempts to introduce topical immunomodulatory therapy have failed; on the other hand, further therapeutic options not primarily expected are being evaluated today such as treatment of severe keratoconjunctivitis sicca. In our own studies, we investigated the pharmacokinetics of topical treatment with different agents including MMF and evaluated the efficacy of topical treatment in animal models for uveitis and keratoplasty. Taken together, topical immunomodulatory therapy will not replace systemic therapy but further treatment options can be expected.

• 2743

Current concepts and future directions in the pathogenesis and treatment of infectious and non-infectious intraocular inflammation

DICK A
Bristol

Purpose Moving away from the morbidity of steroid therapy for inflammatory disease or the overburdonsome adverse events of immunosuppressive therapy, the advent of understanding of immune response during non-infectious uveitis alongside the explosion in biotechnology has facilitated the development of biologic therapy. This has generated a new era for increasing equisitely specific therapy. Improved diagnostics have lead to specific targeting for infectious aetiologies

Methods The review will highlight experimental evidence of targets of inhibiting T cell activation, B cell responses, Trafficking of cells, and cytokine inhibition. However, most importantly is the increasing abibility to predict and therefore target responses. Addiotionally the ability to rapidly identify infectious causes will be discussed

Results We will highlight the strength of predicting response to steroid and highlighting mechanisms of steroid refractiveness has generated avenues of approach for specific therapy. In addition the efficacy of regulating trafficking and inhibiting myeloid cell function shows promise in the future treatments of non-infectious intraocular inflammatory disease.

Conclusion Biologic therapy has the opportunity to not only specifically and powerfully immunomodulate but also with the increase in understanding of individual immune response adapt to generate a more stratified and personalised approach to therapy.

Commercial interest

• 2744

Novel therapeutic strategies for the induction of tolerance in corneal transplantation

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Regenerative Medicine Institute, National University of Ireland, Galway

Purpose To develop novel treatment protocols for the prolongation of corneal allograft survival.

Methods Genetic manipulation of donor corneas prior to transplantation is an attractive approach to protect the graft from allogeneic rejection. A lentiviral construct which encodes for Programmed Death-Ligand 1 (PD-L1) was applied for ex-vivo genetic modification of corneal grafts before transplantation. Moreover, the generation and application of regulatory cell populations such as mesenchymal stem cells (MSCs) and tolerogenic dendritic cells (tolDCs) to modulate immune-mediated rejection in transplanted animals and their mechanism of action will be discussed in this presentation.

Results Overexpression of PD-L1 in ex-vivo cultured corneas prior to transplantation significantly prevents corneal allograft rejection by modulating both innate and adaptive intra-graft allo-immune responses. Moreover, systemic injection of MSCs and tolDCs is able to prolong corneal allograft survival and reduces neovascularisation and graft opacity. A significant reduction of graft-infiltrating inflammatory cells was also recorded for both applications.

Conclusion Local overexpression of immunomodulatory molecules is a promising approach to prevent corneal graft rejection. In addition treatment of transplanted animals with regulatory cells also modulates corneal allograft survival. These novel therapies may have the potential to be further developed towards a clinical application.
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• 2745

Immune modulatory effects of gene therapy to corneal grafts

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(2) Institute of Anatomy, Essen

Purpose To provide an overview of immune modulatory effects of gene therapeutival aproaches to corneal allografting.

Methods The immune reactions caused by corneal allografting will be summarized. Gene therapeutical approaches will be presented, e.g. after transduction of epithelial cells with anti-apoptotic p35 in the mouse model.

Results Transduction with p35 leads to a reduced immune response. Further insight into the immune modulatory effects will be presented.

Conclusion Anti-apoptotic gene transfer leads to a reduced immune response in corneal transplantation. This might offer a way to increase success rate after transplantation of a corneal allograft.

• 2751
Definition and investigative techniques in advanced glaucoma

ZEYEN T
Leuven

According to Hodapp's criteria for visual field (VF) scoring, advanced glaucoma can be defined as having a VF mean deviation index (MD) < -12 dB. With those VF defects, the optic disc cupping is usually very distinct. Advanced glaucoma can also be defined on the basis of patient's skills to perform daily activities. Functional tests are usually more useful than structural parameters to follow-up patients with advanced glaucoma. An overview of the available investigative techniques in advanced glaucoma will be provided.

• 2752
Treatment options in advanced disease

BRON A
Dijon

Glaucoma is still the second cause of blindness worldwide. One of the main reasons is that since glaucoma is a symptom-free disease, at least 50% of glaucoma patients are not aware of their disease. Therefore it is not uncommon to see at the consultation advanced glaucoma cases even in the Western world.The management of these advanced cases is very challenging because if at best the treatment can stop the loss of retinal ganglion cells (RGCs) while lowering intraocular pressure (IOP), it will not prevent from the natural age-related loss of RGCs. Therefore many of these patients will go blind even with a "successful" treatment.The modalities of the treatment are controversial because when surgery is indicated, the fear of the so-called whipe-out syndrome is well known among glaucoma surgeons. Recent papers have highlighted that this complication may occur but may be at a lower rate that previously thought.In any case the treatment has to be customised according to the life-expectancy of the patient, the local and systemic tolerance of IOP-lowering drugs and the status of the other eye. A fair information given to the patients by the ophthalmologist is probably at least important that the suggested treatments for a given patient.

• 2753
Differential diagnosis of advanced glaucoma

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(2) Institute of Ophthalmology, London

Purpose To discuss the value of electrophysiological investigation in the diagnosis of visual pathway disease with particular reference to glaucoma.

Methods Standardised ISCEV electrophysiological recordings to incorporate full-field and pattern electroretinography and visual evoked potentials.

Results A case based presentation will be used to illustrate how appropriate electrophysiological investigation can be used to reach a diagnosis. The correct diagnosis will be discussed in some patients in whom an initial diagnosis of glaucoma was incorrectly made.

Conclusion The findings in patients with glaucoma are not diagnostic. Appropriate electrophysiological testing can usually reach a correct diagnosis when glaucoma is suspected but not present.

• 2754
Counselling the patient with advanced disease

ANSARI E
Eye Ear and Mouth Unit, Maidstone Hospital, Maidstone

Purpose To provide an understanding of how to counsel patients about irreversible sight loss.

Methods Understanding :the patient's perspectivethe grief reactionsharing informationthe role of the clinicianthe role of the counsellor

Results Time- listen listen and listen to the patient and their concerns.Team- you cannot manage this alone! Trust- this happens if time, transparency and team approach are employed.

Conclusion Glaucoma is responsible for irreversible loss of vision. It is very important to inform the patient fully about this from the outset and to be transparent and supportive if blindness supervenes. A solid team approach with the help of a counsellor is very important.

• 2761

Natural compounds as lead therapeutic agents against diabetic eye disease

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Diabetes is a leading cause of new cases of blindness throughout the world. Given the rapid increase in diabetes incidence in recent years, diabetic eye disease will likely become an even bigger problem in the future. There are currently no medical therapies for prevention of early stage ophthalmic complications of diabetes, and treatment for late stage disease is complicated and prohibitively expensive for deployment on a large scale. We have centered our efforts on identifying therapeutic compounds identified as natural products, with a particular focus on plant materials identified over time to be associated with efficacy against diabetes and its complications. The Indian gooseberry (Emblica officinalis), commonly known as Amla, is used in the practice of Indian traditional medicine (Ayurveda) to minimize the effects of diabetes and its complications. We previously showed that treatment of experimentally diabetic rats with crude extracts from Amla fruit delayed the onset and progression of cataracts and prevented the accumulation of sorbitol and diabetes-induced markers of lipid peroxidation and protein oxidation products in the eye. Because these results were consistent with the effects of aldose reductase (AR) inhibition, we embarked on a bioassay-guided scheme to search for putative AR inhibitors (ARI), using human AR (AKR1B1) activity as an assay read out. Fractionation of materials in an Amla extract resolved several compounds with ARI activity. Structure elucidation by NMR identified the major inhibitor as 1-O-galloyl-beta-D-glucose, also known as beta-glucogallin (bGG). We and others have shown that AR inhibition by sorbinil and a variety of other validated ARIs suppresses inflammatory markers associated with exposure to lipopolysaccharide (LPS) endotoxins. Our studies show that treatment of LPS-exposed mice with bGG dose-dependently suppresses infiltration of inflammatory cells in the anterior and posterior chambers and prevents morphological disruption of retinal layers. Using macrophage cell cultures, we demonstrated that bGG down-regulates endotoxin-induced expression of a variety of pro-inflammatory cytokines including TNFa and IL1b. Similar studies are being carried out with a novel drug lead recently identified in a family of flowering plants commonly cultivated in India and Malaysia (Piperaceae). Overall, our studies suggest that natural products may be a rich source of lead compounds useful for development as therapeutic agents against diabetic complications.

• 2762

Protective role of steroids on mouse primary RPE cells under hypoxic stress

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Purpose Angiogenesis is a clinically critical aspect of the pathogenesis of many retinal neovascular diseases. Triamcinolone acetonide (TA) is an important anti-angiogenic and anti-inflammatory agent. This study has evaluated the effect of TA on the expression of pigment epithelium derived factor (PEDF), thrombospondin-1 (TSP-1) and vascular endothelial growth factor A (VEGF-A) in cultured mouse RPE cells under hypoxic stress.

Methods Primary cultures of mouse RPE cells were grown in culture to passage 2-3 and were then subjected to hypoxic stress. TA (50µg/ml) was used to determine the steroid effect under normoxic (95% air/5 % carbon dioxide) and hypoxic (95% nitrogen/5% carbon dioxide) conditions. Hypoxia was continued for 48 hrs with and without TA. Cells were harvested at 0, 24 and 48 hours and both RNA and protein were extracted. Real Time PCR was used to analyze expression levels of PEDF, TSP-1 and VEGF-A. The expression pattern of PEDF, TSP-1 and VEGF-A in the presence of TA were quantifie.

Results After 24 hours of hypoxia, mRNA expression levels of both PEDF and TSP-1 were down-regulated by 2-fold. Hypoxic stress for 48 hours, resulted in 2.2-fold down-regulation of PEDF and a stronger down-regulation of TSP-1 of 3.4-fold. VEGF-A transcripts levels, on the other hand, showed an opposite response to hypoxic stress, an up-regulation of 1.9-fold at 24 hours and 2.7-fold increase at 48 hours. Hypoxic RPE cells, when exposed to TA, led to the rapid recovery of PEDF and TSP-1 transcripts at 24 hours after the initiation of hypoxia. VEGF-A mRNA expression rebounded to control levels in TA treated hypoxic cells. Western blots showed that TSP-1 protein levels correlated with the PCR results. TA significantly induced the expression of TSP-1 protein in hypoxic cells, and the strongest expression was at 48 hours.

Conclusion The results suggests that TA has a protective effect on PEDF and TSP-1 levels, and on the fine balance of PEDF, TSP-1 and VEGF-A levels.

• 2763

R-Ras in retinal angiogenesis

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Purpose R-Ras is a small GTPase belonging to the Ras family of proteins, that regulate cell migration, proliferation and survival. It has been shown to play an important role in vessel maturation. The purpose of this study was to evaluate role of R-Ras in retinal angiogenesis and vascular stability in oxygen induced retinopathy (OIR) model.

Methods Immunohistochemistry, confocal microscopy and qPCR we used to study expression pattern of R-Ras in mouse retinas. R-Ras deficient mice were used to study function of R-Ras during retinal angiogenesis. Retinal vascular permeability was measured using Miles assay where Evans blue (EB) dye is injected into circulation whereafter amount of albumin bound EB in retinas is quantified by spectrophotometer.

Results R-Ras is expressed in retinal vessels during developmental angiogenesis as well as during pathological angiogenesis in OIR model. In R-Ras deficient mice retinal angiogenesis was enhanced in OIR model compared to wt mice. Furthermore, retinal vascular permeability was significantly enhanced in R-Ras mice compared to wt mice in OIR model suggesting that R-Ras can effectively stabilize unstable retinal vessels and reduce the leakiness.

Conclusion R-Ras provides potentially a very interesting new therapeutic target for the treatment of neo-vascular eye diseases.

• 2771

EBO exam: how to succeed?

ACLIMANDOS W
London

ABSTRACT NOT PROVIDED

• 2772

Inventorisation of European education programs

TASSIGNON MJ
Antwerp

ABSTRACT NOT PROVIDED

• 2773

Surgical skills among European students

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Purpose To assess surgical skills of European students at the end of their training

Methods A questionnaire was given to all the students who passed the exam at the end of EBO examination in may 2011. The questions were about the duration of the training program, the beginning of surgical training, the number of different procedures performed by the students like intravitreal injections, lid surgeries, refractive and cataract surgeries. Students were questioned anonymously but they had to precise the country where they have spent their training.

Results We collected 150 questionnaires from the 331 students who have passed the exam. The results showed a great heterogeneity among countries with no surgical training during the residency in some countries while some students have performed more than 50 cataract surgeries without any help at the end of their residencies. Most of the countries do not organize a formal surgical level assessment at the end of the training.

Conclusion These results showed that the organization of surgical training is different among countries in Europe.

• 2774

UEMS-EACCME's new criteria for the accreditation of Live Educational Events (LEEs)

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The criteria set out in its document "The Accreditation of Live Educational Events by the EACCME" (UEMS 2011/30) are a significant change to the standards required for accreditation. The aim is to encourage greater transparency and accountability regarding the financial support of educational activities in the field of healthcare. During the presentation the new criteria and the changes necessary for LEEs will be shown.

• 2775
Evaluation remains a key point

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Purpose European postgraduate medical assessment have developed during the last 25 years. Currently, all European medical specialties examinations use MCQs. The European Board of Ophthalmology Diploma (EBOD) examination uses multiple independent true/false MCQs for the written part of the examination. Since true/false MCQs may be prone to guessing, thorough statistical evaluation has been set-up over the last five years to monitor the performance of the examination and its MCQs.

Methods In 2010, the European Board of Ophthalmology (EBO) decided to introduce negative marks for the MCQs. To study the influence of negative marks on the performance/reliability of the examination, the following statistical performance parameters of test items have been compared: P-value, Rit-value, Cronbach-alpha and 3-parameter item-response analysis.

Results A decrease in average P-value ($P < 0.66$) was observed compared to the situation without negative marks ($P > 0.75$). An increase in average Rit-value ($Rit > 0.15$) was observed compared to the situation without negative marks ($Rit < 0.15$). An increase in Cronbach-alpha (> 0.85) was observed compared to the situation without negative marks (< 0.80). 3-parameter item-response analyses revealed that almost none of the questions was influenced by guessing correctly (average $c <<< 0.33$), while without negative marks all questions were influenced by guessing correctly (average $c \sim 0.33$).

Conclusion Introduction of negative marks at the EBO examination, did lead to a decrease in item-facility (P-value) due to less "wild" guessing; an increase in Pearson correlation (Rit-value) between item and total scores and an increase in reliability (Cronbach-alpha). 3-parameter analysis showed that the portion of correct answers due to guessing is negligible with the use of negative marks.

• 2776
I have got a grant

GRIGORIU D
Oftapro Ophthalmology Clinic, Bucharest

Purpose Ever since the EBO grants have been awarded, the aim was to open communication channels between doctors from all over Europe, particularly linking the East to the West. From my point of view the actual collaboration between the young and the more experienced does just that, enabling the grant recipient to broaden her/his horizon, thus greatly enhancing self-confidence; and my aim is to prove this.

Methods I am going to share some of my personal experience during my stay in VU Medical Center in Amsterdam and speak about the impact that meeting the renowned team there had on the way I perceive my work and my responsibility towards my patients.

Results During my one month stay in Amsterdam I found excellent support in Prof. Ringens and his team – the vitreo-retinal surgeons, strabismus specialists and the retinoblastoma team. I thus made important steps in learning how to use an indirect ophthalmoscope, got to talk about complex retinoblastoma cases and saw some uveitis cases which are more frequent in Latin America or Asia and not so common in Eastern Europe.

Conclusion By receiving this grant I had the opportunity to come into contact with some of the best European ophthalmologists, to get new ideas on how to improve my practice and upgrade my skills in examining the patients. And, above all, I felt more than welcome among them and I feel certain I can count on them for further guidance and support.

• 2777
I have passed the exam

MUSELIER A
Dijon

ABSTRACT NOT PROVIDED

• 2781

A strategy for molecular diagnosis and search for new genes/loci in autosomal dominant retinitis pigmentosa

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Purpose Autosomal dominant retinitis pigmentosa (adRP) affects approximately 1 in 12,000 individuals. To date, 24 adRP genes have been identified accounting theoretically for 44.7% of adRP families; therefore, genetic defects in many patients are yet to be identified. This study was intended to provide information on prevalence of known adRP genes in France and to localize new genes and loci.

Methods The 10 most frequently mutated adRP genes (in full for RHO and RDS, in hot spots only for PRPF31, RP1, PRPF8, IMPDH1, NRL, PRPF3, NR2E3 and SNRNP200) were screened by systematic sequencing to determine the causative mutation in a cohort of 232 French families affected by adRP. We also performed a pilot experiment on 12 families by using whole exome sequencing (WES).

Results The direct sequencing approach was performed on 232 proband DNAs. A causative mutation was found for 99 families (42.7 %), among which 35 out of 68 (51.5 %) were novel. Among the 133 remaining families with no mutation (57.3 %), 12 probands were subjected to WES. This allowed to identify 7 additional families with a causative mutation.

Conclusion The prevalence of the genes was similar to that of the literature for most genes (e.g. RHO with 16 %), but were unexpected for others (e.g. NR2E3 with 3.9 %). The WES approach allowed us to identify a causative gene in 58.3 % of a population previously screened by direct sequencing approach. The 5 remaining families, negative with WES screen, are potentially carrying a mutation in one or more new adRP genes although an intronic mutation cannot be excluded. These 5 families are under active investigation.

• 2782

Search for the identification of new genes causing autosomal recessive retinitis pigmentosa

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Purpose The molecular diagnosis of autosomal recessive Retinitis Pigmentosa (arRP) is challenging because of the large genetic and clinical heterogeneity of this disease: to date, 36 arRP genes as well as 3 loci have been identified accounting for approximately 60 % of arRP families. Two major genes, USH2A and EYS, are responsible for 13 to 19 % of the cases, the other genes being minority. Here, we developed a strategy to search for new genes/loci causing arRP in a series of consanguineous families.

Methods Inbred families were genotyped using microsatellite markers specific for USH2A and EYS genes. Families resulting from this first screening were analyzed using 250K SNP microarrays with TASE software (Transmitted Allele Search Engine). Known genes in homozygous regions were PCR/sequenced. Whole Exome Sequencing is running for a few families.

Results A total of 44 inbred families were analyzed. Among them, 14 (32 %) were fully or partly homozygous for EYS or USH2A markers. We selected 16/30 of the remaining families for SNPs genotyping and homozygosity mapping. We found the causative mutation in 7 families (43 %) in a known gene (RP1, RLBP1, NR2E3, CNGB1, IMPG2, PDE6A) while in 6 others sequencing of known genes in homozygous regions is still ongoing. For the 3 remaining families, potentially new loci were found (in chromosomes 3, 10 and 21) for which the results of whole exome sequencing is being analysed.

Conclusion About 43 % of the tested consanguineous families had a positive molecular diagnosis and a candidate gene approach is ongoing for the 3 loci.

• 2783

Complexity of genetics in keratoconus

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(4) Revemic Systems, Spokane
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Purpose Mapping and genome sharing among affected individuals continue to be important for establishing a link between a genomic variant and its phenotypic consequences. In one large Ecuadorian keratoconus (KC) family a mutation and three other sequence variants were recognized, showing 100% segregation with disease phenotype in DOCK9, IPO5 and STK24 at 13q32 locus. Here we present further linkage and sequencing results of candidate KC genes identified in other Ecuadorian families.

Methods Linkage analyses were performed in 3 large KC families. Next, candidate genes at indentified loci were screened by standard techniques using genomic DNA samples from these families and selected individuals from other Ecuadorian families and control Ecuadorian individuals. Coding exons and intron-exon boundaries of the genes were evaluated.

Results Suggestive keratoconus loci, 2q13-q14.3, 20p13, and 5q31 were identified. Sequencing of IL1A, IL1B and IL1RN at 2q13-q14.3, SLC4A11 at 20p13, TGFBI, PITX1 and IL9 at 5q31 have been completed. Numerous SNV were identified in coding and non-coding regions.

Conclusion Identified keratoconus loci and the sequence variants are specific for the studied families only. Our results indicate high complexity of genetics in familial keratoconus.Support: Polish Ministry of Science and Higher Education, Grant NN402591740 and National Science Center, Grant 2011/03/N/NZ5/01470

• 2784

OPA1-related sensorineural hearing loss

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(7) Genetic, Montpellier

Purpose The OPA1 gene, encoding a dynamin-like mitochondrial GTPase, is responsible for autosomal dominant optic atrophy (ADOA, OMIM #165500), which can be associated with extra-ocular abnormalities including sensorineural deafness. The purpose of this study is to determine, in a large series of patients carrying OPA1 mutations, the prevalence of the R445H mutation and of rarer OPA1 mutations in patients with ADOD and to describe the phenotype associated with these rarer mutations.

Methods We retrospectively reviewed the files of all the OPA 1 patients with documented deafness diagnosed in our laboratory between 2003 and 2011.

Results In our series, deafness occurred in 6.4% of OPA1 patients. Hearing loss occurred as the first sign of the disease in one third of the patients, prior to visual loss. In addition to the most common mutation responsible for ADOA and deafness (R445H), we report 6 additional mutations responsible for this association.

Conclusion Deafness can be associated with dominant optic atrophy, due to OPA1 mutations, other than the classical R445H mutation. Unexplained sensorineuronal hearing loss can even be the first event and its association to optic atrophy and should prompt molecular genetic analysis, which can lead to an appropriate diagnosis.

• 2785 / T003
Detection of a novel premature stop codon in the OPA1 gene in autosomal dominant optic atrophy

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Purpose Autosomal dominant optic atrophy (ADOA) is a genetically heterogeneous disease, with OPA1, OPA4, and OPA5 representing the main ADOA loci. The aim of the study was to identify genetic etiology of inherited optic neuropathy in a Polish family.

Methods We report on a 2-generation Polish family with ADOA in which nine family members are affected. MRI and detailed ophthalmological examination with visual field and electrophysiological testing were performed. DNA was obtained from blood samples and linkage to known ADOA loci as well as sequencing of 29 OPA1 exons were conducted. Amplified fragments were analyzed on an automatic DNA sequencer.

Results MRI and ophthalmological examination confirmed the diagnosis of bilateral optic neuropathy. Pattern visual evoked potentials (PVEP) presented delayed P100 wave latency, reduced N75/P100 amplitude and abnormal morphology of waves. Pedigree analysis demonstrated a dominant mode of inheritance. Linkage studies allowed the exclusion of OPA4 and OPA5 loci but revealed linkage to the major OPA1 locus in the investigated family. Sequencing of the OPA1 gene identified a novel C-to-T transiton in exon 2 prediciting a premature stop codon (Q31X). The mutation co-segratated with the phenotype in this family. No other alteration was found in the OPA1 gene.

Conclusion Occurrence of the premature termination codon at the beginning of the transcript strongly suggest that ADOA in the investigated family is a consequence of OPA1 haploinsufficiency. The novel variant broadens the spectrum of the reported OPA1 mutations causing ADOA.

• 2786 / T004
Analysis of lincRNA at 13q32 keratoconus locus

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Purpose Keratoconus (KC) is a disease of the eye characterized by thinning and protrusion of the cornea. The causes of KC remain unknown. Our mutation screening of genes from 13q32 KC locus have revealed substitution in STK24 showing 100% segregation with KC phenotype in the Ecuadorian family. To continue the KC causes search, some non-coding RNA from 13q32 locus were selected for further molecular analysis. Here, we present sequencing results of lincRNA localized ~1kb from 5' end of STK24.

Methods The lincRNA was screen by sequencing technique using DNA samples from 23 members of KC-014 family and selected affected and unaffected individuals from Ecuador.

Results Sequencing analysis of lincRNA localized ~1kb from 5' end of STK24 have revealed g.99230266C>T substitution showing segregation with KC phenotype in the Ecuadorian KC-014 family.

Conclusion Mutation analysis of lincRNA mapped at the 13q32 locus have revealed sequence alteration segregating with the KC phenotype in Ecuadorian family. Since it is known, that lincRNAs are co-expressed with neighboring coding genes and may function as a regulator of epigenetic marks and gene expression, we suggest that this lincRNA localized in close proximity to STK24 gene might play a role in development and/or progression of familial KC in patients from Ecuador. To our knowledge, this is the first report presenting lincRNA analysis in KC.Support: Polish Ministry of Science and Higher Education, Grant NN402591740

• 2787 / T008
RDH12 mutation and early-onset retinal degeneration

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Purpose To show the clinical evolution of a child with RDH12 mutation (gene typically associated with Leber Congenital Amaurosis,LCA) and early-onset retinal degeneration

Methods A 8-year-old male who came to our department with a complaint of progressive decline in vision in his both eyes. Full clinical ophthalmological examination, including Best Corrected Visual Acuity (BCVA), anterior and posterior segment examination, Optical Coherence Tomography (OCT), color vision test, visual field, electrorretinogram and genetic study, was performed.

Results At first visit, BCVA was 10/100 in both eyes. Anterior segment examination was unremarkable. Fundus eye examination revealed a bilateral and symmetric pattern of macular hyperpigmentation (of three disk diameters in size)with reticular configuration and patches of hypopigmentation between hyperpigmentated areas. No peripheral atrophy with bone spicule nor optic nerve atrophy were observed. OCT showed an intense macular atrophy with severe disruption of complex pigment retinal epithelium-photoreceptors. Farnsworth Munsell 28-hue test revealed preserved color vision. Visual field showed a central scotoma. Electrorretinogram recordings demonstrated a still preserved rod and cone function. Genetic study revealed a compound heterocigotic mutation for RDH12 in exon 6 (p.Ala269fs and p.Arg234His).Two years later VA decreased to <10/100 and we observed progression of the macular damage.

Conclusion RDH12 mutation can be associated, although extremely infrequently, with an early-onset form of severe retinal dystrophy affecting both rod and cone function (preserved at first stages) and having a phenotype distinct from that resulting from mutations in other known LCA genes.

• 2811
Retinal oxygen saturation in health and disease

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Reykjavik

Purpose Measurements of retinal vessel oxygen saturation can provide insight into the nature of several eye diseases.

Methods Dual wavelength oximeters are used by our group and others. They measure light absorbance at one oxygen-sensitive and one oxygen-insensitive wavelength and use the absorbance values to calculate retinal vessel oxygen saturation.

Results Oxygen saturation in the larger retinal venules is decreased in central retinal vein occlusion but increased in diabetic retinopathy and age-related macular degeneration. In glaucoma, retinal venous oxygen saturation increases with increased visual field defect.

Conclusion Oxygen saturation in the larger retinal vessels, particularly the venules, reflects the balance between oxygen supply and oxygen consumption in the retina. In glaucoma, for example, a rise in the retinal venous oxygen saturation is most likely due to tissue atrophy and less oxygen consumption. Oxygen saturation in the larger vessels can also be affected by the efficiency of oxygen distribution by the retinal capillaries. Increased retinal venous oxygen saturation in diabetic retinopathy may for example partly be explained by shunting of blood through preferential channels in the capillary network.

Commercial interest

• 2812
Light flicker and oxygen saturation in diabetes

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Purpose To evaluate the retinal vessel oxygen saturation and its change upon flicker stimulation in patients with diabetic retinopathy.

Methods Dual wavelength oximetry was performed in 41 diabetic patients (65±12.3 years) with mild non-proliferative though proliferative diabetic retinopathy (DR) and 12 healthy controls (61.3±6.2). In a second study, oximetry and vessel diameter (central retinal artery and vein equivalents, CRAE and CRVE respectively) readings were taken before and 90 s after onset of flicker light stimulus in 18 patients with non-proliferative diabetic retinopathy (62.2±8.3 years) and 20 controls (71.2±7.5 years).

Results The venous oxygen saturation was increased in diabetic patients with the severity of the retinopathy: Controls 63±5%, mild non-proliferative DR 69±7%, moderate non-proliferative DR 70±5%, severe non-proliferative DR, 75±5%, and proliferative DR 75±8%.Flicker light increased CRAE, CRVE, and venous SO2 by 1.42%±3.72%, 2.80%*±2.70%, and 2.03%*±2.43% in the patients as well as 4.98%*±6.23%, 8.94%*±5.26%, and 4.20%*±3.71% in the controls (*: $p<0.05$). This increase was significantly higher in the controls vs. patients for all parameters (t-test, $p<0.05$). The arterial SO2 remained unchanged in both groups. After adjustment for the subject's age, the increase of the venous SO2 correlated significantly ($p=0.035$) with that of the CRAE in the controls but not in the diabetics.

Conclusion Retinal blood flow regulation and oxygen supply seem to be impaired in DR. As a key player in blood flow regulation, the vascular endothelium may be involved. Subsequent micro-vascular alterations (occlusions and obliterations in the capillary bead, formation of arterio-venous shunts) may result in a deficient oxygen supply to the retina.

Commercial interest

• 2813
Diabetic retinopathy and oximetry

BEK T
Århus, Denmark

ABSTRACT NOT PROVIDED

• 2814
Oxygen metabolism in age related macular degeneration

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Purpose To determine whether oxygen saturation in retinal vessels of patients with age-related macular degeneration (AMD) is different from that of a healthy population.

Methods The non-invasive retinal oximeter is based on a fundus camera. It simultaneously captures images of the retina at 600 nm and 570 nm and estimates retinal vessel oxygen saturation. Mean oxygen saturation of hemoglobin was measured in retinal arterioles and venules of 28 individuals with AMD, 6 were males. Eight patients had early AMD in at least one eye, 8 patients had untreated exudative AMD in at least one eye, and 12 patients had early AMD in one eye and untreated exudative AMD in the other eye. The age of AMD patients was 78 ± 9 years (mean ± SD) compared to 66 ± 4 years for the healthy controls (n=26).

Results Oxygen saturation of hemoglobin in arterioles, after adjusting for vessel width, was 94.3 ± 3.7% in the healthy population compared to 93.5 ± 3.1% in early AMD (n= ;p=0.42) and 93.7 ± 3.8% in exudative AMD (n= ;p=0.55). The corresponding values in venules were 60.9 ± 5.6% in healthy eyes compared to 64.9 ± 7.0% in exudative AMD (p=0.017). In eleven patients with early AMD in one eye and exudative AMD in the other eye, oxygen saturation in arterioles was 93.5 ± 3.0% and 92.4 ± 2.8% (p=0.52) and in venules 66.3 ± 4.9% and 64.4 ± 5.3% (p=0.080).

Conclusion Oxygen saturation in venules in exudative AMD is higher than in healthy controls and there is a similar trend in early AMD. Arteriovenous difference is smaller in AMD subjects than normals. The study suggests that retinal oxygen metabolism is affected in AMD.

Commercial interest

• 2815
Extraneous factors affecting retinal oximetry

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Purpose To identify extraneous factors that can impact the outcome of retinal oximetry calculations and to discuss how these factors might be negated.

Methods 1. Empiric observation of extraneous factors suspected to impact the outcome of retinal oximetry. 2. Controlled studies of established and suspected extraneous factors.

Results 1. The repeatability of a manual oximetry technique was found to be good. The standard deviations of Optical Density (OD) values ranged from 0.01 to 0.06 OD units and from 0.01 to 0.07 OD units for first degree arterioles and venules, respectively. The Co-efficient of Repeatability (CoR) ranged from 0.02 to 0.11 OD units (relative to a mean OD of 0.15 [0.06-0.23] OD units) for arterioles and 0.03 to 0.14 OD units (relative to a mean OD of 0.25 [0.17-0.31] OD units) for venules. Good reliability ($p<0.001$) was found for arterioles and venules. 2. Dual ratiometric calculations of retinal oxygen saturation (SO2) demonstrated a significant decrease of arterial SO2 during hypoxia. 3. The order of acquisition of spectral images did not influence the outcome of retinal oximetry results. 4. The manual calculation of SO2 values from reflectance data was significantly influenced by the selected retinal locations within and either side of a given retinal vessel. Other extraneous factors included: 5. Variation in retinal pigmentation; 6. Density of retinal pigmentation); 7. Instrument flash intensity; 8. Lenticular irregularities; 9. Tear film irregularities.

Conclusion Although the assessment of retinal SO2 in ocular diseases would seem to be of clinical value, a number of extraneous factors must first be taken into account to avoid erroneous conclusions.

Commercial interest

• 2816
Clinical aspects of retinal oximetry

GIBSON J
Birmingham

Purpose To review the current and future role of retinal oximetry in the clinical management of retinal disorders.

Methods By review of the published literature.

Results Examples of retinal oximetry use in retinal and retinovascular disorders will be presented.

Conclusion In the age of widespread use of anti-VEGF agents in retinal disorders, retinal imaging has become paramount for the treating ophthalmologist. Retinal oximetry enables retinal imaging to be coupled with an assessment of metabolic function of the retina and this may permit more targeted therapies to be given.

• 2817
Oxygen distribution in the retina

POURNARAS CJ
Geneva

Purpose To evaluate the distibution of the preretinal and transretinal partial pressure of oxygen(PO2) in normal and ischemic retinas.

Methods Evaluation of either the preretinal or intraretinal oxygen partial pressure (PO2) distribution, using oxygen sensitive microelectrodes, in normal or ischemic retinal conditions.

Results The distribution of PO2 close to the vitreoretinal interface is heterogeneous, being higher near the arteriolar wall. Preretinal and transretinal PO2 profiles indicate that O2 diffusion from the arterioles affects the PO2 in the juxta-arteriolar preretinal region. Both the preretinal and inner retinal PO2 recorded far from the vessels remain constant in all retinal areas. The oxygen tension (PO2) in the inner half of the retina remains largely unaffected by moderate changes in perfusion pressure, systemic PaO2 changes occuring during either hyperoxia or hypoxia. However, an increase in PaCO2 (hypercapnia), as well as an intravenous injection of acetazolamide (carbonic anhydrase inhibitor) both lead to an increase in preretinal PO2 due to dilation of the retinal vessels. In eyes with experimental branch retinal vein occlusion, PO2 values within the inner retinal layers are indicative of hypoxic conditions, whereas adjacent areas appear to remain normal. In diabetic patients undergoing vitrectomy a lowered vitreal PO2 in the affected retinal areas has also reported.Occlusion of the retinal circulation renders most of the inner retina anoxic.

Conclusion Thanks to the autoregulatory ability of the retinal circulation, the oxygen tension (PO2) in the inner half of the retina, remains largely unaffected during physiological stimuli. In both normal and inner retinal ischemic conditions,the oxygen supply from the choroid is sufficient to support only the photoreceptor inner segments.

• 2821

Novel therapeutic targets in diabetic retinopathy

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The present armatorium for the prevention or treatment of diabetic retinopathy (DR) comprises modulation of systemic factors, laser, surgical approaches, anti-VEGF agents and corticosteroids. In designing new therapies, the clinical targets of the various stages of DR should be clearly defined: these are vasoregression in pre-clinical DR, blood-retinal barrier loss, inflammation and retinal ischemia in macular edema, and angiogenesis and fibrosis in proliferative DR. With regards to early vasoregression, glucose-induced alterations in biochemical pathways, growth factors such as CTGF and Angiopoeitin-2, and leukocyte adhesion are under investigation as targets for prevention, whereas stem cell approaches have been suggested to allow repair of already degenerated retinal capillaries. For non-proliferative DR and macular edema, inflammatory targets such as TNF-alpha, IL-6, IL-10 and the Kallikrein-Kinin system are under investigation as targets for alternative or adjunct treatments for anti-VEGF and laser. However, the growing understanding of the cellular mechanisms of blood-retinal barrier loss may also allow for more directed therapies aimed at the paracellular or transcellular pathways of leakage, while new neuroprotective agents may restrict the ongoing neuronal loss in this stage of DR. For inhibition of angiogenesis in proliferative DR, several novel agents are available to enter clinical development. Finally, recent new insights in the pathogenesis of the angio-fibrotic switch and scarring have identified CTGF and other factors as potential therapeutic targets for prevention of this final blinding phase of DR.

• 2822

Investigator-initiated trials: a corporate perspective

LAMBROU G
Novartis, Strasbourg

The scope, size and regulatory sponsor requirements for Clinical Trials related to Medicinal Products have reached, over the past two decades, a degree of complexity making them increasingly difficult to implement by non-industrial sponsors. In recent years, however, these difficulties are being recognized, and various initiatives and guidelines to facilitate Investigator-Driven Clinical Trials indicate that the situation may be gradually changing. Novartis recognizes that scientifically rigorous Investigator-Initiated Trials with a sound medical rationale can provide essential contributions in furthering knowledge about diseases and their treatments. It therefore encourages implementation by the Healthcare Community of meaningful Clinical Research that adds to better understanding of medical needs and how to address them, with the ultimate purpose of optimizing patient care and treatment outcomes.In this presentation the concept of Investigator-Initiated Trials will be discussed from an industry perspective. The regulatory guidelines and Novartis processes for supporting such trials will be explained, using examples from the field of Ophthalmology, and the potential areas of interest in Retinal Vascular Diseases will be outlined.

• 2823

Perspectives for new treatments at Allergan

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Allergan, Buckinghamshire

Allergan, Inc., with headquarters in Irvine, California, is a global specialty pharmaceutical company that develops and commercializes innovative products for the eye care, neuromodulator, skin care and other specialty markets. We design our clinical trials in a scientific manner to investigate the benefits, risks and value of future or current products.

• 2824

Identifying progression of retinal disease in eyes with NPDR in diabetes type 2 using non-invasive procedures. Protocol nº ECR-RET-2010-02. ClinicalTrials.gov Identifier: NCT01145599

CUNHA-VAZ J
CS n°1, Coimbra

Purpose To identify eyes that show worsening and disease progression (progressor phenotypes)

Methods To identify Diabetic Retinopathy "progressors" to clinically significant retinal edema in type 2 diabetic patients with early NPDR, from baseline to the 12-month visit, assessed by biomarkers. Primary Outcomes: Microaneurysms turnover computed from color fundus photographs using the RetmarkerDR software; Retinal thickness increase in the central subfield. Secondary Outcomes: BCVA changes; ETDRS step changes; and rescue treatment.

Results Observational study with a follow-up at 0, 3, 6 and 12 months in eyes with NPDR (≤35). Color fundus photographs analyzed with the RetmarkerDR software for automated assessment of microaneurysms turnover (MA formation and disappearance rate). Retinal thickness measured with Frequency Domain Optical Coherence Tomography (FD-OCT).

• 2825

Neurodegeneration as an early event in the pathogenesis of Diabetic Retinopathy: A multicentric, prospective, phase II-III, randomised controlled trial to assess the efficacy of neuroprotective drugs administered topically to prevent or arrest Diabetic Retinopathy. EUROCONDOR – EU FP7 Project

CUNHA-VAZ J
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Purpose To assess whether neuroprotective drugs administered topically (somatostatin and brimonidine) are able to prevent or arrest neurodegeneration as well as the development and progression of Diabetic Retinopathy (DR) in its early stages.

Methods Primary: 1) To assess whether somatostatin, administered topically, is able to prevent or arrest the development and progression of neurodegenerative changes. 2) To assess whether, brimonidine, administered topically, is able to prevent or arrest the development and progression of neurodegenerative changes.

Results Primary: Changes in the Implicit Time assessed by mfERG (IT-mfERG). Secondary: 1) Neurodegenerative variables: Retinal Nerve Fiber Layer (RNFL); Ganglion Cell Layer (GCL) and central retinal thickness assessed by SD-OCT. 2) Microaneurysm turnover assessed by Colour Fundus Photography; DR severity. 3) Other variables: BCVA; Visual Fields; Visual-related Quality of Life; Need for rescue treatment.

Conclusion Clinical Trial PopulationType II diabetic patients; ETDRS levels <20 (50%) or ≤35 (50%). 450 patients to be enrolled in 11 or more clinical centres in Europe (41 patients per centre).

• 2826

Prospective, randomized, multicenter, open label, phase II / III study to assess efficacy and safety of ranibizumab 0.5 mg intravitreal injections plus panretinal photocoagulation (PRP) versus and PRP in monotherapy in the treatment of patients with high risk proliferative diabetic retinopathy. PROTEUS

FIGUEIRA J
CS n°1, Coimbra

Purpose To compare efficacy and evaluate safety of intravitreal (ITV) injection of ranibizumab (0.5 mg) plus PRP versus PRP alone in the regression of retinal neovascularization (NV) in eyes with high-risk proliferative diabetic retinopathy (HR-PDR).

Methods Primary Outcome: Regression of neovascularization (NV). Secondary Outcomes: 1) Best-Corrected Visual Acuity (BCVA) loss – changes from baseline; 2) Time to NV regression; 3) Recurrence of neovascularization; 4) Macular retinal thickness by Optical Coherent Tomography (OCT) – changes from baseline; 5) Laser needed for Diabetic Macular Edema (DME); 6) Vitrectomy needed due to the occurrence of vitreous hemorrhage or retinal detachment; 7) Drug safety profile.

Results This is a prospective, randomized, multicenter, open label, phase II / III study to assess efficacy and safety of ranibizumab plus PRP versus PRP alone in the treatment of subjects with HR-PDR. Number Patients:94 eyes from 94 diabetic patients: Randomized 1:1; Group 1: 47 eyes (PRP group); Group 2: 47 (ranibizumab + PRP).

• 2831

Interface quality of endothelial keratoplasty buttons obtained with optimised femtosecond laser settings

BOURGES JL
Paris

ABSTRACT NOT PROVIDED

• 2832

Microkeratome vs femtosecond laser assisted endothelial transplant cut

TOUBOUL D
Bordeaux

ABSTRACT NOT PROVIDED

• 2833

The interest of imaging for corneal lamellar grafting

NUBILE M
Chieti

ABSTRACT NOT PROVIDED

• 2834

New trends in endothelial transplantation: DSAEK vs DMEK

SCORCIA V
Catanzaro

ABSTRACT NOT PROVIDED

• 2835

Is there still room for penetrating keratoplasty in 2012

GICQUEL JJ
Poitiers

Penetrating keratoplasty (PK) is the most commonly performed graft in the western world. Recent advances in the medical management of corneal diseases and the advent of lamellar surgeries have considerably changed patterns in the indications of PK. Hence we will apprehend what indications are left for PK, as well as the enhanced PK techniques.

• 2841
New therapeutic approaches in uveitis

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Purpose Autoimmune uveitis is a severe disease, responsible for approximately 10% of acquired blindness. The side effects induced by systemic steroids or immunosuppressive therapies have prompted us to search for more specific treatments. Recently, tyrosine kinase inhibitors, including imatinib and sunitinib, have shown interesting properties in several autoimmune diseases. Their immunomodulating properties make them potential interest in the treatment of autoimmune uveitis and we analyzed their therapeutic effects in the mouse model of experimental autoimmune uveitis.

Methods We induced uveitis to C57BL6 mice by immunization with IRBP protein, and we performed a randomized blinded controlled trial in 30 mice treated with either sunitinib (50mg/kg/day), imatinib (50mg/kg/day) or placebo. We then compared the efficiency of these treatments by measuring the frequency and the severity of the uveitis induced.

Results An effect of sunitinib in the prevention of experimental autoimmune uveitis was observed, with an average uveitis clinical score of 1.1 in the control group, 0.70 in the imatinib group (p=0.28) and 0.36 in the sunitinib group (p=0.02). This effect was confirmed by retina histological examination, with a histopathological score of 0.95 in the control group versus 0.19 (p=0.003) in the sunitinib group. We furthermore demontrasted that sunitinib efficiency is most likely related to the immunomodulation of the immune response, with a reduction in the Th17 response and an inhibition of T cell proliferation.

Conclusion Thus, we report for the first time that a tyrosine kinase inhibitor can prevent experimental autoimmune uveitis or decrease its intensity. In particular, sunitinib could be considered as a potential treatment for autoimmune uveitis.

• 2842
Inflammasome activation by oxidative stress in ARPE-19 cells

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Purpose It is known that oxidative stress and inflammation are associated with the age-related macular degeneration (AMD). Retinal pigment epithelial (RPE) cells are responsible for the immune defense of retina, and they are constantly exposed to oxidative stress, a condition where the amount of intracellular oxidizing agents becomes increased with a concurrent decline in the cell´s defensive systems. Inflammasomes are intracellular protein complexes which become activated by danger signals encountered by the cell. They play a major role in innate immunity responses but their detailed contribution has still largely remained to be elucidated. In the present study, we have examined the association of oxidative stress with the inflammasome activation in human ARPE-19 cells.

Methods The cells were pre-treated or not treated with the bacterial endotoxin LPS, and thereafter exposed to the lipid peroxidation end product 4-hydroxynonenal (HNE).

Results Our data show that HNE significantly increased the production of proinfammatory cytokines IL-1beta and IL-18 but LPS by itself did not. Pretreatment of the cells with LPS, however, further enhanced the HNE-stimulated cytokine production. PCR analysis revealed that HNE induced a significant increase in the amount of the receptor component NLRP3 mRNA compared to control cells. The amount of NLRP1 mRNA remained unchanged.

Conclusion Our results suggest that LPS provided the first signal needed for the inflammasome activation. Thereafter, HNE triggered the assembly of the NLRP3 inflammasome complex.

• 2843
IL-17A as a possible target of anti-inflammatory and anti-parasitic treatment in toxoplasmic uveitis

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Purpose Toxoplasmosis is the most common cause of posterior uveitis in immunocompetent subjects. Taking into account the opposing needs of limiting parasite multiplication and minimizing tissue destruction, the immune imbalance implies especially Th17 and T regulatory (Treg) cells.

Methods In a multicenter prospective clinical study of intraocular inflammation (PHRC 3964), we evaluated the cytokine pattern in aqueous humors of 10 T. gondii infected patients. To determine the immunological mechanisms, we evaluated intraocular inflammation, parasite load, and immunological responses using mRNA and protein levels in a mouse model. Anti-IL-17A monoclonal antibodies (mAbs) were administered with the parasite in order to evaluate the role of IL-17A.

Results We observed severe ocular inflammation and cytokine patterns comparable to human cases, including IL-17A production. Neutralizing IL-17A decreased intraocular inflammation and parasite load in mice. Detailed studies revealed upregulation of Treg and Th1 pathways. When IFN-γ was neutralized concomitantly, the initial parasite multiplication rate was partially restored.

Conclusion Local IL-17A production by resident cells plays a central role in the pathology of OT. The balance between Th17 and Th1 responses (especially IFN-γ) is crucial for the outcome of infection. This data reveals new in vivo therapeutic approaches by repressing inflammatory pathways using intravitreal injection of IL-17A mAbs.

• 2844
Immune responses to model antigen elicited by immunization via conjunctiva associated lymphoid tissue

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Purpose There is an excessive demand to develop vaccines against many of the pathogens that infect mucosal tissues or have a mucosal port of entry. Parenteral vaccination may protect in some instances, but usually a mucosal vaccination route is of vital importance as the strongest immune response is obtained at the site of vaccine application and in anatomically adjacent mucosae. The aim of this study was to assess the efficacy of conjunctiva-associated lymphoid tissue (CALT) as a mucosal route of immunization.

Methods BALB/c and C57BL/6 mice were immunized via conjunctiva with tetanus toxoid (TTd) as a model antigen. 100 µg/mouse of TTd was applied onto conjunctiva of each eye, together with merthiolate-inactivated B. pertussis, which served as adjuvant. Control mice were immunized subcutaneously with 100 µg/mouse of TTd.

Results We found TTd-specific IgG and IgA in tears and sera of both mice strains, in addition to IgG positive TTd-specific cells. There was strong correlation between the amount of TTd-specific antibodies in sera and the presence of TTd-specific B cells in draining lymph nodes. B. pertussis enhanced IgG and IgA immune responses in both mouse strains. T cell activation (increase in CD25 expression and in percentages of CD4+, CD8+, and CD3+ cells) and B cell activation (increase in percentages of CD19+ CD25+ cells) occurred in all mice, but mice immunized with TTd in combination with B. pertussis had the strongest responses.

Conclusion Immunization via conjunctiva induced TTd-specific local and systemic immune responses. The strongest immune responses developed in mice that received TTd together with B. pertussis.

• 2845
Secondary choriocapillaritis in infectious choroiretinitis

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Purpose Primary choriocapillaritis is the mechanism at the origin of diseases such as MEWDS, APMPPE, multifocal choroiditis and serpiginous choroiditis. In case of severe chorioretinal inflammation as in infectious posterior uveitis, indocyanine green angiography (ICGA) shows much more widespread involvement than seen by funduscopy or fluorescein angiography (FA) in form of hypofluorescent areas. The aim of this work was to analyse this occult choroidal involvement.

Methods Charts of patients with toxoplasmic retinochoroiditis (TRC), syphilitic and tuberculous posterior uveitis seen in the Centre for Opthalmic Specialised Care (COS) in Lausanne, Switzerland from 1995 to 2011 were reviewed and patients with occult choroidal ICGA lesions were analysed.

Results Occult ICGA lesions were characterized by a ring of hypofluorescence around the focus as well as small hypofluorescent satellite lesions in TRC and tuberculous posterior uveitis. In syphilitic posterior uveitis the ICGA hypofluorescence was characterized by more extensive areas that could contrast with minimal FA and fundus findings. For all three entities these hypofluorescent areas responded well to treatment, completely regressing in syphilitic posterior uveitis and regressing to a size equivalent to the foci seen on funduscopy and FA.

Conclusion The aspect and the quick response to therapy of occult hypofluorescent areas on ICGA seen in severely inflamed infectious posterior uveitis most probably correspond to inflammatory choriocapillaris hypo or non-perfusion and its extent needs to be assessed by performing a global appraisal of these cases including ICGA.

• 2846
Central serous chorioretinopathy misdiagnosed as posterior uveitis: frequency and consequences

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Purpose Central serous chorioretinopathy (CSC) is one of the differential diagnoses to be kept in mind in case of posterior uveitis. Its diagnosis is of utmost importance as CSC misdiagnosed as posterior uveitis can worsen related to the prescription of corticosteroid therapy. The purpose of this study was to determine the proportion of cases of CSC misdiagnosed as a posterior uveitis.

Methods Charts of patients seen in the section of inflammatory eye diseases at the Centre for Opthalmic Specialised Care (COS) in Lausanne, Switzerland seen from 1995 to 2011 were reviewed and referred cases of CSC misdiagnosed as posterior uveitis were studied.

Results In a collective of 1268 patients seen from 1995 to 2011 at the COS, 12 patients (0.95%) with CSC were misdiagnosed as posterior uveitis. Erroneous diagnoses were Ocular tuberculosis in 3 cases, Vogt-Koyanagi-Harada disease in 2 cases, lupus (LED) in one case and undetermined uveitis in 3 cases. In 3 cases CSC developed following corticosteroid therapy for uveitis (2) or systemic inflammatory disease (1) and was misdiagnosed as worsening of the underlying inflammatory disease. Bad functional outcome was proportional to the diagnostic delay of CSC. The most useful means to diagnose CSC retrospectively was either the original angiography, especially indocyanine green angiography (ICGA), or OCT.

Conclusion CSC is not a rare misdiagnosis in posterior uveitis representing a percentage of nearly 1% in a total collective of uveitis cases but reaching a proportion of about 3% when only posterior uveitis cases are considered. Investigative methods such as angiography including ICGA, and OCT are crucial for reaching a diagnosis as quickly as possible to avoid disease worsening corticosteroid therapy.

• 2847 / F096
Atypical panuveitis parasitic and Herpes virus co-infection in immunocompetent adults: real co-infection or false positive?

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Purpose Acute panuveitis with retinitis diagnosis may sometimes be difficult. Contribution of microbiological analyzes of intraocular samples currently allows a rapid diagnosis to guide therapeutic management when visual function is severely threatened.

Methods We report three original cases of panuveitis with retinitis for which analyzes showed concomitant infection with Toxoplasma and Herpes viruses.

Results PCR techniques have increased the sensitivity and specificity of diagnostic tests for ocular pathogens, including Toxoplasmosis and Herpes viruses. For Toxoplasmosis, Western blot and Desmonts coefficient remain standards tests in immunocompetent adults. As for central nervous system infections, Herpes viruses PCR is the gold standard test for intraocular samples. The clinical cases described here are atypical and the clinical examination failed to set the diagnosis. The detection of two infectious agents has led to the establishment of a double etiologic treatment, due to the severity of the ocular involvement. However, we may suppose that certain viruses in dormant states can be liberated in an inflammed eye, causing DNA to be detected on PCR testing, making more than one true positive result both possible and clinically relevant.

Conclusion In actual clinical use, false-positive results are possible from contamination, and false-negative results are possible from polymorphism, specimen degradation, or failure to sample in the acute stages of disease. It remains difficult to determine the responsibility of both infectious agents revealed. Is it a real co-infection, or false positive?

• 2851
Intracranial pressure and glaucoma

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Purpose There are facts and myths. The fact is, that the orbital cerebrospinal fluid pressure (CSF-P) is the real counter-pressure against the intraocular pressure across the lamina cribrosa. The myth is that an abnormally low orbital CSF-P is involved in the pathogensis of normal-(IOP)pressure glaucoma.

Methods The talk will present the results of recent studies which may shed some light on the question wherther CSF-P is related to glaucoma

• 2852
Quantitative assessment of the visual pathway by DTI-MRI in Glaucoma

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Purpose In glaucomatous optic nerve atrophy (glOA) damage of retinal ganglion cells may continue to the linked optic radiations (OR). This study investigated differences between glOA and non-glOA in relation to impairment of the optic radiations using DTI-MRI.

Methods We examined 42 patients with healthy optic nerve head and no ophthalmological signs of an affected visual pathway, 134 glOA patients, and 35 non-glOA patients (mean age 54±15.9 years, 64±12.4 years, and 49±15.2 years, respectively). The participants underwent the diffusion tensor imaging (DTI) to measure the axonal integrity, i.e. fractional anisotropy (FA) and mean diffusivity (MD), and demyelination, i.e. radial diffusivity (RD), in the semi-automatically outlined optic radiations. The results were correlated with the retinal nerve fiber layer thickness (RNFL) acquired by the Spectralis optical coherence tomography and with the mean defect provided by standard automatic perimetry.

Results Age correlated significantly with the DTI parameters in all groups. If corrected for age only in the glOA patient group the mean defect correlated with FA (r=-0.31; p=0.004) and RD (r=0.22; p=0.043). In the non-glOA group the RNFL correlated with MD (r=-0.57; p=0.027) and RD (r=-0.59; p=0.019). The control group did not show a correlation of DTI parameters with the mean defect or RNFL.

Conclusion In both types of optic nerve atrophy a correlation was found between visual field and axonal integrity/ demyelination of the optic radiations, and the reduction of the RNFL was associated with an impairment of the axonal integrity/ demyelination of the optic radiation. The damage of the optic nerve was significantly associated with loss of RNFL and ageing.

• 2853
Autonomic nervous system dysfunction in glaucoma

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Although abnormal intraocular pressure (IOP) is the main risk factor for the development of primary open-angle glaucoma (POAG), other culprits including ocular microvascular dysregulation and systemic vascular abnormalities have been implicated in its etiology. The status of autonomic nervous system (ANS) is an important determinant of the systemic hemodynamic parameters implicated in glaucoma pathogenesis. Nevertheless, assessing the ANS function is not a practice in glaucoma diagnosis and management. Consequently, there is a lack of alternative therapies tailored to address associated systemic risk factors for POAG on a case and chronological wise basis; this approach could possibly be more effective in preventing the progression and visual loss in selected glaucoma cases.

• 2854
Neurodegeneration of the visual pathway in glaucoma

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Glaucoma has recently become recognized as a neurodegenerative disorder. This has been predominantly because that neuronal and axonal changes occur throughout the visual pathway from the retina to the brain. Furthermore, as in other neurodegenerative conditions, there are numerous studies investigating neuroprotective agents in glaucoma, using vitro and in vivo models. Historically, there has been a problem translating results however, from the laboratory to the clinic. In fact, there is a real shortage of good clinical trials in this area. In glaucoma, it is recognized that there is a need an alternative therapeutic approach, independent of IOP reduction. Several mechanisms have been implicated in initiating the apoptotic cascade in glaucomatous retinopathy and numerous drugs have been shown to be neuroprotective in animal models of glaucoma, although translating to the clinical arena has been difficult to date. This lecture will summarize neurodegeneration of the visual pathway in glaucoma and review current potential neuroprotective strategies.

• 2855

Neuroprotective therapy of the visual pathway in glaucoma

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Purpose To review our results of experiments relating to neuroprotective therapy of glaucoma at various levels of the visual pathway.

Methods Using isolated retinal ganglion cell (RGC) culture system, drug effects on hypoxic stress-induced damage of RGCs were studied. Using monkey unilateral experimental glaucoma model, 1) drug effects on the optic nerve head (ONH) circulation, and 2) neural degeneration secondary to experimental glaucoma in the CNS visual pathway were studied. Drug effects on CNS degeneration secondary to RGC death were also studied in a mice model. A double-masked placebo-controlled trial was conducted to investigate the effect of oral nilvadipine, a Ca2+-blocker, on the visual field in normal tension glaucoma (NTG) patients.

Results Ca2+-blockers and some of the beta-blockers were found to be neuroprotective against hypoxia-induced cultured RGC damage. Both nilvadipine and lomerizine, another Ca2+-blocker, increased the ONH circulation not only in normal, but also experimental glaucoma eyes in monkeys. In the lateral geniculate nucleus (LGN) of experimental glaucoma monkeys, M-cells were first damaged, and then both M- and P-cells damaged, where endoplasmic reticulum (ER) stress in apoptotic processes and activation of glial cells were involved. Systemic lomerizine and memantine were found to alleviate CNS damages secondary to NMDA-induced RGC death in mice. In a clinical trial, a low dose of oral nilvadipine (4mg/day) significantly decreased the rate of mean deviation (MD) deterioration in NTG patients as compared to placebo.

Conclusion A systemic drug administration such as oral nilvadipine which can alleviate damage at various levels of visual pathway may have potential in neuroprotective therapy in glaucoma.

• 2861
Retinal vessels as biomarkers

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Purpose In the recent years much interest was directed towards the analysis of retinal vessel diameters. This is related to our improved understanding of the systemic, ocular, environmental and genetic factors that control retinal vascular calibers.

Methods Methods to assess retinal vessel diameters are described. In addition, more sophisticated analyses of vessel structure are presented based on fractional analysis. Finally, techniques to study retinal vascular responses during stimulation, such as diffuse flicker light, are presented.

Results Narrower retinal arteriolar caliber is associated with aging, systemic hypertension and obesity. Wider retinal venular caliber is associated with impaired fasting glucose and diabetes, dyslipidemia and cigarette smoking. In addition, wider venular calibers are considered markers of inflammation and endothelial dysfunction. Reduced flicker-induced vasodilatation is an early process in diabetes.

Conclusion Assessment of retinal vessel diameters is an interesting approach for risk stratification based on ophthalmological findings. Refined technology and longitudinal studies are required to fully explore the potential of these techniques.

• 2862
Combining vessel analysis with Doppler OCT

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Purpose It has been recognized that morphological and functional changes of retinal vessels do not only reflect ocular vascular pathologies, but are also associated with systemic disease. Changes of the retinal vascular system may therefore serve as an indicator for systemic vascular related disorders such as diabetes and hypertension. The resolution of classical fundus-camera based systems is, however, limited, and vessels smaller than 40 -60µm cannot be adequately imaged.

Methods As such, much emphasis has been put into the development of new and sophisticated methods to assess retinal blood flow in vivo. One approach is based on Doppler optical coherence tomography (OCT), yielding in principle information on both, velocity and diameter. We investigated the validity of this approach by comparing vessel diameters with values as obtained using the Dynamic Vessel Analyzer (DVA) and blood velocities as obtained with laser Doppler velocimetry (LDV).

Results Comparison of velocity data as obtained with bi-directional Fourier Domain Doppler OCT showed good correlation with LDV data during both normoxic and hyperopic conditions ($p < 0.01$ each). Diameter data as obtained from OCT images were, however, significantly lower as those measured with DVA ($p < 0.01$). This was the case when data were extracted from both the amplitude and the phase images. In some cases the OCT technique underestimates the vessel diameter by as much as 20 µm.

Conclusion Whereas velocity data are adequately measured using Doppler OCT velocity data are significantly underestimated. As such adequate data on retinal blood flow can only be extracted using a combination of fundus camera-based vessel analysis and OCT-based velocity extraction. This technique may have considerable potential for risk stratification of cardiovascular patients.

• 2863
Retinal vessel analysis and oximetry - technical advances and clinical applications

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Purpose To develop and evaluate a method for simultaneous measurements of retinal vessel oxygen saturation and vessel diameter change upon flicker light stimulation.

Methods Dual – wavelength (548 nm and 610 nm) fundus images were taken before (baseline) and during luminance flicker stimulation (12.5 Hz, modulation depth: 1:25). Retinal vessel oxygen saturation (OS, dual – wavelength optical oximetry) and diameters (central retinal arterial and venous equivalents – CRAE and CRVE) were determined. Investigations were performed in 19 healthy volunteers (mean age: 26 ± 2.5 years), 18 patients with diabetic retinopathy (62.2±8.3 years), 16 glaucoma patients with IOP (≤22 mmHg, mean 16±3.5 mmHg, mean age 66±14 year), and 20 age matched controls (71.2±7.5 years).

Results In the young population, the flicker increased CRAE, CRVE, and venous OS statistically significant from 193 ± 20 µm, 228 ± 20 µm, and 60 ± 5.7% at baseline to 202 ± 19 µm, 242 ± 17 µm, and64 ± 5.9% (all $p<0.0005$).. Flicker light increased CRAE, CRVE, and venous OS by 1.42%±3.72%, 2.80%*±2.70%, and 2.03%*±2.43% in the patients as well as 4.98%*±6.23%, 8.94%*±5.26%, and 4.20%*±3.71% in the controls (*: $p<0.05$). Also in glaucoma patients, the increase of venous OS upon flicker was smaller in the patients than in the controls (1.9±4.9%).

Conclusion Oxygen supply or consumption is reduced in diabetic retinopathy as well as glaucoma. The simultaneous measurements of retinal vessel oxygen saturation and vessel diameter change upon flicker light stimulation should be considered for the investigation of such impairment of oxygen supply.

Commercial interest

• 2864
Retinal vessel analysis in animal models

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Purpose Measurements of retinal blood flow in the rodent is a major challenge because of the small size and the poor optical quality of the eye. We present a technique based on the measurement of retinal vessel diameters using a fundus camera specifically designed for the rodent eye. This is combined with a Doppler OCT technique for measuring retinal blood velocities.

Methods In the rat retinal vessel diameters and retinal blood velocities were measured during several stimuli. These included systemic hyperoxia by breathing 100% oxygen, systemic hypercapnia by breathing increasing concentrations of CO2 and by stimulation with diffuse flicker light.

Results Retinal blood flow was quantified in larger retinal venules in our studies. As expected systemic hyperoxia induced a pronounced decrease in retinal vessel diameter, retinal blood velocity, and retinal blood flow ($p < 0.01$ each). Breathing increasing concentrations of CO2 on the other hand induced a dose-dependent increase in retinal vessel diameter, retinal blood velocity and retinal blood flow ($p < 0.01$ each). Finally, stimulation with flicker-light also increased retinal vessel diameter, retinal blood velocity and retinal blood flow ($p < 0.01$ each).

Conclusion Our data indicate that changes in retinal blood flow in the rodent can be adequately measured using combined fundus photography and Doppler OCT. This technique can also be used to study neurovascular coupling. Our results are important, because the mechanisms of retinal blood flow regulation remain largely obscure.

• 2871
Biology of metastatic disease

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Purpose Despite successful treatment of the primary tumour, uveal melanoma (UM) disseminates haematogeneously in approx. 50% of patients, usually to the liver. In a few patients, metastases can be treated surgically; however, in the majority, there is no effective chemotherapy, as the "magic bullet" for metastatic UM has yet to be found.

Methods Literature review to provide an overview of the morphological, immunohistochemical and molecular genetic features of metastatic UM. In addition, immunohistochemical studies for various proteins, including BRCA1 associated protein 1 (BAP-1), were performed on tissue microarrays of matched primary and metastatic UM. The percentage of tumor cell positivity was scored blind by independent assessors, and correlations were measured with statistical tests.

Results Literature review revealed only a few studies of human UM metastases, including some on fine needle aspiration biopsies, liver resections, or on autopsy material. Occasional studies examined matched primary and metastatic tumour samples. The majority of investigations had performed immunohistochemistry, with only a few examining the genetic changes of these tumours. The results of our analyses of a cohort comprising >100 metastatic UM will be presented. We confirm that absence of BAP1 correlates with metastasis of UM; however, metastasis can occur despite BAP1 expression.

Conclusion In order to understand the dissemination process of UM, including the mechanisms involved in successful tumour cell colonisation, the tumour microenvironment-, the immunophenotype-, genotype and possible susceptible signalling pathways of the melanoma cells, it is essential that greater efforts are made to access and investigate these samples. Only in this way can treatment of the systemic phase of UM be successful.

• 2872
Genetic analyses of uveal melanoma metastases

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Purpose To identify genes linked to metastasis development in uveal melanoma (UM), transcriptome analysis linked to comparative genomic hybridization was performed with 63 primary tumors and 115 liver metastasis. 9 primary tumors and their matched metastasis (couples) were also analyzed. A biostatistical approach was used to define the genetic prognosis parameters. BAP-1 mutations reported to be frequently present in class 2 UM were investigated.

Results Fifteen percent of the metastases were found disomic for the chromosome 3 (suggesting a class1 profile) and the couples were monosomic for chromosome 3 (suggesting a class2 profile). Examination of the genomic imbalances in couples (all with monosomy 3, suggesting a class2 profile) indicated that no major alterations occurred at the metastatic step. Very few genes (30) were found differentially expressed between the primary tumor and the metastasis after removal of liver expressed genes.

Conclusion These results suggest that the events leading to the metastasis spreading are already present in the primary tumor.

• 2873
Prediction of metastasis

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Purpose To describe the Liverpool approach to the prediction of metastasis from uveal melanoma.

Methods The Liverpool Ocular Oncology Research Group (LOORG) has developed the Liverpool Uveal Melanoma Prognosticator Online (LUMPO), which is available free on the internet at www.ocularmelanomaonline.com. This estimates the survival probability according to age, sex, largest basal tumour diameter, tumour thickness, ciliary body involvement, extraocular spread, melanoma cytomorphology, mitotic count, extravascular matrix pattern and chromosome 3 status. An all-cause survival curve is generated using the accelerated failure time mathematical model. A survival curve for the general British population of the same age and sex is also generated. By subtracting one curve from the other it is possible to estimate metastatic mortality.

Results LUMPO has been developed with data on more than 3000 patients and has been thoroughly validated. The results depend greatly on the accuracy of clinical measurements, mitotic counts and genetic typing. We have found FISH to be inadequate and have replaced this with MLPA and MSA, reserving the latter for small biopsy samples. Biopsy techniques have also improved and these have enhanced the results of prognostication.

Conclusion With advances in biopsy, genetic testing and multivariate analysis, we are now able to provide personalised prognostication. This enhances the quality of life of patients with a good prognosis while enabling us to target intensive care,such as counselling and screening, at high-risk patients. Improved prognostication has also enhances opportunities for basic science research, facilitating the identification of molecular abnormalities influencing the metastatic process.

• 2874
Serum biomarkers of metastatic disease: current practice and future perspectives

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Purpose Molecular genetic testing of primary uveal melanoma (UM) specimens is being integrated into clinical practice for prognostication purposes. However, the current screening protocol for metastatic disease (MD) it is not able to detect micrometastases. There is a clear need for easily assessable biomarkers that would allow earlier detection of MD and aid monitoring of systemic adjuvant therapy. As UM disseminates haematogeneously, it is reasonable to search for blood-borne biomarkers as indicators of MD.

Methods Review of the literature to provide an overview of blood biomarkers studies in UM.Outline of the workflow, which could lead to new biomarker discovery using a discovery proteomics approach.

Results Conventional biomarkers described in other cancer types have been investigated in blood samples from UM patients. These markers have failed to provide reproducible results and therefore their usefulness in the clinical senario has been questioned. The enumeration of circulating tumour cells shows good potential, but results are influenced by the technique used for detection. Proteomic technology has been applied to UM tumour tissue, secretome and cell lines, mainly using 2D gels. Quantitative mass spectrometry-based discovery proteomics comparing high risk tumours versus low risk ones, followed by system biology analysis to select a panel of meaningful candidates among the differential expressed proteins, bears the potential to be a more accuare and effective approach.

Conclusion None of the blood biomarkers tested in UM patients have demonstrated the necessary sensitivity and specificity to guide clinical decisions. A rational development of clinically relevant blood biomarkers can be achieved applying proteomic technologies.

• 2875

Staging of uveal melanoma metastases

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Purpose To summarize the need and methods available to stage metastatic uveal melanoma.

Methods Literature review and personal experience.

Results In the Tumor, Node, Metastasis (TNM) classification, metastatic disease is assigned to category N1 (regional lymph node metastasis) and M1 (systemic metastasis) and stage IV by definition. For practical purposes, uveal melanoma spawns only systemic metastases. The latest 7th TNM edition, effective from January 2010, introduced subcategories of M1 based on the largest diameter of the largest metastasis (LDLM) at diagnosis of disseminated disease: M1a corresponds to LDLM 3.0 cm or less, M1b to LDLM 3.1-8.0 cm and M1c to LDLM 8.1 mm or above. In addition to the TNM system, a staging system based on three variables: performance index as a measure of the general health of the patient, serum or plasma alkaline phosphatase level as a measure of the hepatic function and non-measurable metastases and to LDLM as a measure of measurable metastases is available. It was developed at the Helsinki University Central Hospital and has been validated by the European Ophthalmic Oncology Group. An underlying multivariate model assigns patients into stages IVa, IVb and IVc with predicted median survival of less than 6 months, 6 to 12 months and over 12 months. In the validation data set, the corresponding observed median survival times were 18.6 months for stage IVa, 10.7 months for stage IVb, and 4.6 months for stage IVc.

Conclusion Staging of cancer at diagnosis is important because it enables the physician to assess the extent of disease in a standardized way. This will help in choosing appropriate treatment and in assessing treatment outcomes between studies in a more comparable way.

• 2876

Metastatic uveal melanoma: A liver disease or a systemic disease?

KEILHOLZ U
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ABSTRACT NOT PROVIDED

• 2877

Therapeutic options in metastatic uveal melanoma

PIPERNO-NEUMANN S
Paris

Purpose Despite the advances in the treatment of uveal melanoma (UM), randomized studies have demonstrated that the metastatic risk was similar after enucleation or conservative treatment. Survival has not improved and enucleation remains the treatment of choice for large tumors.

Methods Up to 50% of patients develop metastases, to the liver in 90% of cases,usually leading to death. Metastases are rarely detected at the time of diagnosis, and in contrast with cutaneous melanoma, occur via hematogenous spread. There is no standard adjuvant treatment to prevent metastases. Today, genome-wide techniques of genomic and expression profiling make it possible to improve the characterization of high-risk UM. Recently, mutations in the GNAQ/11 genes have been described as oncogenic drivers in UM and consequently potential therapeutic targets. Since the identification of genomic abnormalities correlated with the metastatic risk, techniques of fine needle aspiration biopsies have been developed and systematic genetic analysis of UM became recommended for the next years, in the prospect of future adjuvant trials based on potential biological targets to be tested in preclinical animal models.

Results Relevant clinical data and dedicated studies in metastatic UM patients are lacking. Only 25 prospective clinical trials were published in the last 30 years,none of them reported a randomized phase III trial. In a retrospective series of 470 metastatic patients managed at Institut Curie (2000-2008), the median overall survival was 13 months, with a significant difference according to the first treatment in the metastatic setting: 28, 12 and 4 months for liver surgery, any systemic treatment, best supportive care respectively

Conclusion We will review current options and future developments for UM treatment.

• 2881
Difficult counselling issues

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Purpose Families present to the genetic ophthalmic clinic in a wide variety of challenging situations. Unexpected, complex diagnoses have an impact on individuals and their families that require multidisciplinary genetic counselling and support. While there is limited research into the impact or service needs of families with inherited eye disease, we can learn a great deal from the cases presenting in clinic.

Results In this presentation, we describe clinical situations that have presented challenges for the genetic eye team in order to highlight counselling issues and improvements in care. Examples will include the diagnosis of multisystemic disease, approaching sudden and unexpected vision loss in children and the impact and ethical challenges in cascade screening in families.

Conclusion Genetic counselling as part of a multidisciplinary approach for inherited eye disease is required to support families around diagnosis, impact of vision loss and testing in the wider family.

• 2882
Syndromic ophthalmic genetics

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Purpose This presentation will provide an overview of recent scieitific progress in understanding multisystemic genetic ophthalmic disorders with specific examples including early-onset developmental disorders as well as syndromic cataract and retinal disorders.

Methods A review, including case presentations, to illustrate novel insights into pathways underlying common and rare syndromic ophthalmic disorders, the importance of recognising such disorders and the utility (and limitations) in clinical practice of high throughput technologies including next generation sequencing.

Results Syndromic ocular disorders are an important contributor to childhood visual disability. There are many common issues regarding diagnosis and counselling apply to the entire group allowing the development of unified care pathways. An important challenge is to improve diagnosis since management of non-ocular manifestations is likely key. While current diagnostic genetic testing still focuses on single genes, which will be illustrated through discussion of multisystemic retinal phenotypes such as bardet Biedl and Cohen syndromes, future prospects will employ high throughput technologies (e.g. next generation sequencing, microarray analysis) to enable efficient diagnosis of poorly recognised conditions (eg CTX, ocular auricular syndrome, mitochondial cytopathies)

Conclusion The continued and accelerated identification of genes underlying syndromic disorders associated with microphthalmia; corneal and lens developmental abnormalities or retinal dystrophies sheds light on the underlying pathways. Their identification has a direct bearing on clinical management, allowing the improvement and development of individualised care pathways.

• 2883
Mitochondrial optic neuropathies

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Purpose This update will focus on recent and exciting new developments in mitochondrial optic neuropathies after reviewing the background, including clinical and molecular features.

Methods Mitochondrial optic neuropathies are a group of conditions which are currently untreatable and which comprise non-syndromic conditions such as Leber's Hereditary optic neuropathy, dominant optic atrophy, recessive optic atropby, as well as syndromic optic neuropathies. A number of key developments in genetic testing, counselling and potential therapies will be reviewed together with difficult or challenging cases as examples.

Results Understanding the pathophysiology of the mitochondrial optic neuropathies will aid in our quest for new diagnostic, management and therapeutic interventions. The focus of the update will be to highlight some key developments and encourage discussion and participation from the floor.

Conclusion This is a rapidly advancing field with a potential for future therapies emerging on the horizon.

• 2884
Inherited retinal disease

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Purpose To illustrate several inherited retinal dystrophies and dysfunctions and their management in the ophthalmic genetic clinic.

Methods A case presentation format will be used to illustrate different genetically determined retinal dystrophies and dysfunctions. Case descriptions will include clinical and electrophysiological phenotypes as well as genotypes.

Results Phenotypes and genotypes of genetically determined retinal diseases are very different. An important distinction to be made is the one between stationary and progressive diseases, as the visual outcome differs considerably between different conditions.

Conclusion Inherited retinal diseases are very diverse. Taking a thorough history in combination with an extensive clinical examination and psychophysical and electrophysiological tests most often allows a to make a specific diagnosis. It is important to distinguish between progressive and stationary conditions.

• 3211
CSCR/ DRPE : a same disease?

GAUDRIC A
Paris

ABSTRACT NOT PROVIDED

• 3212
Correlation between spectral-domain OCT features and fundus auto-fluorescence patterns in CSCR

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Purpose Central serous chorioretinopathy (CSCR) is characterized by the development of a macular serous retinal detachment with a focal or multifocal areas of leakage at the level of the retinalpigment epithelium (RPE) that can be identified by fluorescein angiography. Aim of the study is to show the changes on optical coherence tomography (OCT) and on fundus autofluorescence (FAF).

Methods Patients affected by CSCR underwent a complete ophthalmological examination including best corrected visual acuity measurement, OCT and FAF with blue-light FAF and near-infrared FAF.

Results Eighty-nine patients affected by CSCR were recruited for the study. OCT reveals many changes, including swelling of thesensory retina, disruption of the RPE, thickening of the outerretinal surface, and loss of the boundary of the photoreceptor inner/outer segments. Blue-light FAF can disclose dot-like deposits located in the sensory retina orsubretinal space. Near-infrared FAF shows the development of some granular changes according to the fluid changes typical of CSCR.

Conclusion The combination of OCT and FAF imaging provides useful insights to characterize CSRC stages.

Commercial interest

• 3213
Role of corticosteroids in CSCR

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Geneva

Purpose Central serous chorioretinopathy (CSCR) is a relatively common retinal disease characterized by the accumulation of subretinal fluid at the posterior pole of the fundus, creating a circumscribed area of serous retinal and/or pigment epithelium detachment.

Methods Numerous reports during the past few years have provided us with arguments strengthening the hypothesis of a possible association between CSCR and glucocorticoids.

Results It has been noted that central serous chorioretinopathy is associated with different conditions, characterized by exposure to increased levels of endogenous or exogenous glucocorticoids. In fact, central serous chorioretinopathy has been described in patients with endogenous Cushing's syndrome. It is also prevalent in patients with type-A personality; it has been reported following stressful events, whereas pregnancy represents another possible risk factor. These conditions are all characterized by endogenous hypercortisolism. In addition, many cases of central serous chorioretinopathy have been described during or following treatment with glucocorticoids, administrated by any route, for various systemic or ocular conditions.Central serous chorioretinopathy, when related to exposure to exogenous glucocorticoids, has a less prominent male predilection, presents more often with a chronic or atypical form, and is frequently bilateral. Furthermore, treatment of CSCR with glucocorticoids was found to exacerbate the clinical picture.However,very few patients worldwide are suffering from CSCR, while under systemic steroid treatment.

Conclusion It could be suggested that glucocorticoids may be involved in the development of central serous chorioretinopathy. Glucocorticoids should not be used in the treatment of central serous chorioretinopathy.

• 3214
Photodynamic therapy in the treatment of CSCR

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Alicante

Purpose To evaluate the efficacy of photodynamic therapy (PDT) to treat chronic central serous chorioretinopathy (CSC) and changes in neural retina (NR) thickness and best corrected visual acuity (BCVA) induced by PDT.

Methods Non randomized, multicentric, interventional case series. 82 eyes of 72 patients with chronic CSC were treated by conventional PDT. LogMAR BCVA and central foveal thickness (CFT) measured by optical coherence tomography (OCT) before and after PDT, number of PDT treatments and complications were considered as outcome indicators. In 26 eyes LogMAR BCVA and OCT were evaluated before treatment and one year after PDT. 24 eyes from 24 patients with non chronic, non PDT treated forms of CSC were evaluated as a control group.

Results BCVA changed from 0.53 before PDT to 0.48 at 6 months (p=0.007). Subretinal fluid disappeared in all the cases. CFT decreased from 325 µm, to 229 µm one month after PDT; to 206 µm at three months; and to 202µm at six months (p<0.0001 in the three cases). No cases developed severe visual loss or complications derived from PDT. In subgroup studied at one year NR CFT before PDT was 181.4±42.6 µ vs. 149.0±30.6 µm one year after treatment (p=0.004). NR CFT in the untreated eyes was 204.6±30.7 µ vs. 192.5±26.4 µ after self resolution (p=0.03). Basal NR thickness was not statistically significant different between both groups (P = 0.31); this difference became significant at the end of the follow-up (P<0.01).

Conclusion PDT may be useful in chronic CSC improving BCVA and reducing subretinal fluid and CFT. The use of PDT in chronic CSC induces NR thickness thinning. This change is not correlated with a decrease in BCVA. Randomized studies with longer follow-up are needed to asses the real role of this treatment in chronic CSC.

• 3215

Other therapeutic options

BEHAR-COHEN F
Paris

ABSTRACT NOT PROVIDED

• 3221
Markers of disease progression in atrophic AMD

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Geographic Atrophy (GA) is a common cause for severe visual loss in age-related macular degeneration (AMD). In contrast to neovascular AMD in which efficient therapy is now available with intravitreally administered inhibitors of VEGF, there is as yet no therapy available for patients with GA. Natural history studies have demonstrated a continuous progression of outer retinal atrophy in patients with GA. Hereby, a high interindividual variability has been documented with regard to enlargement rates of GA ptaches over time. Various markers of disease progression have been identified including phenotypic charatersitcs on fundus photographs such as soft drusen and hyperpigmentary changes. Furthermore, certain abnormal patterns of increased fundus autofluorescence (FAF) on confocal SLO images have been shown to represent risk characteristics for GA evolution and aloow disrimintaion of slow vs. fast progressors. The status of the fellow also has an imapct on progression rates. SD-OCT imaging is currently evaluated in ongoing longitudinal studies with respect to specific microstructural alterations in the junctional zone of GA and their impactz for future progression. Idenfication of progrnostic markers is not o9nly important for a better understandibng of the disease process, but also for the design and conduct of interventional clinical trials in patients with GA as enrichment for fast progressors allows to perform such trials in an acceptable time period in a relatively slowly progressing disease, to reduce costs for clinical developments and to increase the likelyhood for the identification of a therapeutic signal.

• 3222
Gene therapy in rare diseases

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Purpose Stargardt disease is caused by a mutation of the ABCR gene leading to photoreceptor degeneration and vision loss. Genetic replacement StarGen™ uses LentiVector® technology to deliver a corrected version of the ABCR gene. A single administration of the product directly to the retina could provide long-term or potentially permanent correction. The primary objective of StarGen™ study is to assess the safety and tolerability of ascending doses of StarGen™ in adult patients with Stargardt macular degeneration. Up to 28 patients 18 years or older with a differing level of advancement of SMD will be included in this study in which a dose-escalation phase of StarGen™ is followed by a dose confirmation phase. In Retinitis Pigmentosa, preservation or partial restoration of impaired cone function offers very promising perspectives based on neuroprotection, prosthetics or optogenetics. We demonstrated that cone cell function loss might result from the loss of expression of Rod-derived Cone Viability Factor (RdCVF) consecutive to degeneration of rod photoreceptors directly affected by causative mutations. Administration of RdCVF, irrespective of the gene defect, induced in relevant animal models a strong preservation of cone cell function related to the maintenance of rod outer segments (1). Recently, work conducted by Botond Roska and our group showed that in advanced cases, cone cell bodies of dormant cones can be reactivated by vectorization of halorhodopsins (2).Over the past years we have followed a cohort of over 3000 patients and studied the morphology and function of cone photoreceptors, using novel high resolution imaging.. We showed that cone outer segment degeneration during the disease course can be documented and that patients suitable for clinical trials testing neuroprotection or optogenetics can be selected on this basis. A comprehensive personalized set of therapeutic strategies can be tailored on this basis. Such advances, unprecedented in the field of currently untreatable retinal diseases, offer hope for visual rehabilitation. To evaluate and document such functional outcomes, we have developed novel tools for assessing reproducibly visual impairment and restoration, as well as palliative aids and associated training protocols.

Conclusion StarGen™: A Phase I/IIa Dose Escalation Safety Study of Subretinally Injected StarGen™ Administered to Patients With Stargardt Macular DegenerationSponsored by Oxford BioMedica UK Ltd. Principal Investigator Prof. Jose-Alain Sahel Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris France – Professor David Wilson -Casey Eye Institute, Portland Oregon Léveillard T, Sahel JA. Rod-derived cone viability factor for treating blinding diseases: from clinic to redox signaling. Sci Transl Med. 2010 Apr 7;2(26):26ps16.Busskamp V et al. Genetic reactivation of cone photoreceptors restores visual responses in retinitis pigmentosa. Science. 2010 Jul 23;329(5990):413-7.

• 3223
Perspectives for new treatments at Novartis

BURIAN G
Novartis

Clinical research in the current clinical practice and regulatory environment related to development of Medicinal Products has evolved in recent years to encompass areas beyond the primary aim of achieving a Marketing Authorization. A model of "development continuum" appears to recently emerge to address key aspects in this new setting: the area of personalized medicine and specialty care, and associated outcomes research, which together aim to achieve therapeutic optimization at individual patient level, in both endemic as well as in rare diseases. This type of clinical research is conducted in late development phase of drugs, most often post-marketing, under continuous regulatory guidance for drug label optimization. Novartis recognizes and is interested in this changing environment, and is hence committed to address these emerging unmet medical needs that impact clinical practice. Collaboration with the wider group of healthcare professionals in the global community to facilitate the design and implementation of clinically relevant research projects is an important aspect to drive scientific and medical progress in this area.In this presentation, concepts of clinical development and trials design for optimization of drug outcomes and therapeutic patient management will be discussed from an industry perspective. The regulatory and Novartis guidelines for supporting them will be explained, using focussed examples from the field of Ophthalmology, particularly areas of research interest in chorioretinal vascular diseases.

• 3224
Perspectives for new treatments at Alcon - part 2

RICH C
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In an effort to continue to meet unmet medical needs for ophthalmology conditions Alcon continues to have a well developed pipeline of products in the Ophthalmology space. This presentation will give the audience an overview of how we identify a wide variety of potential products to develop and how we condense this list down to the final candidates that will establish our pipeline strategy. This process is conducted across the 3 main franchises of Alcon: Pharmaceuticals, Surgical and Vision Care. This presentation will review products in development in the area of Retina and this is an exciting area for Alcon with several projects in development for the treatment of a number of conditions.Alcon is conducting multiple projects in the area of vitreo-retinal diseases including products for vitreolysis, dry and wet AMD, retinal vein occlusion and diabetic retinopathy. In the area of rare diseases Alcon currently has a program to evaluate the treatment of multifocal choroiditis. During this presentation we will discuss these programs on a high level and also discuss our approach to retina, which we see as a growing area within ophthalmology. The treatment of retinal conditions is still early in its evolution and Alcon looks forward to developing products that treat significant unmet medical needs in the area of Retina.

• 3225
Study Assessing Double-masKed Uveitis tReAtment (SAKURA)

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Purpose The purpose of this study is to evaluate the safety and efficacy of intravitreal injections of DE-109 ophthalmic suspension.

Results Primary Outcome Measures:Proportion of subjects with vitreous haze score [Time Frame: 5 months] [Designated as safety issue: Yes]

Conclusion Study Design:Allocation: RandomizedEndpoint Classification: Safety/Efficacy StudyIntervention Model: Parallel AssignmentMasking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)Primary Purpose: Treatment

• 3226
Stargardt macular dystrophy

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Initiation of a number of upcoming clinical trials for patients with Stargardt disease emphasizes the urge of determining objective outcome measures derived from retinal imaging. Especially novel techniques such as fundus autofluorescence (AF) and quantitative AF imaging as well as spectral domain optical coherence tomography (SD-OCT) now allow assessing the characteristic pathology of Stargardt disease at different disease stages. Fundus AF highlights lipofuscin accumulation in the retinal pigment epithelium (RPE), the phenotypic finding that defines Stargardt disease. Also, fundus AF delineates areas of RPE atrophy with high contrast, allowing to longitudinally monitoring respective changes with high accuracy. SD-OCT, on the other hand, is a clinically meaningful outcome measures since is allows to delineate the photoreceptor layer of the retina. Structural alterations within this layer have been shown to correlate directly with retinal function. Relevant functional parameters include visual acuity and microperimetry. Disease phenotyping (including comparison of various imaging modalities) as well as analysis of longitudinal imaging data, structure-function-correlations and genotype-phenotype correlations will be prudent. In a prospective, multicenter, non-interventional, non-randomized, unmasked, observational study the natural history of patients with Stargardt's disease will be characterized, prognostic markers identified and microstructural alterations and functional variations determined. Allö probands will be ABCA4-genotyped.

• 3227
Sparing of the fovea in geographic atrophy

HOLZ F, SCHMITZ-VALCKENBERG S, FLECKENSTEIN M
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Geographic Atrophy (GA) is a common cause for severe visual loss in age-related macular degeneration (AMD). Typically, atrophic patches initially occur in the parafoveal retina. Over time, several atrophic areas may coalesce, and new atrophic areas may appear. This can temporarily result in a horseshoe configuration of atrophy. In advanced stages, atrophic areas may form a ring encompassing the intact and still functioning fovea. On clinical examination, the fovea may remain untouched by the atrophic process until late in the course of the disease, a phenomenon referred to as 'foveal sparing.' When the fovea finally becomes involved, a dramatic deterioration in visual acuity results. Prognostic factors indicating a pending foveal involvement are yet unknown. So far, spread of geographic atrophy has been quantified with regard to the area enlargement of all atrophic patches in an eye. Further clarification of the natural history of the disease needs to include analyses of the directional spread and identification of prognosdtic markers fopr foveal involvement as well as disease modeling. In a prospective, multi-center, non-interventional, non-randomized, unmasked, observational study the natural history will be characterized, prognostic markers identified and to microstructural alterations determined in eyes with a 'foveal sparing" in GA secondary to AMD by serial simultaneous confocal scanninglaser ophthalmoscopy (cSLO), fundus autofluorescence imaging and spectral domain (SD)-OCT imaging.

• 3231
Autophagy: a new way to retinal neuroprotection

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Purpose Autophagy is a highly conserved catabolic pathway in which proteins and organelles are engulfed by autophagic vacuoles (AVs) that are then targeted to lysosomes for degradation. Basal autophagy serves homeostatic function and it is induced during periods of cell stress. Defects in the autophagic machinery have been described in several neurodegenerative diseases. In this study we investigated the role of autophagy in the retinal neurodegeneration associated to ischemic conditions.

Methods Retinal ischemia was induced in adult rats by acute elevation of intraocular pressure. Expression of autophagy related proteins, beclin-1 and LC3, was studied by western blotting and immunofluorescence. NMDA antagonists, calpain inhibitors or siRNA were intravitreally administered. Effects of autophagy modulation on retinal ganglion cell (RGC) survival was evaluated in serum-starved RGC-5 treated with autophagy inhibitors or transfected with beclin-1 siRNA.

Results Beclin-1 is part of the complex involved in the induction of autophagy, while LC3 plays an essential role in the expansion of AVs. Retinal ischemia produced a reduction of the autophagosome-associated form of LC3 (LC3II) and induced a significant decrease of beclin-1 expression. The latter event was dependent on NMDA receptors and calpain activation as shown by the prevention afforded by MK801, calpain inhibitors or calpain siRNA. Inhibition of autophagy or beclin-1 silencing in RGC-5 significantly reduced cell viability under serum starvation conditions.

Conclusion Our results, while provide the first in vivo evidence of a calpain-mediated cleavage of beclin-I, show that retinal ischemia alters the dynamic of the autophagic process and suggest a neuroprotective role of autophagy in RGCs exposed to detrimental stimuli.

• 3232
Neuroprotective factors against retinal injury in response to hypoxia: new perspectives

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Purpose In the retina, hypoxia is considered one of the key factors to trigger angiogenesis and to promote apoptosis by reducing photoreceptors and other retinal neurons, each of them contributing to vision loss. We recently demonstrated that the beta-adrenergic system interferes with angiogenesis-dependent diseases in the retina by regulating endogenous VEGF. Aim of the present study was to investigate the role of distinct beta-adrenergic receptors (BARs)in neurodegenerative processes in response to hypoxia.

Methods Ex vivo mouse retinal explants and in vivo models were used. BARs were blocked with antagonists or silenced with siRNAs. VEGFR2 was blocked with SU1498, whereas iNOs and eNOS with AG, L-NIO or L-NAME. mRNA levels were evaluated with quantitative RT-PCR. BARs, iNOS, eNOS and apoptotic signals were determined with Western blot. Immunohistochemistry was used to localize BARs and to assess neovascularization. VEGF release and NO production were measured with colorimetric assays. Hoechst and TUNEL were used to evaluate cell loss.

Results Among the BARs, BAR3 is localized to blood vessels, is upregulated by hypoxia and acts through iNOS/NO to control VEGF levels and degenerative responses to the hypoxic insult. In particular, BAR3 blockade is accompanied by increased levels of apoptotic signals and cell loss. Pharmacological interaction with the VEGF signalling demonstrates that BAR3 exerts a protective action on retinal cells through a modulation of endogenous VEGF.

Conclusion Our findings demonstrate that modulation of BAR3 activity during ischemia may be a powerful means to achieve neuroprotection. VEGF's role in retinal cell survival has important implications for treatments with VEGF blockade within the context of ocular vascular diseases.

• 3233
Retinal neuronal death caused by ocular hypertension

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Purpose To characterize the anatomical and functional changes that follow ocular hypertension (OHT).

Methods In adult albino rats or mice, the episcleral and perilimbar veins were photocauterized with laser diode. This resulted in OHT that reaches basal levels by one week in mice and by three weeks in rats.

Results OHT induces anatomical and functional degenerative retinal changes. One week after lasering there is impairment of the retrograde axonal transport which is first functional and then mechanic. By two weeks there is loss of approximately 80% of the RGC population without further progression. RGCs loss occurs mainly in pie-shaped sectors but is also diffuse throughout the retina. The intraretinal RGC axons and somas show signs compatible with a slow retrograde axonal degeneration resembling an optic nerve crush. OHT induces loss of RGCs but not of other non RGC neurons present in the ganglion cell layer, namely the displaced amacrine cells, for periods of up to six months after OHT. There is a protracted and progressive affectation of the outer retina which results in a major loss of LM- and S-cones. This anatomical data are supported by functional analyses. Electroretinogram recordings show maintained and significant diminutions of the scotopic threshold responses as well as of the a- and b-waves indicating permanent alterations of the inner and outer retinal layers, respectively.

Conclusion OHT results both in RGC axonal crush-like injury and in an ischemic damage to the outer retinal layers. Thus, this model may be used to study axotomy- or ischemia-induced neuronal death in the innermost retina or in the outer retina, respectively.

• 3234
RIP Kinases, necroptosis and redundancy in neuronal cell death

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Purpose Neuronal cell death is the major cause of vision loss in many eye diseases. The exact mechanism remains unknown. Apoptosis has been thought to be the major form of regulated cell death and the main modality of neuronal cell death in degenerative ailments. However, neuroprotective strategies based on apoptosis have failed to materialize. We wanted to investigate the presence of alternative cell death modalities in various models of degenerative eye diseases.

Methods Neuronal cell death was studied in a variety of animal models, including retinal detachment, RD10 juvenile degeneration, Cx3Cr1/CCL2/rd8 triple mutant, optic nerve crush, and chemical toxicity models (NMDA, PolyI:C, Na-Iodate, Lipid peroxide, and chloroquine). Analysis of cell death was performed by transmission electron microscopy (TEM), TUNEL staining and standard molecular techniques.

Results Caspase dependent apoptosis was the major cell death modality in most models of cell degeneration. However, RIP regulated necrosis accounted for a significant portion of cell death morphology. Under conditions of selective caspase inhibition, RIP regulated necrosis became the predominant cell death modality. Simultaneous caspase and RIPK inhibition lead to significant neuroprotection. Autophagy accounted for small portion of cell death in the models that it was examined.

Conclusion RIP Kinase regulated necrosis (necroptosis) is a significant redundant cell death pathway in many animal models of ocular degenerative diseases. It becomes the predominant form of cell death under conditions of caspase inhibition. Combination treatments may be needed for successful neuroprotection.

Commercial interest

• 3235

Neuroprotection and autoimmunity in glaucoma

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In glaucoma, the elevated intraocular pressure cannot explain the disease in all patients. However, the pathogenesis of the disease is widely unknown. Biomarker research could be help to understand the disease process. Beside some genetic and proteomic biomarkers, immunoproteomics could play a significant role. Several studies could provide hints for an involvement of autoantibodies in the pathogenesis of the disease. The complex profiles of natural occurring autoantibodies were analyzed by Western Blotting and mass spectrometry based techniques combined with multivariate statistics and artificial neural networks. In several studies we could demonstrate consistent up- and down-regulations of immune reactivities against ocular antigens in glaucoma patients. These findings could lead to a better understanding of the pathomechanisms involved in glaucoma, but could also lead to new innovative ways of early detection and neuroprotective treatment options of the disease.

• 3241
Molecular pathology of inflammation in age-related macular degeneration

CHAN C
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Purpose To review molecular pathology of inflammation in age-related macular degeneration

Methods Personal and collaborative research in addition to literature review

Results Risk for AMD is multifactorial, relating to age, environmental and genetic factors. Genome-wide and targeted genetic association studies have identified various polymorphisms important for AMD susceptibility. Many are within immune-related genes, including complement factors, e.g. CFH, C2, C3, CFB, and CFI; Toll-like receptors, e.g., TLR-3 and TLR-4; and chemokines and receptors, e.g., CX3CR1 and CCR3. In addition, copy number variation/polymorphism, miRNA and epigenetics related to immune relevant genes could also contribute to AMD pathogenesis and patient responses to specific therapies. Inflammatory cells (mainly macrophages and microglia) and inflammatory factors (complement factors, cytokines/chemokines, oxidative stress-related inflammatory products) are demonstrated in AMD lesions at various stages.

Conclusion The molecular characterization of AMD captures the localizations and interactions among the inflammatory elements, relevant molecules (e.g., oxidative stress products and lipoprotein), and retinal/choroidal cells, in particular, the photoreceptors and RPE.

• 3242
Parainflammation and the ageing retina

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Purpose To review para-inflammatory responses in the ageing retina, and the role of dysregulated para-inflammation in age-related retinal degeneration.

Methods Published and unpublished data from personal study in in vivo models and literature review.

Results Para-inflammation is an immune response to chronic noxious stimuli at a low magnitude that lies between the basal homeostatic state and overt inflammation. The physiological role is to maintain tissue homeostasis and functionality. The retina, particularly the macula, is constantly subjected to a low-level of insult mediated by oxidized molecules such as unsaturated fatty acid, and the insult accumulates with age. Retinal homeostasis in the ageing eye is maintained by a para-inflammatory response executed by resident microglia, retinal pigment epithelial (RPE) cells and the complement system. A dysregulated para-inflammation may not be able to maintain retinal homeostasis, and age-related retinal degeneration may occur. The presentation will discuss how microglial activation is controlled in the retina, and the potential contribution of uncontrolled microglial activation to age-related retinal degeneration.

Conclusion Para-inflammation is important to retinal homeostasis in the ageing eye. Uncontrolled or dysregulated para-inflammation may contribute to the pathogenesis of age-related retinal degeneration.

• 3243
Imaging and the ageing retina

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Until recently, assessment of ageing in the living human retina has principally depended on fundus photography and related techniques (e.g., fluorescein/indocyanine green angiography and fundus autofluorescence). Since the 1990s, however, the discovery of a wholly new imaging modality - optical coherence tomography (OCT) - has revolutionised the diagnosis and management of retinal diseases by providing high resolution cross-sectional images of the retina in a non-invasive manner. In this presentation, I will review existing methods in use for imaging of the ageing human retina, with a particular focus on the latest advances in OCT imaging. I will also describe the attempts that are underway to address the shortcomings of current retinal imaging modalities; for example, the use of adaptive optics to provide cellular level image resolution, the use of Doppler and spectral imaging techniques for the assessment of retinal blood flow and oxygenation, and a number of new technologies with the potential for assessment of novel functional parameters, such as photoacoustic and magnetic resonance imaging.

• 3244
Macrophages and the ageing and diseased retina

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Purpose Recruitment and activation of microglia and macrophages are controlled by local cytokine and chemokine signals that also determine neurotoxic or protective responses of these cells. I will review our current understanding of how the behaviour of macrophages and microglia in the retina is controlled by Ccl2-Ccr2 and Cx3cl1-Cx3cr1 chemokine signalling during ageing, in retinal degenerations and choroidal neovascularisation (CNV).

Methods We investigated recruitment and activation of myeloid cells in wildtype and chemokine single-(Ccl2, Cx3cr1) and double-knockout (Ccl2/Cx3cr1) mice in vivo (by AF-SLO, OCT, fluorescein angiography) and ex vivo (by FACS, immunohistochemistry, morphometric semithin histology and 3D serial block-face scanning electron microscopy). We studied these mice during ageing, in combination with a monogenetic inherited retinal degeneration (RD8) and in the laser-induced CNV model.

Results Ageing is associated with alterations in myeloid cell populations in the retina and the choroid that are specifically altered by chemokine signalling dysfunctions. Ccl2 deficiency leads to an age-related accumulation of subretinal macrophages and an attenuated CNV response with reduced infiltration of neutrophils, but no significant effect on degenerative processes in inherited (RD8) or age-related retinal degenerations. In contrast, and despite an apparently similar accumulation of subretinal macrophages, Cx3cr1 deficiency leads to a more pronounced degenerative phenotype caused by the RD8 mutation, which was similar in Ccl2/Cx3cr1 knockout mice.

Conclusion Myeloid cell behaviour, controlled by Ccl2-Ccr2 and Cx3cl1-Cx3cr1 chemokine signalling, differentially modulate the manifestation of inherited and age-related retinal degenerations and contribute to the increase of CNV lesions with age.

• 3251

Why should we care about rate of progression in glaucoma management?

STALMANS I
University Hospitals Leuven, Leuven

During this short introduction, the meaning and importance of measuring the rate of progression in glaucoma care will be explained and illustrated with a patient example.

• 3252

Detecting progression using visual fields

ROSSETTI L
Milano

ABSTRACT NOT PROVIDED

• 3253

Detecting progression using structural measurements

BRON A
Dijon

The management of glaucoma is driven by the changes of functional and structural endpoints overtime. Is the disease stable or not? In this presentation we will cover the practical aspect of structural progression assessment which follows the same rules that apply to functional tests; good baseline material and sufficient further examinations whatever the technique. We will detail the methods used to assess structural progression which are similar to those used for evaluating functional progression.Although challenging, the evaluation of structural progression is very helpful in the follow-up of the glaucomas. However it must be combined with functional progression to achieve clinical relevance.

• 3254

Linking it together: structure-function correlation

SUNARIC MEGEVAND G
Rothschild Foundation, Geneva

In this part of the course we will discuss the implication of the combination of the structural and functional measurement. In glaucoma structural and functional measurements provide largely independent information, and most studies indicate that their agreement is generally poor. There is some evidence in the literature that structural damage may precede a correlative functional deterioration. However as concordance of measures is limited, combining longitudinal information from structural and functional tests can improve detection and assessment of glaucoma progression. New technological tools and statistical modeling approach combining structure and function may improve detection of progression today.

• 3255

Into practice: clinical examples

STALMANS I
University Hospitals Leuven, Leuven

Clinical examples on the use of visual field and structural measurements in the management of glaucoma patients will be presented, and discussed with the audience.

• 3261
GCA diagnosis controversies

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Purpose To report on different clinical presentations of giant cell arteritis (GCA, temporal arteritis) and diagnostic and therapeutic approach. GCA is the most common primary vasculitis of adulthood. Ocular symptoms present in 30-75% of patients and include visual loss, amaurosis fugax, ophthalmoplegia, diplopia and ocular pain. Approximately 15-50 % of patients suffer from permanent visual loss. Temporal artery biopsy and corticosteroid treatment is essential for diagnosis and preservation of vision.

Methods Review and retrospective study of 50 eyes (36 patients) with giant cell arteritis treated at Eye Hospital Ljubljana. There were 67% female and 33% male patients with average age of 79 years, range 62-92 years, with typical clinical picture and/or positive biopsy (78%, 18/23 performed).

Results Loss of vision was unilateral (65%) or bilateral (35%). The most common ischaemic lesions were anterior ischaemic optic neuropathy (AION; 16 unilateral, 4 bilateral) and posterior ischaemic optic neuropathy (PION; 5 unilateral, 5 bilateral). Other lesions included central retinal artery occlusion and internuclear ophthalmoplegia. More than half of patients (53%) had visual acuity of counting fingers or less in affected eye. In AION various peripheral defects almost universally showed respect for horizontal meridian. Nasal and inferior halves of visual fields were most often affected. PION most often presented with scotomas with or without peripheral defect.

Conclusion Severe loss of vision is present in affected eye in most patients. Bilateral loss of vision can occur if the diagnosis is not established early and corticosteroids given. Very few affected eyes recover to small extent. It is essential to recognise this disease even in absence of typical signs and symptoms. In elderly, all the patients to report amaurosis fugax, sudden loss of vision or diplopia should be suspected to have temporal arteritis.

• 3262
Strabismus surgery: minimally invasive or not?

MOJON D
Airport Medical Center Eye Clinic, Zurich

Purpose To present the advantages and disadvantages of minimally invasive strabismus surgery (miSS).

Methods Review of available literature and experience from surgeons starting with MISS.

Results MISS has the following advantages: less visibility of surgery, decrease of postoperative discomfort and pain, hospital stay and working disability, and preservation of limbal stem cells. Disadvantages of MISS are: long learning curve, need of microscope, difficulties visualizing anatomical variations, and increased risk of globe penetration.

Conclusion For skilled surgeons with already experience in microscope assisted strabismus surgery transition to MISS will be easier.

• 3263
Atropine use in childhood myopia treatment

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Purpose To discuss the role of atropine use in childhood myopia treatment.

Methods The analysis of the literature and studies of the subject.

Results The prevelance of myopia the population in the United States, Europe and Australia is about 30-40%, whreaes in some southern Asian countries is up to 80-90%. Moreover, it was shown that this prevalence has been increasing in the recent 20 years. Although the pathogenesis of myopia is unknown, it is argued that, at least in the case of school myopia, environmental factors are of major imprtance, whrease genetic factors play secondary role. The role of atropine in the lowering the rate of myopia progression was analysed in recent 10 years in many studies, differing with the atropine concentration, studied group characteristics, the time of treatment and the the time of observation, etc. The lowering effect of atropine was proved, however, its effectiveness decreased with the time of drug use, and after the drug discontuinuation the effect was partially reversed. On the other hand, it is well-known that atropine use is related to significant side-effects, including mydriasis, cycloplegia, increased exposure to UV light. Moreover, some argue that results of the therapy, i.e. lowering of the magnitude of school myopia, cannot be be balanced by the problems and unknown longterm effects related to the therapy.

Conclusion The atropine use in childhood myopia treatment remains controversial and possible benefits and weaknesses of the therapy should be carefully analysed.

• 3264
Is the eye a window to the mind? RNFL thickness measurements by OCT as a biomarker for neurodegenerative diseases

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Purpose Optical coherence tomography (OCT), a noninvasive imaging technique that assesses the retinal nerve fiber layer (RNFL) thickness, macular thickness and volume, is widely used in various ophthalmologic disorders including glaucoma and macular diseases. A decreased RNFL thickness can correspond to neuronal death and axonal loss. Therefore, OCT measurements might be of particular interest in numerous neurodegenerative diseases with axonal loss.

Methods A significant reduction in the peripapillary RNFL thickness has been reported in patients with various neurologic diseases, such as multiple sclerosis, neuromyelitis optica, Alzheimer´s disease, and Parkinson´s disease, suggesting that OCT might also prove useful in other neurodegenerative disorders. Thus, we have studied for the first time these neurodegenerative changes in patients with schizophrenia and obstructive sleep apnea syndrome (OSAS). The goals of these studies were to determine by OCT the differences in the peripapillary RNFL thickness, macular thickness and volume, between controls and patients with several neurodegenerative disorders in which there is axonal loss, and to assess whether a correlation exists between the RNFL thickness and the clinical severity of the disease.

Results Most neurodegenerative disorders show a significant thinning of the peripapillary RNFL; however, the patterns of change differ in some aspects. The findings indicate loss of retinal ganglion cells and may reflect degenerative brain changes in these conditions. This topic reviews the application of OCT imaging of the retina in Neurology and Psychiatry.

Conclusion RNFL thickness may be used as a biological marker and might help to the early diagnosis of several neurodegenerative conditions.

• 3265

Controversies related to mfVEP use

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Purpose To address the usefulness of mfVEP use in clinical research on neurophthalmology, with a focus on optic neuropathies (Leber and Kjer Optic Neuropathies) as well as acquired cortical scotomas.

Methods We have tested a sample of 17 asymptomatic Leber's hereditary optic neuropathy (LHON) who were mtDNA 11778G>A mutation carriers from two generations of the same pedigree (mean age ± SD = 27.94 ± 12.97 years; mean visual acuity ± SD= 1.25 ± 0.11). We included an age-matched control group (n=18; mean age ± SD = 33.29 ± 14.22 years; mean visual acuity ± SD= 1.09 ± 0.14).We have also studied 22 subjects (44 eyes) from 13 families with Autosomal Dominant Optic Atrophy (ADOA) submitted to OPA1 mutation analysis. Quantitative psychophysical methods were used to assess konio and parvocellular chromatic pathways. Electrophysiological assessment included the Multifocal Electroretinogram (mfERG) and Pattern Electroretinogram (PERG), respectively. Global Pattern and Multifocal VEP (visual evoked potentials) were used to assess retinocortical processing. Finally we performed multimodal studies (mfVEP and structural and functional MRI) to study visual loss in a patient with a cortical scotoma.

Results We found evidence for functional impairment in color vision pathways in LOHN carriers, with relative preserved VEP and mfVEP responses. In ADOA mfVEP showed distinct evidence for cortical impairment that is only moderately explained by the retinal phenotype, suggesting additional damage mechanisms at the cortical level. fMRI based visual field cortical mapping revealed changes in retinotopic organization that were more difficult to identify using mfVEP.

Conclusion mfVEP is an interesting tool in clinical research , but its application in the clinical diagnosis setting is still difficult.

• 3271
Visual, ocular and refractive development in children

SCHAEFFEL F
Ophthalmic Research Institute, Tübingen

Purpose To describe visual, ocular and refractive development in children, possible reasons for deviations and some of the underlying mechanisms.

Methods Literature review and own data.

Results Contrast sensitivity and visual acuity develop slowly, reaching adult-like performance around 5 years of age. Refractive development is very different if measured with and without cycloplegia but typically emmetropization was successful at 5 years of age, before the risk of myopia comes in. These developments require continuous visual feedback. If the retinal image is not focused or clouded by cataract, irreversible amblyopia develops. Eye growth represents by no means a linear scaling of the initial ocular dimensions. The decline in optical power of the cornea levels off already in the second year of life but axial eye growth continues at least until puberty. There is a built-in risk factor for myopia because the crystalline lens has limited capacity to compensate for further axial elongation. These observations do not explain the environmental input to myopia development. In animal models, further axial eye growth is triggered by negative defocus, loss of image contrast, or abnormal light cycles or intensities. The retina is the major controller of axial eye growth. It uses image focus to control the growth of the underlying sclera bi-directionally, depending on sign of defocus. Growth inhibition, induced by positive lenses, involves a biochemically different mechanism which is very responsive - but can apparently still not save the human eye from myopic.

Conclusion A lot can go wrong during postnatal ocular development since appropriate visual input is obligatory for normal development. Natural eye growth patterns include a built-in risk factor for myopia development in early adolescence.

• 3272
Myopia - Its etiology and prevalence

SANKARIDURG P
Brien Holden Vision Institute, Sydney

Purpose Myopia (short- sightedness) is a significant health problem that is fast rising in prevalence in many parts of world including Europe and USA and at a much higher percentage for population in parts of Asia. Also high myopia is associated with the risk of developing other sight threatening eye conditions.

Methods An analysis of the published prevalence rates for myopia with the risks and morbidity associated with high levels of myopia. Also factors that are considered to play a role in the development and progression of the condition will be discussed with emphasis on published data for the role of these factors.

Results Whilst the role of individual factors is yet to be elucidated both environmental and genetic factors have been considered to play a role. An increased prevalence of myopia in urban versus rural populations, association with outdoor/indoor work, supports and provides evidence for the role of environment. In this regard, many of the previous efforts have focussed on accommodative effort and blur at the central retina during near visual tasks. More recent evidence suggests that the peripheral retina also plays a role in emmetropisation and development of refractive errors.

Conclusion This presentation will discuss the rates and differences in the prevalence of myopia across various populations. In addition, current hypotheses considering the aetiology of development and progression of myopia will be discussed.

Commercial interest

• 3273
The influence of peripheral refractive errors on myopia development

OHLENDORF A
Carl Zeiss Vision, Aalen

Purpose This talk will present research about the role of peripheral refraction on the development of central refractive errors in human eyes as well as in various animal models of myopia.

Methods The interconnection of peripheral refractive profiles and central refractive error will be described. Studies investigating the role of the peripheral refractive error on central refractive development will be presented.

Results Myopes typically show relative hyperopia in the periphery of the eye, while emmetropes and hyperopes show a relative peripheral emmetropia or myopia. Studies in humans as well as in various animal models of myopia indicate that the management of the peripheral refraction can change the development of central myopia. More recently, Smith et al. confirmed the influence of peripheral refraction on myopia development in monkeys, by influencing peripheral refraction with either form-deprivation (2005) or minus lenses (2009).

Conclusion Research in animal models of myopia and in humans found strong evidence that the peripheral refraction of the human eye can guide the development of central refractive errors. More studies are needed investigating the efficiency of "peripheral refraction management" with various kinds of correction methods (e.g. Contact lenses, Ortho-K, spectacle lenses). Additionally, there is a need for long term studies on central refractive development based on peripheral refraction in the human eye.

Commercial interest

• 3274
Correction of peripheral refractive errors and its impact on visual performance

ATCHISON DA
institute of Health and Biomedical Innovation, Kelvin Grove

Purpose There has been considerable recent interest in modifying peripheral refraction for the purpose of treating myopia. Correcting peripheral refraction can affect peripheral visual performance. The purpose of this study was to consider the extent of such improvement and the feasibility of making spectacle lenses for this purpose.

Methods Peripheral refraction was used as a basis for designing lenses to correct refraction out to 30 degrees along the horizontal meridian. Visual performance tests were conducted at 20 degrees nasal, 30 degrees nasal and 25 degrees temporal visual field. Tests were detection acuity for high contrast sinusoidal gratings and contrast thresholds for 1 min arc diameter spots.

Results Correcting peripheral vision has limited influence on visual acuity as this and other resolution-like tasks are limited more by retinal sampling than by image quality. However, Lewis et al (ARVO abstract 2012) found that correcting vision at 20 degrees nasal visual field could improve low contrast resolution acuity by an average of 0.06 log unit and up to 0.16 log unit for people with large off-axis astigmatism. Detection tasks, such as deciding in which of two presentations a grating appears without necessarily being resolvable, give up to 0.7 log unit (5 times) better acuity than resolution tasks at 20 deg N, but are sensitive to defocus such that performance reduces close to those of resolution tasks with about 2 D defocus (Wang et al, IOVS 1997). Results like the above indicate the potential value of peripheral correction for people with macular lesions. Our own results with specially designed lenses will be presented.

Conclusion The lenses were partially successful in improving peripheral vision. Difficulties included variability in peripheral refraction measurements and lack of sensitivity of some subjects to peripheral correction. Whether or not correcting peripheral refractive errors will influence myopia progression is not yet known.

• 3275

(New) Approaches to reduce progression of myopia with spectacles from Carl Zeiss Vision

KRATZER T
Carl Zeiss Vision, Aalen

Purpose This talk will present a dedicated spectacle lens design that has indicated to reduce the progression of myopia in a group of Asian children in a randomized and double blind clinical study.

Methods In contrast to conventional spectacles lenses for myopes, the ZEISS MyoVision lens uses a special peripheral treatment zone to bring the peripheral focus back or in front of the retina while providing a clear and undisturbed asymmetric central vision. A clinical trial has been conducted to evaluate the performance of this new lens design.

Results The combination of a peripheral treatment zone and a clear central viewing zone in a single vision lens show positive results by indicating a reduction of the progression of myopia by 30% on average in Asian children age 6-12years old with a history of parental myopia while providing stable and clear vision without adaption problems of the wearer.

Conclusion This lens has been successfully trialed in a randomized and double blind clinical study on Chinese school children. Modern spectacle lens designs with special treatment zones can lead to a reduction of the progression of myopia.

Commercial interest

• 3281

A comparison of HLA genotype with inflammation in uveal melanoma

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Purpose HLA (Human Leukocyte Antigen) polymorphisms have been associated with the development of autoimmune diseases. In uveal melanoma, a high expression of HLA class I and II and infiltration with lymphocytes and macrophages are associated with a bad prognosis, and Natural Killer cells are thought to play a role in the killing of metastasizing cells. The goal of this study is to determine whether specific HLA alleles are associated with increased inflammation.

Methods Records were analyzed of 45 patients who underwent enucleation for uveal melanoma. HLA typing, tumor HLA expression and tumor macrophage infiltration were determined in each case.

Results Before correction for multiple testing, macrophage infiltration was less in HLA-A2 positive patients. Patients with HLA-DR6 had a higher tumor cell expression of HLA-DR. After correction for the number of analyses, no associations remained statistically significant.

Conclusion The results before correction suggest that the HLA genotype may influence inflammation as indicated by HLA expression and macrophage infiltration in uveal melanoma. Comparing HLA expression with the genetic presence of specific HLA alleles is a new approach to obtain insight into the role of the immune system in uveal melanoma.

• 3282

Proteomic analysis of uveal melanoma

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Purpose To further the molecular biological understanding of the events governing the development of metastatic disease and to identify potential targets for therapy.

Methods 8 metastatic vs 8 non-metastatic fresh uveal melanoma tissue with a minimum follow-up of 10 years were subjected to quantitative, label-free proteomic analysis. Strict criteria was applied in the Progenesis LC-MS software to filter out statistically non-significant peptides and proteins. These were anova $p < 0.05$, power > 0.8 and protein confidence score > 100. Differential expression of proteins and their relative abundance in the 2 disease groups were determined using the same software.

Results 653 proteins were identified (global proteome of all 16 samples). Of these, 61 proteins met the statistics criteria applied. 9 of those had good separation between metastatic and non-metastatic disease groups. 4 proteins were selected for further follow-up and validation. Currently, immunohistochemistry studies are being performed to confirm expression levels in paraffin embedded tissue slides. Then, siRNA knockdown and immunoprecipitation experiments will be performed in uveal melanoma cell lines (primary and metastatic) to determine downstream effects and potential targets for therapy.

Conclusion Proteomic analysis of 8 metastatic vs 8 non-metastatic fresh uveal melanoma tissue has identified 4 proteins which are currently being validated using immunohistochemistry, siRNA knockdown and immunoprecipitation experiments.

• 3283

Pre-clinical analysis of Crizotinib in uveal melanoma

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Purpose Uveal melanoma (UM) is an intraocular neoplasm with an annual incidence of 7 per million. UM originates from melanocytes just like cutaneous melanoma (CM) and similar to CM, the MAPK pathway is involved in the development of UM. However, not all UM seem to depend on the activation of this pathway. Loss of ERK signalling may be correlated with progression as the ERK negative cells are derived from UM metastasis. Here, tumours apparently use different mechanisms to proliferate and survive. In this study, we aimed to determine the pathway that is up-regulated in UM metastases and to inhibit its function with targeted kinase inhibitors.

Methods We used pathway profiling to identify the pathways that are important in metastases. Furthermore, the c-Met inhibitor (Crizotinib) was used to inhibit the c-Met receptor and to identify downstream targets. Colony formation assays and 3D sphere assays were used to characterize UM cells in a three dimensional environment.

Results Reduced c-Met activation rather than reduced expression was induced with Crizotinib treatment. Subsequently, c-Met inhibition was correlated with reduced colony formation. c-Met positive UM cells captured in 3D spheres revealed a reduced capacity to migrate upon Crizotinib treatment compared to cells that lack activated c-Met.

Conclusion c-Met activation was observed in metastasizing UM where it serves as biomarker for Crizotinib treatment. Efficacy of treatment was shown by inhibition of growth and migration. Combined our data reveals c-Met signalling in progression of UM and support the use of Crizotinib for UM metastasis.

• 3284

Temperature-dependent vascular endothelial growth factor (VEGF) induction in human retinal pigment epithelium – implications for transpupillary thermotherapy in uveal melanoma

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Purpose Transpupillary thermotherapy is a hyperthermia treatment for small uveal melanomas but its use is controversially discussed. In uveal melanomas, vascular endothelial growth factor (VEGF) increase is correlated with metastases, and VEGF increase can be found in treated melanomas. In this study, the effect of hyperthermia on the VEGF secretion in human RPE cells was studied.

Methods Immortal human retinal pigment epithelium (RPE) cell line Arpe-19 was exposed to 40°, 42°, 45° and 50°C for 1 min, 5 min and 15 min. Toxicity was evaluated using trypan blue exclusion assay and VEGF secretion was evaluated by ELISA. Involvement of Mitogen activated protein kinase (MAPK) pathways and Transient Receptor Potential Vanilloid (TRPV) channels on VEGF induction was investigated using commercially available inhibitors.

Results Hyperthermia induces cell death in a time and temperature dependent manner. VEGF expression and secretion is strongly induced by hyperthermia in a time and temperature dependent manner. VEGF induction is mediated by p38 and to a lesser degree by JNK. TRPV channels are only involved in VEGF secretion at lower temperatures.

Conclusion Hyperthermia induces a temperature dependent secretion of VEGF in human RPE, which is mediated by p38. As VEGF may be involved in the development of micrometastases, these findings indicate that thermotherapy for the treatment of uveal melanomas should be regarded with caution.

• 3285

Primary transpupillary thermotherapy for small suspicious choroidal nevi

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Purpose The purpose of this study was to assess the ocular and systemic outcomes of patients treated by transpupillary thermotherapy (TTT) for suspicious choroidal nevi at our oncology centre.

Methods A retrospective chart review was conducted for all patients with a newly diagnosed small suspicious choroidal nevus treated by TTT at our oncology centre from the date of acquisition of the laser (2002) to September 2011. Standard treatment consisted of three TTT sessions. Patients with two or more risk factors for tumour growth were systematically treated. Ocular and systemic outcomes were reviewed and compared with those of similar patients that were observed between 1990 and 2008.

Results Our preliminary data include 8 patients treated by TTT and 56 patients that were followed-up without treatment. Of the treated patients, 3 (37.5%) showed progression with a mean time to recurrence of 13 months. Of the observed patients, 23 (41%) showed progression with a mean time to recurrence of 41 months. There were no reported deaths in the treated group, and 3 (5.4%) deaths due to metastatic melanoma in the observation group.

Conclusion Despite careful patient selection, primary TTT for small suspicious choroidal nevi showed poor local tumour control. No deaths due to metastatic melanoma were reported in the follow-up of treated patients, and mortality remained low in the observation group.

• 3286

Ultrasound features changing during uveal melanoma local treatment

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Purpose The aim of our study was to estimate the echographic sighs (acouctic densitometry characteristics and hemodynamic changes in tumoral vascular network) of uveal melanoma during the local irradiation.

Methods 58 patients (31-74 years old) with uveal melanoma underwent the investigation. Acoustic densitometry and hemodynamic characteristics in tumoral vessels were estimated both before and during brachytherapy using high-resolution duplex scanning (using ultrasound system Voluson® 730Pro, GE Medical Systems, Kretz Ultrasound).

Results There were estimated some alterations in echographic sighs which included the increasing of blood flow velocity in tumoral vessels and decreasing the acoustic densitometry characteristics during the local treatment in comparison with those before the treatment. The dimension and the degree of intensity those alterations depended on tumor size, it's localization in the eye, facility of the irradiation, angioarchitecture of the lesion.

Conclusion The estimation of echographic alterations in uveal melanoma during the local treatment allows indirectly to judge about tumor radiosensivity and probably to assume the local treatment efficiency.

• 3411

Prevention of endophthalmitis in cataract surgery

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Purpose To review data from the Swedish prospective endophthalmitis (E) registry which is linked to the National Cataract Register.

Methods 14 years of reporting was reviewed.The registry contains data on demographics, type of surgery,the prophylactic protocol and surgical complications

Results Thanks to the introduction of intracameral cefuroxime, the rate of E. in Sweden has not exceeded 0.05% which is considerably lower than other nation-wide reports. In the most recent 3-year period, the rate has approached 0.02% which has been parallel to a decline in capsule breaks and procedures in patients aged > 85 years, two independent risk factors for E. Moreover, an intracameral antibiotic, mainly cefuroxime, is practically always employed nowadays and alternative agents to cefuroxime are presently tried.

Conclusion Analysing the effect of prophylactic disinfecting protocols in large-scale clinical observational studies is necessary to reach a well supported strategy aimed at preventing E.In addition, identifying risk factors for E and avoiding them is a supplementary means to reduce the rate of this dreaded complication.

• 3412

Is there a rational for the use of topical antibiotics before and after intravitreal injections

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Among the possible complications of intravitreal injections (IVI), postoperative endophthalmitis is the most severe. On the first series, the incidence was between 0.7 and 1.6%. Through improved practices, it was quickly reduced to around 0.09% to 0.03%, according to two recent retrospective series. The guidelines for IVI generally recommend performing the surgery under conditions close to those of the anterior segment surgeries, i.e. in compliance with aseptic conditions. The instillation of antibiotic eye drops was initially recommended, three days before and three days after IVT. Several publications have evolved strategies. Recent studies showed low rates of endophthalmitis despite the lack of preoperative antibiotics and a retrospective study found no significant difference whether or not topical antibiotic therapy was used pre-and postoperatively. One study showed that instillation of antibiotics before surgery does not contribute to the sterility of the conjunctiva immediately before injection, from the moment the surgical site has been prepared with povidone iodine. It therefore appears that antibiotic treatment in IVIs is essentially aimed at reducing the contamination of the conjunctiva from the immediate post-op period to the time the site of injection is considered healed. In this respect, the ideal antibiotic should combine several of the following properties: rapid efficiency on bacteria potentially responsible for endophthalmitis, broad spectrum, no lasting change in the conjunctival flora, no selection of resistance to this antibiotic or other antibiotics by crossover mechanism, reusability without additives adverse reactions with repeated cures.

• 3413

Microbiological diagnosis of bacterial endophthalmitis

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Purpose The systematic microbiological documentation of endophthalmitis allows the confirmation of the infectious nature of the disease and the possible adaptation of treatment at the individual level and, at the collective level, the epidemiological characterization of the bacterial spectrum of endophthalmitis.

Methods different microbiological techniques will be presented: conventional techniques (media), eubacterial PCR, real time PCR

Results It is preferable to inoculate intraocular samples into culture media (a paediatric blood culture bottle or in Brain Heart Infusion (BHI) broth) under sterile conditions in the operating room and to transfer the sample intended for PCR into a sterile tube without residual DNA (DNA-free) and with a screw cap. Bacterial identifications and antibiograms are then obtained using phenotypic methods. Real time PCR is more sensitive than culture, allows the detection and identification of specific micro-organisms, DNA quantification, and has a faster turn around time (no post-PCR step). The PCR amplification of 16S rDNA uses consensus primers (panbacterial PCR) and is followed by identification from analysis of 16S rDNA sequence. This technique has the advantages of amplification of DNA from all bacteria, and identification of bacteria difficult to identify phenotypically (e.g. coagulase-negative Staphylococcus species). However drawbacks are the possible contaminations, the duration (2-3 days including sequencing), and the impossibility of differentiating mixed bacterial species in the same clinical sample.

Conclusion PCR techniques are complementary tools to culture. New techniques of PCR are needed in order to be faster and more sensitive. Genomic characterization of strain virulence of bacteria involved in endophthalmitis will be further studied.

• 3414

Management of postoperative endophthalmitis

BRON A
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Postoperative endophthalmitis remains a devastating condition both for the patient and the surgeon. Even with careful prophylaxis such an ocular infection may occur.The EVS (Endophthalmitis Vitrectomy Study) has shed light and provided robust guidelines for the management of acute postcataract endophthalmitis. However since the publication of the EVS in 1995 we may wonder whether the findings of this major trial are still valid in 2012. Vitrectomy techniques have improved, the choice of the systemic antibiotics used in the EVS was not optimal and the widespread use of local antibioprophylaxis may have changed the presentation and prognosis of postoperative endophthalmitis. Others questions are not fully answered; what about the use of intravitreal corticosteroids, how do the EVS data apply to other endophthalmitis presentations (traumatic, glaucoma or chronic endophthalmitis?).In this presentation we will give some very practical and useful clinical tips for postoperative endophthalmitis management, mainly based on the FRIENDS group (FRench Institutional ENDophthalmitis Study) which has gathered about 100 cases of endophthalmitis.

• 3421

EVICR.net Reading Centre Network

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Purpose To promote understanding of the work of Reading Centres in Europe in order to allow for greater collaboration both between existing reading centres and reading centres and clinical investigators.

Methods During the 90 minutes session, the members of the European Reading Centre Network will introduce their work. Detailed discussion will take place on how reading centres currently contribute to different studies. These will cover anterior and posterior segment images and their grading protocols in general and then will continue with detailed analysis plan of these.

Results The results of this session will be that better and more detailed understanding of the needs of the studies and what the Reading Centres can and cannot provide. These will lead to better communication from the start of the study in order to satisfy grading and reporting criteria of the studies.

Conclusion In conclusion, the Reading Centre network will present its work and will invite collaboration from the attendees of the session with the view of developing this unique collaboration further.

• 3431

Risk factors for endothelial cell loss after corneal transplantation

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Purpose To analyze risk factors for endothelial cell loss after corneal transplantation.

Methods Cohort study including 1438 consecutive eyes of 1438 patients who underwent Penetrating Keratoplasty, Anterior Lamellar Keratoplasty, or Descemet Stripping with Endothelial Keratoplasty between 1992 and 2010. To describe post-operative endothelial cell loss, the biphasic linear model was fitted to grafts with at least 2 (early phase) or 3 (late phase) endothelial cell density (ECD) measurements in time: ECD = ECD0 – (t * E), for t < 1 year (early phase); ECD = A – (t * L), for t > 1 year (late phase). The least squares estimates were used to calculate the coefficients of the various equations for each eye.

Results The average follow-up time was 45.9+39.3 months (mean+SD). The early-phase and late-phase annual endothelial cell loss (ECL) were, respectively, -24.7+18.8% (n=921) and -10.8+10.3% (n=664). Overall, the model-predicted cell loss was lower than the observed cell loss in the early phase and higher in the late phase. In multivariate analysis, 5 variables significantly influenced the early-phase endothelial cell loss: graft storage time, recipient rejection risk, preoperative hypertony, surgical group, and rejection episodes. Three variables significantly influenced the late-phase endothelial cell loss: recipient rejection risk, surgical group, and rejection episodes.

Conclusion Extending the graft organ culture time beyond 3 weeks results in higher early cell loss. High-risk recipient and rejection episodes are important risk factors for cell loss. ALK induces minimal cell loss whereas keratoplasty in eyes with impaired recipient endothelium is associated with high cell loss.

• 3432

Delivery of molecules into corneal endothelium using nanoparticles activated by femtosecond laser pulses: proof of concept

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Purpose NanoFemtoTransfection (NFT) is an innovative and promising non-viral technique to transfer molecules into cells (Chakravarty. Nature Nanotechnology 2010;5:607). It consists in temporarily permeabilizing cell membrane by a photoacoustic effect obtained by nanoparticles of black carbon activated by Ti-Saphir femtosecond laser (fsL) pulses. Calcein (622 Da), tagged bovine serum albumine (70 kDa) and one eGFP plasmid (5 MDa) were transfected into two non-adherent cell lines (DU145 prostate-cancer and GS-9L rat gliosarcoma). Our aim was to adapt the NFT to adherent human corneal endothelial cells (HCEC)

Methods We tested the NFT of calcein in vitro on the HCEC line HCEC-12 seeded at 1500cells/mm2 in 6 wells plates and ex vivo on whole human organ cultured corneas. A matrix of experiments comprising 4 exposition times, 6 fluences and 2 fsL beam movements was performed in order to obtain transfection with minimal toxicity. After exposition to fsL, nuclei were counterstained with Hoechst33342 and transfection efficiency was determined by observation on a fluorescence inverted microscope (IX81, Olympus, Japan) and further quantified by flow cytometry (FACSCalibur, BD, CA). Viability was assessed by Trypan blue staining

Results In HCEC-12, a fluence of 100 mJ/cm² and a laser beam movement of 3,5 mm/s gave a transfection of 17% and a viability of 97%. In whole corneas, with the same parameters, transfection was detectable in disseminated EC

Conclusion We obtained the proof of concept of the NFT in HCEC. Further optimization is ongoing to increase the transfection rate while maintaining minimal toxicity, especially for bigger molecules, like plasmids

• 3433

Characterization of cell cycle modifications induced by electric pulses in human corneal endothelium

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Purpose We recently described the possibility of gene electrotransfer into endothelial cells (EC) of human organ cultured corneas (He. OphthalmicRes2010;43:43). Parallel to the transfection of plasmids, trains of electric pulses alone also triggered mitosis of EC, despite human endothelium is normally considered unable to proliferate. Our aim was to further characterize the effect of electric pulses on the cell cycle of EC

Methods The short-term (3 days) and long-term (30 days) effects on EC of 8 square pulses lasting 100 ms, at 1 Hz frequency and 125 mA intensity were studied on 20 human organ cultured corneas. EC proliferation was evaluated by quantification of Ki67 expression, a proliferation marker of G1 to M phase, and by 5-Ethynyl-2'-Deoxyuridine (Clik-it EdU) incorporation during DNA replication (S phase marker) EC viability was assessed using the triple labeling with Hoechst33342/Ethidium/Calcein-AM with calculation of the viable EC density by image analysis (Pipparelli.IOVS2011;52:6018) and using an apoptotic marker, pSIVA-IANBD

Results Three days after stimulation by electric pulses, a significant activation of EC proliferation was observed with S-phase revealed by EdU staining and G1 to M phase, including mitosis, revealed by Ki67 staining. 90% of proliferating EC were located in area with ECD bellow 2000cells/mm2. For long-term effect, ECD did not increase and nuclear fragmentation and cell death were detected

Conclusion Electric pulses activate the cell cycle of EC on ex vivo corneas but cell division seems to abort and result in cell death. Mechanisms of cell cycle trigger and of mitosis abortion are currently being studied.

• 3434

Inhibition of Apaf-1 as a potential therapeutic strategy to improve corneal quality

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Purpose About 12 million people in the world live with visual impairment due to corneal diseases while there's a shortage of corneal tissue suitable for transplantation. One of the major causes of inappropriateness of corneas to be transplanted is to have a low endothelial cell density being apoptosis a key mechanism mediating cell loss. The protein Apaf-1 is a key regulator of the mitochondrial apoptotic pathway. We have developed a family of Apaf-1 inhibitors that have shown to be active in other apoptosis based-pathologies.

Methods We have established a corneal storage model.Corneas were preserved at 4°C for 7 days followed by a rewarming period that resembles the implant. At 4°C the endothelium was intact but not the tight junction (TJ) integrity. Throughout the rewarming, apoptosis was induced as indicated by caspase 3 activation, resulting in cell loss.

Results The addition of Apaf-1 inhibitors in the storage media reduces apoptosis activation. Caspase 3 activity was diminished; anti-apoptotic genes were up-regulated and pro-apoptotic down-regulated resulting in a reduced endothelium loss. Apaf-1 inhibitors not only probed to be active during the rewarming period but also at 4°C: surprisingly, their presence inhibited the TJ breakdown. Integrity of TJ is known to be crucial to maintain cellular morphology and corneal transparency.

Conclusion The results hereby presented demonstrate a dual role of Apaf-1 inhibitors in preserving the cornea integrity by keeping TJ integrity and inhibiting apoptosis. The use of these inhibitors in the clinical setting could increase the availability and quality of tissue to be transplanted.

Commercial interest

• 3435

Impact of corneal donor post-mortem time on the rate of culture medium contaminations

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Purpose In the majority of European countries there is a shortage of donor corneas for corneal transplantations. In 2007, the EU Directive 2006/17/EC on 'technical requirements for the donation, procurement and testing of human tissues and cells' was introduced restricting the usability of post-mortem donor blood sampling from 72 hours to 24 hours. As a consequence, post-mortem time for donor cornea acquisition was shortened, resulting in a further reduction of corneal allografts. This study analyzed the effect of donor cornea post mortem-time on medium contamination in organ culture storage.

Methods Contamination rates during corneal organ culture during extended (2008-9, Group I) versus restricted post-mortem time protocols (2010-11, Group II) were retrospectively analyzed. Data were collected at LIONS Cornea Bank North Rhine-Westphalia, University Eye Hospital Duesseldorf, Germany.

Results In the years 2008 and 2009 (Group I) 1272 corneal grafts with a post-mortem time of 30.05 ± 15.77 hours were collected and cultivated in LIONS Cornea Bank NRW. After introduction of the new guidelines, the overall number of acquired donor corneas dropped by 29.88% to 892. Post-mortem time was significantly lower during the restricted post-mortem time protocols (24.2 ± 12.37 hours, $p<0.05$, t-test). Interestingly, there was no significant difference of culture medium contamination rates between the two groups (Group I: 9,0%, n=115 versus Group II: 7.3%, n=65; Chi-squared test).

Conclusion Restriction of donor cornea acquisition time down to 24 hours seems to be without benefit regarding the contamination rates during corneal organ culture.

• 3436 / T076

Big bubble technique dissection plane: histological and ultrastructural comparative analysis on both white and clear margin dissected corneas

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Purpose Pneumodissection or 'big-bubble' technique (BBT) is used to separate Descemet's membrane (DM) and stroma in both deep anterior lamellar keratoplasty and Descemet's membrane endothelial keratoplasty. It has been reported that BBT may produce two typer of bubble outlines: clear or white margin. It seems that the components of the posterior lamella obtained with each bubble rims also differ. Our aim is to compare BBT dissection plane using histological and electron microscopy (EM) analysis on eye-bank corneas.

Methods BBT was carried out on donor corneas unsuitable for transplantation for reasons other than corneal disease.Corneoscleral discs were mounted on an artificial anterior chamber and BBT was carried out using a 27G needle. 5 samples which had a bubble with white margin and 5 with clear margin were fixed in formalin and sent for histology followed by EM.

Results Samples in which the edge of the bubble had a white margin showed variable residual stroma adherent to DM. When the edge of the bubble was clear no residual stroma was seen attached to a bare, smooth DM. The anterior lamellae of the cases without residual stroma were also analysed. These showed no evidence of DM elements excluding the unlikely possibility of intra-Descemet's dissection plane. The findings were confirmed by EM in all cases. These showed intact banded DM in all posterior lamellae but only those with a white bubble outline had attached residual stromal collagen.

Conclusion In eye bank corneas the histological elements of the posterior lamella dissected using BBT can be predicted depending on the margin of the bubble obtained. Assumptions that pneumodissection in BBT routinely bares DM need to be revisited.

• 3437 / T075

Rabbit, rat and pig corneas: main characteristics and storage in organ culture

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Purpose Except for primates, animal models of corneal are far from human. Animal models of corneal storage are virtually non-existent. Aim: to update the main characteristics (especially for endothelial cells (EC)) of the cornea of 3 easily available animals, as well as their ability to be stored in organ culture (OC)

Methods 30 corneas of 6 month-old Large White pig, 20 of 10 week-old California rabbits and 10 of 8 week-old Lewis rats were investigated. Macroscopic data: 1/ horizontal and vertical diameters (digital calliper), 2/transparency (analysis of modulation and contrast transfer functions), 3/ corneal thickness (CT) (ultrasound pachymetry). Microscopic data: 1/ histology on Hematein-Eosin-Safran stained cross sections and ultrastructure, 2/ EC density (ECD) and morphometry, 3/ EC proliferative status (Ki67 and 5-Ethynyl-2'-Deoxyuridine incorporation (Clik-it EdU)), differentiation status (Na+/K+ ATPase, ZO-1, JAM-1), and existence of stem cells (Nestin, ABCG2, Telomerase). Fresh corneas were organ cultured in 2 commercially available media. CT was measured every 2h during 6h, then every 12h. Transparency and EC survival was determined after 2, 3 and 4 days of OC

Results We constituted a complete database of ex vivo corneal characteristics of the 3 species. ECD, polymorphism and polymegathism were higher than in human. CT increased rapidly (up to 3 times) in both OC media, resulting in biconvex tissues with almost complete loss of transparency and significant endothelial folding. EC survival decreased especially in folds

Conclusion Corneas of the 3 animals cannot be stored more than 2 to 3 days in OC media designed for human. Specific media should be developed to obtain reliable models of animal corneal OC

• 3441
Clinical challenges of ocular anti-microbial therapy

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Purpose To discuss the different clinical challenges in ocular anti-microbial therapy as they pertain to bacteria, fungi, viruses, and acanthamoeba.

Methods An overview of how the different infections often seen and how available medications might be utilized.

Results With the large number of medications available to ophthalmologists these days, deciding what medication to use can be complicated. The initial choice of fourth-generation fluoroquinolones has raised questions about bacterial resistance. This may highlight the importance of cultures in cases where infections are not responding as expected. Recognition of certain infections, such as early acanthamoeba, which can look similar to herpetic keratitis, may be difficult. The use of newer diagnostic tests, such as PCR, may be helpful to ensure appropriate treatment is started in a timely fashion. This may also be helpful in targeting treatment in fungal infections. The use of long term wear contact lenses, such as with a keratoprosthesis, has raised questions as to whether antibiotics are efficiently reaching the corneal surface and treating biofilms that form on contact lenses. Understanding what flora is present in cases of long term contact use may allow clinicians to better prevent infections. There have also been many clinicians who have advocated the treatment of viral conjunctivitis to help reduce the number of lost work and school hours. There is still debate as to the efficacy of these treatments and how it might impact the continually growing cost of health care.

Conclusion Newer testing modalities and understanding what long term use of ocular anti-microbials does on the ocular surface will improve our treatment of ocular infections and hopefully prevent them too.

• 3442
Is there an anti-adenoviral drug on the horizon?

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Adenovirus ocular infections (epidemic keratoconjunctivitis [EKC], follicular conjunctivitis, and pharyngeal conjunctival fever) are the most common ocular viral infections worldwide, including more than 1,000,000 cases annually in Japan. To date, there is no US FDA or European Medicines Agency approved antiviral therapy for these infections. Little progress on anti-adenoviral development was made until our group developed the first reliable animal model for ocular anti-adenoviral testing 20 years ago. Using that animal model, our group was instrumental in the preclinical development of the first topical antiviral drug for the treatment of adenoviral conjunctivitis tested in clinical trials, the nucleoside analog cidofovir. However, toxicity concerns, not efficacy, caused the sponsor to discontinue development. Since then, there has been considerable progress made regarding the discovery and development of antivirals by both academia and the pharmaceutical industry. Preclinical in vitro and in vivo studies have identified several new antiviral candidates such as 2,3-dideoxycytidine (ddC), cyclopentenylcytosine (CPE-C), intravenous immune globulin (IVIG), NVC-422, and FST-100. These preclinical studies have led to industry sponsored clinical trials which have been initiated with several agents NVC-422 (NovaBay), Zirgan (0.15% Ganciclovir gel, Bausch + Lomb), and FST-100 (0.4% povidone-iodine/0.1% dexamethasone, Foresight Biotherapeutics). The first antiviral to treat adenovirus ocular infections will hopefully be available in the not too distant future.

Commercial interest

• 3443
Biofilms in ocular infection

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Purpose To discuss the evidence for microbial biofilms in ocular infections.

Methods A description microbial biofilms and a review of the evidence in the literature for bacterial biofilms in ocular infections.

Results Microbial biofilms are surface attached communities of microbes that are recalcitrant to antibiotic therapy and associated with a wide number of human diseases including, but not limited to as cystic fibrosis, dental caries, otitis media, osteomyelitis, and chronic wounds. There is an increasing body of evidence supporting the potential role of microbial biofilms in ocular infections.

Conclusion The model that biofilms contribute to ocular infections is an exciting new arena of study.

• 3444
Is antibiotic resistance a major problem in ophthalmology?

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Purpose Ocular antibiotic bacterial resistance becomes problematic when: 1) intrinsically susceptible bacteria become resistance, 2) antibiotic resistance spreads from patient –to-patient, and 3) effective antibiotic treatment is unavailable. The "Standard of Care" of ocular bacterial infections will be accordingly evaluated.

Methods Based on the findings of our dedicated ophthalmic microbiology laboratory, the trends in ocular susceptibility in regards to bacterial pathogen and disease (endophthalmitis, keratitis, conjunctivitis, and blepharitis) were analyzed for evidence of acquired resistance, possible infection spread, and the armament of treatment.

Results Our studies indicate that based on the bacterial pathogen, bacterial resistance is most prevalent with endophthalmitis isolates of Staphylococcus aureus and coagulase-negative Staphylococcus. There is evidence that endophthalmitis isolates of Staphylococcus aureus may be hospital acquired. Although Haemophilus influenza and Streptococcus pneumonia isolated from conjunctivitis are probably spread patient-to patient, an increase in antibiotic resistance has not occurred. There does not appear to be a treatment problem for Pseudomonas aeruginosa keratitis based on in vitro antibiotic resistance.

Conclusion Our study concludes that antibiotic resistance does occur for ocular bacterial pathogens, but ocular infection does not spread from patient to patient. There is a plethora of effective topical antibiotic agents to treat all types of bacterial ocular infections. It is important to culture all severe ocular infections to optimize therapy and to guard against the creation of antibiotic resistant bacteria. The future of antibacterial therapy may rely on preventing infections instead of the production of new drugs.

• 3451
Historical concepts of glaucoma

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Purpose To present different historical concepts of glaucoma in relation to the thought-styles of their time.

Methods Historical analysis of the old medical treatises and modern history of ophthalmology articles.

Results The pathogenesis of glaucoma is one of the most important and puzzling issues in the 21st century ophthalmology.Many concepts were recently presented, including light-damage theory, local and systemic ischaemic injury, oestrogen deficiency and low CSF pressure. It shows its multifactorial profile and our present deficiency in understanding its real nature. The possible reason for this might be our scientific thought-style, which determines our present perception of the disease and possible concepts of its pathogenesis, which are verified in clinical and experimental research. The collective thought-style, in this case regarding the nature of glaucoma, might easily eliminate any new idea or non-conventional hypothesis. The scientist is a part of the thought-collective. Every observer has been shaped by a particular culture and represents a thought-style of a definite scientific group, and his style determines the range of his observations. The historical glaucoma concepts reflected usually historical thought-styles typical for the period of scientific development.

Conclusion Understanding the principles that govern the development of science in the historical perspective allows for an understanding of our own limitations in this respect (contemporary thought-style), which frequently prevent us from looking at the matter in a non-standard way.

• 3452
Pathogenesis of glaucoma: does light play a part in the process?

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Pathogenesis of glaucoma: does light play a part in the process?By: Neville N. OsborneFundación de Investigación Oftalmológica, Instituto Oftalmológico Fernández-Vega, Oviedo 33012, Spain.Neurones are absolutely dependent on their mitochondria for their energy needs unlike dividing non-neuronal glial cells. Retinal ganglion neurones are particularly dependent on their mitochondria because a lot of energy is required to propagate the action potential along the non-mylinated axons within the globe. We have propose that glaucoma is initiated by an alteration in the blood flow dynamics in the optic nerve head causing a defined "ischemic-like" insult to the retinal ganglion neurone axon mitochondria and also surrounding astrocytes and microglia. While this results in ganglion cells being metabolically weaker, but still functionally normally, they are now susceptible to secondary insults that they would have normally tolerated. The major secondary insults to subsequently result in ganglion cells dying at different times probably arise from chemicals released from activated optic nerve head astrocytes and microglia. Yet another factor may be the very same light that is involved in vision. This is because basic science studies have shown that light as impinging on ganglion cell axons can affect mitochondrial function. Thus while it is not suggested that light causes glaucoma it is proposed that particularly the blue light component impinging on the retina can exacerbate already metabolically effected ganglion cell mitochondria.

• 3453
Non-IOP lowering treatment

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The classical glaucoma treatment focuses on IOP reduction. Better knowledge of the pathogenesis has opened up new therapeutical approaches. Whilst most of these new avenues of treatment are still in the experimental phase, others, are already used by some physicians. Blood pressure dips can be avoided by intake of salt or fludrocortisone. Vascular regulation can be improved locally by carbonic anhydrase inhibitors, systemically with magnesium or with low doses of calcium channel blockers. Experimentally, glaucomatous optic neuropathy (GON) can be prevented by inhibition of astrocyte activation, either by blockage of epidermal growth factor receptor or by counteracting Endothelin. GON can also be prevented by nitric oxide-2 synthase inhibition. Inhibition of matrix metalloproteinase-9 inhibits apoptosis of retinal ganglion cells and tissue remodelling. Upregulation of heat shock proteins protects the retinal ganglion cells and the optic nerve head. Reduction of oxidative stress especially at the level of mitochondria also seems to be protective. This can be achieved by gingko, dark chocolate, polyphenolic flavonoids occurring in tea, coffee or red wine and anthocyanosides found in bilberries.

• 3454
Biomechanical concepts in Glaucoma

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Purpose Title: Corneal biomechanics and glaucoma risk- where are we now?

Methods The impact of central corneal thickness (CCT) on intraocular pressure (IOP) measurement accuracy has been well documented, and CCT has become part of the routine work up of a glaucoma suspect patient. What is relatively unclear is whether corneal properties, such as CCT and in vivo measures of corneal biomechanics, give an indication of the risk of glaucoma susceptibility. This talk will consider whether there is a role for the cornea that lies beyond the limits of IOP measurement accuracy, discussing the evidence as to whether current measures of corneal biomechanics may be used as a surrogate marker of optic nerve compliance.

• 3461

Vascular tumours of the retina and choroid : classification, diagnosis and treatment

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Purpose Retinal vascular tumors consist of capillary hemangioblastomas, associated with Von Hippel Lindau's disease, cavernous or racemous hemangiomas, and vasoproliferative pseudotumors. Coat's disease is typically diagnosed in male children presenting retinal telangiectasia, complicated by retinal exudates. Choroidal vascular tumors are most frequently circumscribed, more rarely diffuse hemangiomas, the latter being associated with Sturge Weber syndrome

Methods Diagnosis is often made by ophthalmoscopy and ultrasonography, and confirmed by fluorescein and/or ICG angiography. OCT and panoramic angiography have improved visualization with regard to the extent of the vascular tumor(s).

Results Therapeutic approach can consist of periodic observation, laser photocoagulation, cryotherapy, photodynamic therapy (PDT), irradiation by plaque or protons, and anti-VEGF injections.

Conclusion Controversy exists as to the optimal management of these benign but potentially blinding tumors. This review therefore serves as an introduction to the different topics of this symposium as well as the debate at the end with different experts sharing their experience.

• 3462

Coats' disease : classification and current treatment

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Purpose Coats' disease is characterized by idiopathic telangiectasia with lipid exudates and retinal ischemia. Advanced cases develop total retinal detachment (RD)(stage 3B) and neovascular glaucoma (stage 4), resulting in enucleation in 7% and 78% of cases respectively.

Methods Nine consecutive cases of Coats' disease stage 3B (n=5) and 4 (n=4) received 1 or more intravitreal injections of 0.5 ml ranibizumab. In 3 cases, subretinal fluid drainage by sclerotomy was performed. Mean age at diagnosis was 17.9 months (range 1-38). At the end of treatment, ERG was recorded (n=4) and amblyopia treatment was attempted in 6 patients. Mean follow-up was 42.9 months.

Results Rubeosis disappeared during the first week with the retina reattaching within 4 months, rendering pathological vessels and ischemic retina accessible to conventional therapy. A single injection was sufficient in 6 cases, 2 injections were necessary in 1 patient and another needed 4. One patient developed 10 months after complete retinal reattachment a severe fibrous vitreo-retinopathy evolving to subtotal tractional RD. Amblyopic treatment was performed in 4 patients and restored measurable visual acuity in two patients. Scotopic ERG was unrecordable with a severely reduced photopic b wave in 3 patients. The last patient had a reduced scotopic b wave (50%) and a normal photopic ERG with slightly increased implicit time.

Conclusion There is an increasing interest in anti-VEGF therapy in Coats' disease. To our knowledge, this is the largest series of stage 4 and 3B Coats' disease treated by ranibizumab, demonstrating that it is a well-tolerated and safe therapy in young children with advanced disease. Ranibizumab facilitates the management by suppressing rubeosis in stage 4 and decreasing exudation.

• 3463

Coats' reaction and angiomas of the retina from mutations affecting telomere maintenance

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Purpose To describe retinal abnormalities other than Coats' reaction in 4 of 6 Finnish patients with CRMCC, also known as Coats' plus.

Methods An observational series of genotyped children imaged with RetCam. The children (5 girls, 1 boy) were born prematurely on gestational week 30-39 and were small for date with birth weights from 770 to 2170 g. Four are alive at age 4-22 y and two have died at age 6 and 18 y.

Results Of the 6 children, 2 presented with bilateral, asymmetric Coats' reaction at age 7 and 11 months. The more advanced eye had an exudative retinal detachment (RD). Three children had retinal angiomas without exudation, accompanied with preretinal and vitreous bleedings, and abnormally running circular vascular loops at age 2-11 months. In two of the latter, traction RD developed. Regardless of the phenotype, the retina peripheral to the vascular anomalies was avascular but without ROP changes. One patient did not have clinically visible retinal vascular anomalies. All patients with retinal changes had the common c.1994T>G [p.Val665Gly] mutation, three with c.2831delC [p.Pro944Leufs*7] and one each with c.3583C>T [p.Arg1195*] and c.3425_3426delTCinsAT [p.Leu1142His] mutations. The genotype did not predict the phenotype. The patient without retinal changes had c.680C>T [p.Ala227Val] mutation with c.2831delC [p.Pro944Leufs*7]. Other Finnish patients with the latter ccombination have had retinal changes since early childhood.

Conclusion It is important to appreciate that CRMCC can present with retinal phenotypes other than Coats' reaction, and a minority may not have any visible retinal changes. Also angiomas call for neuroimaging to identify brain cysts and calcifications which characterize CRMCC

• 3464

Von Hippel-Lindau's disease : general and ocular management

GALDRIC A
Paris

ABSTRACT NOT PROVIDED

• 3465

Choroidal hemangioma : photodynamic vs. radiotherapy

ZOGRAFOS L
Lausanne

ABSTRACT NOT PROVIDED

• 3466

Debate : Epi- and peripapillary capillary hemangiomas and hemangioblastomas : in search of an optimal therapeutic approach

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ABSTRACT NOT PROVIDED

• 3471

Predicting chromatic sensitivity in normal trichromats and in subjects with congenital deficiency

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Purpose Differences between M- and L-class variant pigments arise largely because amino acid substitutions in M-class pigments contribute less to the corresponding shifts in spectral responsivity. Other factors such as the relative numbers of L and M cones, their optical density and the midpoint between their spectral peaks can also contribute to the subject's overall, red/green (RG) chromatic sensitivity. The purpose of this study was to examine how these differences affect chromatic sensitivity in normal trichromats and in subjects with deutan- and protan-like deficiency.

Methods RG thresholds were measured in 269 deutans, 132 protans and 330 normal trichromats using the CAD test. The colour vision of every subject was also examined using the Nagel anomaloscope. Classification into normal, deutan and protan classes was based on the results obtained on CAD and anomaloscope tests.

Results RG thresholds measured within each group were ranked in increasing order. Samples equal to the number of subjects within each group were taken from a single Gaussian distribution, in the case of normal trichromats, or from more than one distribution in the case of deutan and protan groups. The distribution parameters were optimised to predict the rank order of the measured RG thresholds in each group.

Conclusion The rank order of thresholds measured in normal trichromats can be predicted by a single Gaussian distributions. Deutans produced the most complex rank order which could only be predicted adequately with a minimum of four Gaussians. In contrast, the rank order for the protan group was much simpler and could be predicted well with only two or at most three Gaussian distributions.

• 3472

The contribution of the rod/melanopsin driven ganglion cells to the dynamic pupil light reflex response

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Purpose Intrinsically photosensitive retinal ganglion cells have been shown to contribute to the control of the steady-state pupil response. The extent to which melanopsin contributes to rapid pupil responses elicited with brief stimuli remains less clear. The principal objective of this study was to examine how the dynamic pupil light reflex response changes with the level of light adaptation for stimuli that isolate luminance, colour or combined rod and melanopsin. The range of light levels that yield useful rod signals was also investigated.

Methods The study involved ten normal subjects, one patient with rod deficiency, one patient with retinitis pigmentosa (RP) and one rod monochromat. The pupil responses were measured to stimuli that isolate photopic luminance, colour or combined rod and melanopsin at three light levels (456, 74.4 and 4.8cd/m2). Visual acuity, contrast sensitivity and chromatic sensitivity were also measured in all subjects.

Results The patients with rod deficiency and RP exhibit pupil responses to luminance and colour modulation, but much reduced or absent response to rod/melanopsin modulation. Conversely, the rod monochromat shows complete absence of pupil colour and luminance responses, but exhibits large pupil rod/melanopsin responses at all light levels.

Conclusion The findings from this study suggest that pupil responses to briefly presented stimuli are mediated largely by rod and cone signals with no contribution from melanopsin. The results also suggest that rod signals remain unsaturated and can contribute to dynamic pupil responses at much higher light levels.

• 3473

Colour vision as a screening tool for sub-clinical retinal disease

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Purpose Age-related retinal diseases start developing at a subclinical level, as gradual photoreceptor dysfunction, ganglion cell apoptosis etc. Subtle retinal changes disturb the fine intraretinal signal transmission and despite the lack of clinically detectable signs can cause an impairment of chromatic sensitivity that precedes the loss of performance in processing other stimulus attributes. Colour vision can be used as a sensitive screening tool for retinal diseases when the tests are carried out at lower light levels.

Methods The health of the retina (HR) index was introduced to detect early changes caused by disease by capturing the worsening of chromatic sensitivity as the light level changes from photopic to mesopic (J Opt Soc Am A Opt Image Sci Vis 29,2:A27-A35,2012). This approach makes it possible to separate changes caused by normal aging from the effects of sub-clinical retinal disease. Chromatic sensitivity was measured in 60 subjects (mean age 47.6 years, range 16-79 years) at four light levels using the Colour Assessment and Diagnosis (CAD) test; measurement of pre-receptoral absorption by the crystalline lens and the macular pigment and the size of the pupil allowed an estimation of retinal illuminance.

Results The HR index proved largely independent of age (r2~0.2), but ~11% of clinically normal older subjects showed impaired chromatic sensitivity that could reflect the development of retinal pathology. Some of these subjects developed AMD and Glaucoma 2.5 years after the assessment. Patients with identified retinal disease also show abnormal HR indices.

Conclusion The HR index is a single number that captures information about the health of the retina irrespective of age and can be used to screen for sub-clinical signs of retinal diseases.

• 3474

Effects of viewing time of pseudoisochromatic plates

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Purpose Effects of viewing time on the recognition of red/green and blue/green pseudoisochromatic plates were evaluated to improve clinical application.

Methods Special pseudoisochromatic "C" or "E" plates (in following referred to as "spic-plates") allow repeated exams with identical demands on color vision. The study included 5 daltonian subjects with a best corrected visual acuity BCVA of 1.0, 5 diabetic patients with non proliferative diabetic retinopathy NPDR, BCVA 0.8 or better, and 10 normal observers. Under standard illumination and viewing distance, the viewing time was 1 s, 3 s, or unrestricted until the subject had arrived at his or her final estimate.

Results Daltonian subjects were unable to recognize the red / green spic-plates during a viewing time of 1 s or 3 s. Under unrestricted observation, 3 of 5 daltonian subjects deciphered the red/ green spic plates. Blue/green spic-plate results in the daltonian subjects matched those of normal observers. 3 of 5 diabetic patients failed in the blue/ green spic plate at 1 s, one at 3 s of viewing time. With one exception at 1 s, the diabetic patients passed the red/green spic plates, as normal observers did.

Conclusion Besides the angle of observation and the level and spectral composition of illumination, the viewing time has an influence on the results of color vision testing by pseudoisochromatic plates. In clinical application, viewing time should be considered e.g. following Ishihara's advice of 3 s

Commercial interest

• 3475

Age-corrected monocular limits of normal trichromacy

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Purpose Chromatic sensitivity worsens gradually with increasing age, but the inherent variability in normal colour vision makes this difficult to detect and to separate from very early changes caused by either retinal or systemic diseases. In this study we developed new approaches to identify and screen for changes that cannot be attributed to normal aging. This approach made it possible to produce reliable, age-corrected limits for normal colour vision.

Methods Red-green (RG) and yellow-blue (YB) thresholds were measured monocularly in each eye (using the Colour Assessment and Diagnosis (CAD) test) in 394 subjects (age range: 16 to 90 years). Only clinically normal subjects according to medical history and eye / fundus examination were included. All subjects with congenital colour deficiency were excluded. A new filter based on right / left eye asymmetry for RG and YB thresholds was also employed to exclude subjects with significant differences in monocular thresholds. After filtering, the analysis of the effects of normal aging was based on 178 subjects (age range: 16-79 years).

Results The effects of age (in the range 20 to 80 yrs) can be accounted for well by a linear trend with just over two-fold increase in both RG and YB mean colour thresholds. Statistical limits of variability ($\pm 2\sigma$) were computed from the normal subject data in order to provide limits of age-corrected RG and YB colour vision.

Conclusion The age-corrected CAD thresholds limits established in this study provide a more accurate way of detecting monocular changes in colour vision caused by either retinal diseases or systemic conditions that affect the eye.

• 3476

Detection of colour vision changes in patients with systemic diseases that can affect the eye

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Purpose Changes in colour vision can provide the earliest signs of vision loss caused by either retinal or systemic disease (Expert Rev.Ophthalmol. 6(4):409-420,2011). Both yellow-blue (YB) and red-green (RG) mechanisms are affected in acquired deficiency, but some diseases may cause different patterns of colour vision loss. Patients with different systemic diseases were examined to discover abnormal changes in colour vision using a newly developed, age-corrected system for colour assessment.

Methods 334 subjects (age range: 41 to 91years) were investigated. The subjects were classified as normal, hypertensive, diabetic, diabetic and hypertensive, idiopathic and other systemic conditions. RG and YB colour thresholds were measured monocularly in each eye using the Colour Assessment and Diagnosis (CAD) test.

Results Subjects with early stage pathology were excluded using a number of criteria including the discovery of right / left eye asymmetric loss in colour sensitivity. Age-corrected limits of normal colour vision were employed to detect significant changes in chromatic sensitivity. The results reveal significantly higher RG and YB thresholds in all groups (including the idiopathic and other systemic conditions group).

Conclusion The use of age-corrected normal limits of chromatic sensitivity makes it possible to detect reliably significant loss of colour vision in systemic disease. Loss of chromatic sensitivity that precedes retinopathy is present in every systemic condition examined. Further studies are needed to discover the extent to which the pattern of selective RG and YB losses can be attributed to specific diseases of the eye.

• 3481

Evolution of cataract surgery: Barraquer experience

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Purpose To describe the evolution of cataract surgery at the Barraquer Eye Center

Methods Several videos are presented showing the different techniques of cataract surgery over the last century

Results Intracapsular cataract extraction using the eysiphake was first developed by Prof. Ignacio Barraquer and the surgery was done with topical anesthesia, sutureless technique. This technique was later on enhanced with zonulolysis using alpha-chymotrypsis as discovered by Prof. Joaquin Barraquer. Anterior chamber intraocular lens implantation using the Strampelli lens thru a small corneal incision is also shown. Finally we show the present day technique femtosecond laser assisted phacoemulsification thru a 2 mm incision with implantation of foldable intraocular posterior chamber lens.

Conclusion Several changes have taken place thru the last century in cataract surgery. Techniques have been developed for less intra operative and postoperative complications, faster visual rehabilitation and excellent refractive results.

• 3482

Efficacy of surgical simulator training versus traditional wetlab training on the complication rate during capsulorrhexis portion of cataract surgery in trainees

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Purpose The purpose of this study is to determine the translational effectiveness of surgical simulation as part of resident training on their performance on the task of casulorhexis during their first surgeries, as compared to traditional wetlab training.

Methods Second Year Residents on rotation at the Veterans Affairs Boston Healthcare System were randomized to continuous capsulorrhexis training (CCC) in the traditional wetlab (n=10) with silicone eye versus on the EYESI surgical simulator (n=11). After completion of the training, residents' initial CCCs in the operating room on real patients were videorecorded. Videos were reviewed and scored by two anterior segment attending surgeons.

Results Scores on 12 measures of performance were reasonably close in all cases; there was no statistical significance in any of the differences in individual scores.Correlation across all 12 measures of performance is 0.919 (p<.001). Overall score was calculated as the sum of the 12 individual performance scores.There was no significant difference in overall score between the two groups (p=.527).

Conclusion Study suggests surgical simulator training when compared to traditional wetlab training is a safe, non-risk method of preparing trainees to perform capsulorrhexis during their initial surgical experiences on real patients in the operating room.

• 3483

Intracameral cefuroxime injection at the end of cataract surgery reduces the incidence of endophthalmitis, a French study

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Purpose To show the interest of intra-camerular injection of cefuroxime at the end of cataract surgery to decrease the incidence of post-operative endophthalmitis.

Methods 5115 patients operated from cataract between april 2003 and june 2008 were prospectively and exhaustively included in a survey for operative site infection. Intracameral Cefuroxime injection started in june 2006, so 2289 patient received Cefuroxime, and 2826 did not. Pre-operative data (betalactamin allergy, history of endophthalmitis, age, sex) and intraoperative data (use of trypan blue, capsular ring or iris retractors, surgical time, senior or junior surgeon, corticosteroids injection, iris retractors), and postoperative infections at 8 days and 1 month were prospectively collected.

Results Respectively, the incidence of endophthalmitis without and with cefuroxime intracamerular injection was 35 of 2826 patients (1,238 %) and 1 of 2289 patients (0,044 %) (p < 0,0001).None of intraoperative factors we considered has been significantly associated to postoperative infection. No allergic reaction has been reported.

Conclusion Intracamerular Cefuroxime injection at the end of cataract surgery is a safe procedure to significatively decrease the incidence of endophthalmitis.

• 3484

Morphology of age-related cuneiform cortical cataracts: the case for mechanical stress.

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Purpose To study the morphology of age-related cuneiform cortical cataracts.

Methods We evaluated the gross morphology, location, and fiber cell architecture of equatorial cortical opacities in the aging human lens. Using dark-field stereomicroscopy, we photographed donor lenses in toto and as thick slices. In addition, we investigated the details of the fiber cell architecture using fluorescent staining for membranes and by scanning electron microscopy. We then combined our data with data from recent studies on lens viscoelasticity.

Results We found that small cortical and cuneiform opacities are accompanied by changes in fiber structure and architecture mainly in the equatorial border zone between the lens nucleus and cortex.

Conclusion Because the lens cortex and nucleus have different viscoelastic properties in young and old lenses, we hypothesize that external forces during accommodation cause shear stress predominantly in this border zone. The location of the described changes suggests that these mechanical forces may cause fiber disorganization, small cortical opacities, and ultimately, cuneiform cataracts.

• 3485

Contribution of 3D anterior segment reconstruction by rotative UBM to the sizing of phakic IOL

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(2) LaTIM Inserm UMR 1101, Brest
(3) Quantel Medical, Clermond-Ferrand
(4) CHU Morvan, Service d'ophtalmologie, Brest

Purpose Posterior phakic implantation is the recommended procedure for high ametropia correction but it is harmed by a difficult sizing inducing errors. We designed a 3D rotative UBM prototype in order to take into account the volume of the posterior chamber to improve the sizing.

Methods 7 myopic eyes (mean MRSE: -10.8) of 4 patients underwent a phakic implantation by one surgeon with a "white to white"-based sizing method. During the 3rd postoperative month, we evaluated several mesures that we assessed by anterior segment OCT (2D) and by our UBM prototype (3D), designed by the LaTIM -Inserm U1101 in association with Quantel Medical®. It contains a linear scanning probe of 50 MHz with a rotative motor (acquisition of 30 coaxial slides).

Results 3D reconstruction gives us a representation of one eye on 360°. For each eye, we have compared data pre and postoperative implantation and our results reflect the conventional impact of implant.

Conclusion Our rotative probe has allowed the first 3D reconstruction of the ocular anterior segment. This initial approach reports high anatomical variations and non uniformity of intraocular clearances, explaining potentially some unexpected IOL positioning. Our goal is to have an accurate visualization of relationship between phakic IOLs and intraocular surrounding structures. Perspectives could be the evaluation of the impact of accommodation on intraocular volumes in addition to preoperative simulations in 3 dimensions.

Commercial interest

• 3486

Influence of multifocal intraocular lenses on standard automated perimetry test results

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Purpose To evaluate the influence of multifocal intraocular lenses (MFIOLs) on standard automated perimetry (SAP) and size V perimetry test results.

Methods Sixteen eyes of 16 patients with a diffractive MFIOL (median age 64 years) and 45 phakic eyes of 45 healthy subjects (median age 49 years) were included in this cross-sectional case-control study. All eyes underwent (1) SAP with the Humphrey Field Analyzer using a 30-2 grid and the Swedish Interactive Threshold Algorithm standard strategy and (2) a full threshold test with stimulus size V (instead of the default size III). Our Main Outcome Measures were the mean deviation (MD; for SAP) and mean sensitivity (MS; for both SAP and size V perimetry).

Results The MD of the SAP test results was on average 2.18 dB lower in MFIOL patients than in controls (P<0.001). For all 16 cases and an age-matched subgroup of 18 controls, this difference was 2.05 dB (P=0.001). The age-adjusted difference in MS between cases and controls was -2.34 dB (P<0.001). For size V perimetry, this was -1.67 dB (P<0.001). For a subset of test locations within 10 degree eccentricity, the age-adjusted difference in MS between cases and controls was -2.35 dB for size III (P<0.001) and -1.96 dB for size V perimetry (P<0.001).

Conclusion Patients with a diffractive MFIOL have a clinically relevant reduction of the visual sensitivity as assessed with SAP and size V perimetry.

• 3511
Inflammation in retina disease

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ABSTRACT NOT PROVIDED

• 3512
Early markers of inflammation

BEHAR-COHEN F
Paris

ABSTRACT NOT PROVIDED

• 3513
Clinical markers of inflammation

COSCAS G
Creteil

ABSTRACT NOT PROVIDED

• 3514
Inflammation in uveitis

DE SMET M
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ABSTRACT NOT PROVIDED

• 3515

Management of inflammation in RVO

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Macular edema (ME) is a leading cause of vision loss in retinal disease including retinal vein occlusion.The development of macular edema is mediated by angiogenic as well as Inflammatory processes. There is increasing evidence that management of the inflammatory part is important in the treatment of the edema. Therefore, theoretically steroid therapy has a good potential in the treatment of macular edema.Regarding retinal vein occlusion specifically treatment by Ozurdex implant, containing dexamethasoe provides visual recovery with excellent safety outcomes.

• 3611

Revisiting transconjunctival sutureless 25 gauge vitrectomy for macular surgery

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Purpose To report the results of 25g vitrectomy with ILM peeling, SF6 tamponade and strict face down posturing for the treatment of idiopathic macular holes.

Methods This is a retrospective study of 106 eyes with idiopathic macular hole, treated with 25g PPV, brilliant peel assisted ILM peel , SF6 gas tamponade and face down posturing for 1 week. The patients were followed up at 1 day, 1 week, 1 month, 3 months and 9 months postoperatively clinically and with OCT. Preoperative and postoperative logMAR visual acuity was recorded

Results 106 eyes were included in this study. 88 phakic (83%) and 18 pseudophakic (17%). 32 males (30%) and 74 females (70%). Mean age was 66.5 years. Mean preoperative visual acuity was 0.69 logMAR and improved at 0.39 logMAR at 9 months postoperatively.Anatomical macular hole closure rate was 100% (106/106). 102/106 patients (96%) had anatomical closure of the hole after the 1st operation. 4/106 patients had an open hole noticed at 1 week and received an additional SF6 injection at the office and strict face down posturing for another week. 4/4 patients had the hole closed at month 1.Postoperative complications included a case of macular toxicity due to accidental intravitreal leak through the sutureless port of gentamycin which was injected subconjunctivaly at the end of surgery. Early postoperative raised intraocular pressure was noticed in 6 patients (5.6%) . No retinal detachment and no case of endophthalmitis was noticed.

Conclusion 25g PPV, ILM peeling, SF6 gas tamponade and posturing is a safe and effective technique for the treatment of idiopathic macular holes. Additional gas injection combined with extended strict posturing can increase the anatomical closure rate without the need of additional surgery.

• 3612

Myopic foveoschisis: OCT findings, surgical indications and results

GAUDRIC A
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ABSTRACT NOT PROVIDED

• 3613

Clinical and OCT outcomes for full-thickness and lamellar macular hole surgery

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Purpose Macular hole surgery has been long-established practice in vitreoretinal surgery and yet there is still controversy over its management especially around the value of postoperative face-down posturing on its outcome.Surgical indications for lamellar macular holes (LMH) are far more controversial.OCT has become the standard assessment tool for success evaluation and may even yield prognostic value.

Methods Review of current published literature regarding posturing vs. non-posturing for full-thickness macular holes (FTMH), surgery vs. observation in lamellar macular holes (LMH).

Results 21 studies investigating the effect of face-down posturing on the outcome of macular hole surgery were identified. 11 studies included a comparison group and were deemed suitable for inclusion in the meta-analysis. Of three RCTs, two suggested a benefit in larger holes but none demonstrated evidence of benefit in smaller holes. The lamellar macular hole group is much more heterogenous with some authors distinguishing between lamellar macular holes (LMH) and macular pseudoholes (MPH). Some morphological OCT changes, such as oedema, cystic spaces and lamellar holes were commonly seen in patients with epiretinal membrane (ERM). The presence or absence of an intact IS/OS layer may correlate with visual outcome.

Conclusion The field surgery is constantly changing even for what is considered standard surgery in macular holes. The trend towards postoperative posturing seems to recur, especially for macular holes larger than 400µm. CONSORT-adherent RCTs would be required to provide future guidance.Lamellar macular holes are still a poorly defined group with proponents and detractors in balance. The presence of concurrent ERM on OCT may tip the balance towards surgery.

• 3614

Morphology of surgical ILM-specimens in epiretinal membranes, macular holes, and diabetic retinopathy

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Purpose Myofibroblasts play a major role in the production of retractile phenomena causing contraction or shrinkage of the epiretinal membranes (ERM) in proliferative vitreoretinopathy and diabetic retinopathy. The purpose of our study was to evaluate the expression of myofibroblasts on epiretinal tissues in eyes with epiretinal membranes, diabetic macular edema (DME) or macular holes.

Methods Samples of ERM and ILMs (internal limiting membranes) following macular epiretinal membrane removal in eyes with diabetic maculopathy, refractory to conservative treatment, idiopathic epiretinal membrane and macular holes, were collected. Double immunofluorescence staining, with antibodies recognizing a smooth muscle actin (a-SMA) and fibronectin (ED-A FN) or vimentin in myofibroblasts, followed by confocal and electronic microscopy was performed.

Results a-SMA in association with either ED-A FN or vimentin were detected in all ERM specimens. a-SMA and ED-A FN were also detected in ILMs removed in cases of stage IV macular holes. ED-A FN was expressed in close relation to a-SMA–positive myofibroblasts, predominately located close to the border of the macular hole area. In all idiopathic ERMs, ED-A FN was expressed in close relation to a-SMA–positive myofibroblasts. In those cases, no a-SMA staining was observed in ILM specimens.

Conclusion Scanning electron microscopy indicated that active contraction mechanisms are always expressed in epiretinal macular membrane and underling ILM tissues in eyes with diabetic maculopathy and late stages of macular hole.ILM folding seems to be myofibroblast-independent in idiopathic epiretinal membrane cases.

• 3615

Vitrectomy with subretinal t-PA, gas tamponade and intravitreal ranibizumab for the treatment of submacular hemorrhage due to AMD

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Purpose This lecture aims to summarize what is known about the effect of vitrectomy with subretinal t-PA, gas tamponade and intravitreal anti-VEGF in the management of submacular hemorrhage in neovascular age-related macular degeneration.

Methods Submacular hemorrhage associated with neovascular age-related macular degeneration is a complication known to have potentially devastating effects on visual acuity. The exact incidence of submacular hemorrhage in patients with neovascular age-related macular degeneration is unknown, and risk factors for its occurrence ill defined. It is known, however, to be a relatively common problem and important because the visual prognosis of these patients is poor.

Results Multiple treatment modalities have been suggested including intravitreal anti-vascular endothelial growth factor injections, photodynamic therapy, pneumatic displacement with or without adjuvant intravitreal tissue plasminogen activator, and pars plana vitrectomy with or without adjuvant subretinal tissue plasminogen activator. However, there remains no consensus on optimal treatment, as clinical trials for neovascular age-related macular degeneration have excluded patients with submacular hemorrhage.

Conclusion Although the final visual outcome is often limited by progression of age-related macular degeneration, significant and stable visual recovery is possible in selected eyes. Prospective clinical trials are needed to clarify the role for vitrectomy/tPA/gas/anti-VEGF and to provide definitive outcome comparisons with other management approaches.

• 3631
Gene therapy approaches in corneal pathologies

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Purpose This lecture will provide an overview over past and current gene therapy approached to treat corneal pathologies.

Methods The presentation will include both viral and non-viral gene transfer strategies and will present data from the authors and other research groups.

Results Depending on the carrier transduction rates of corneal cells vary. However, outcome has ben promising, also during corneal storage and after corneal transplantation.

Conclusion Gene therapy to the cornea is a relatively new but promising field.

• 3632
Nanoparticles for drug delivery

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Purpose To test dorzolamide cyclodextrin microparticle eye drops applied once a day (QD)for intraocular pressure control,compared with Trusopt® 3 times a day (TID).

Methods Self aggregating cyclodextrin microparticle eye drops (DorzNP) containing 3% dorzolamide were formulated. The effect of the DorzNP eye drops QD was compared to Trusopt® TID in a prospective randomized single masked crossover trial over 24 hours. Seventeen healthy volunteers with intraocular pressure (IOP) over 18 mmHg were recruited. IOP was measured with an Icare tonometer pro and each patient underwent full eye examination.

Results DorzNP eye drops QD and Trusopt® TID lower IOP in a similar manner. At no time point was there a significant difference in IOP between the two groups. The peak effect in both groups was at 4 hours: In the DorzNP group IOP decreased from 21.7 ± 2.4 mmHg at baseline to 17.9 ± 3.9 mmHg, which is 3.8 ± 2.6 mmHg and 18% IOP decrease. In the Trusopt® group IOP decreased from 20.9 ± 2.2 mmHg at baseline to 17.9 ± 3.3, at 4 hours which is 3.1 ± 3.7 mmHg ,14%, (p = 0.97 between groups) IOP drop. At trough at 24 hours the IOP drop was 1.4 ± 2.8 (6%) in DorzNP eyes and 1.5 ± 2.0 (7%) in Trusopt eyes (p = 0.23).Burning in DorzNP eyes on the scale 1-100 was 12±15 and in Trusopt® eyes 37±30 (p=0.0038). Vision aquity and redness did not differ between the two groups

Conclusion The results suggest that once a day dorzolamide nanoparticle eye drops have a similiar effect on intraocular pressure as Trusopt® applied 3 times a day. The dorzolamide microparticle eye drops are well tolerated, less burning than Trusopt®and significantly reduce intraocular pressure.

Commercial interest

• 3633
Recombinant NFG for treatment of ocular surface diseases

BONINI S
Rome

ABSTRACT NOT PROVIDED

• 3634
SEGRAs a new therapeutic option on the horizon?

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Fifty years after their initial clinical use glucocorticoids (GC) are still the most important and most frequent used anti-inflammatory agents in the treatment of acute and chronic inflammatory diseases. Unfortunately the anti-inflammatory and immunosuppressive effects of GC are frequently accompanied by undesired side effects. Beside unknown individual factors, recent investigations have idientified molecular mechanisms of GC action that may reveal new antiinflammatory agents with a better effect/side effect profile.The effect of GC on target cells is mediated by the regulation of transcription of steroid-responsive genes. After binding to cytosolic glucocorticoid receptors (GR) the complex translocates into the nucleus and modulates gene transcription either by a positive (transactivation) or negative (transrepression) mode of regulation. There is growing evidence that beneficial effects as well as undesired effects are related to the dissociation of these two major mechanisms, e.g. steroid diabetes and steroid induced glaucoma seems to be mainly related to transactivation mechanisms.The dissociation of these mechanisms has recently led to the development of new agents that may predominantly induce transrepression over transactivation and subsequently lead to potent anti-inflammatory effects while displaying less dominant side effects. Indeed, transgenic mice carrying a defective GR could demonstrate the anti-inflammatory potential of transrepression. The purpose of this presentation is to provide an up-date on recent developments in this field.

• 3635

Synthetic eye prosthesis

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Purpose Development of synthetic eye prosthesis to provide a long term stable keratoprostesis

Methods Synthetic hydrophobic and hydrophilic biomaterials were selectively modified by physical and chemical nanotechnological methods. The modified biomaterials were tested in cell culture experiments (fibroblasts L929 and primary epithelial cells, porcine) and implanted into rabbits eyes. The hydrophobic material was implanted finally into eyes of ultima ratio patients.

Results After very successful in vitro evaluation, keratoprostheses were implanted to rabbit eyes (New Zealand white rabbit) and showed excellent in vivo performance in the animal experiment.As for the hydrophibic material, no adverse reaction was observed after follow up of 2.5 years in human eyes.

Conclusion We could develop a new keratoprosthesis which is well tolerated in human eye.

• 3641

Translating ocular immunology from the laboratory to the clinic - keratoplasty -

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Keratoplasty has definitely its paradoxes. It has been the first successful transplantation in man and is with approx.100.000 grafts/year easily the most frequent allograft in human medicine. At the same time it is still the least understood form of transplantation in respect to its biology. It is both, the most successful as well as probably the most underestimated procedure regarding its risks in clinical transplantation. Indeed, the common assumtion, that corneal transplantation is a safe procedure with good prognosis may have hindered more intensive effort of research in this field. There are still limitations to corneal transplantation, and allograft rejection still poses the greatest challenge. In the last two decades, graft survival has been greatly improved by the introduction of efficient immunosuppressive drugs. This lecture aims to highlight the most novel and successful strategies to achieve a better outcome of pkp and e.g. tolerance via induction of Tregs. In addition, the use of lamellar grafts (e.g. DMEC) has significantly changed our perception and will be discussed.

• 3642

Exploiting the immune response to halt progression of ocular melanoma

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Purpose The purpose of this study was to characterize the requirements for spontaneous rejection of tumors transplanted in the anterior chamber (a.c.) of splenectomized mice as a first step toward identifying how to harness the immune reponses to eliminate intaocular tumors.

Methods Luciferase expressing E.G7-OVA (Luc E.G7) tumors were injected in the a.c. of the eye of wildtype, CD8 depleted, perforin deficient, IFNγ deficient, IFNγ receptor 1 deficient (IFNγR1), or inducible nitric oxide synthase (NOS2) deficient mice that were splenectomized or left untreated prior to tumor challenge. In some experiments intraocular macrophages were depleted by subconjunctival administration of clodronate liposomes. Luc E.G7 tumor growth was measured by bioluminescent imaging using an IVIS imager. Tumor-specific OT-I CD8+ T cells were monitored in vivo by flow cytometry.

Results Luc-E.G7 tumors grew progressively in the a.c. of nonsplenectomized mice but were spontaneously rejected in splenectomized mice. Rejection of ocular tumors in splenectomized mice required CD8+ T cells, macrophages, IFNγ and IFNγR1 expression by host cells. Infiltration of ocular tumors by CD8+ T cells and their expression of IFNγ were equivalent in splenectomized and nonsplenectomized mice. Perforin expression and nitric oxide production were not required for rejection of intraocular tumors.

Conclusion These data suggest a model of ocular tumor regression in splenectomized mice in which CD8+ T cells express IFNγ to induce nitric oxide-independent tumoricidal activity within intratumoral macrophages. Therefore, restoring tumoricidal activity in intratumoral macrophages is critical for CD8+ T cell mediated elimination of ocular tumors

• 3643

Regulatory T cell therapy for uveitis

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New therapeutic strategies, including novel generation of immunosuppressors and biologic agents are currently available for the management of noninfectious uveitis. However, adverse events remain an important issue to consider and other options need to be evaluated. We have previously controlled experimental autoimmune uveoretinitis by administrating activated polyclonal regulatory T cells (T-regs) intravitreally. Based on these preliminaru results, a clinical study has been initiated to evaluate the safety and efficacy of this approach in patients with uveitis and low vision. Tolerance and efficacy will be monitored with clinical examination, laser flare photometry and imaging. Intraocular levels of pro and anti-inflammatory cytokines will be determined in each patient at baseline and after T-reg administration. Cell therapy may become an interesting strategy, expanding the anti-inflammatory armamentarium.

• 3644

Immunological aspects of age-related macular degeneration: implications for treatment

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Purpose To review immunological aspects of AMD with implications for treatment

Methods literature review and personal collaborative studies

Results As inflammation is recognized to play a role in AMD pathogenesis, systemic and local anti-inflammatory therapies have been recently used for disease prevention and/or in combination with anti-VEGF medications for the treatment of exudative/neovascular disease. Several small AMD clinical trials have demonstrated potential benefits of immunomodulatory medications such as corticosteroids, non-steroidal anti-inflammatory drugs (NSAID), immunosuppression (methotrexate and sirolimus), and biologics (infliximab and daclizumab); ongoing studies are now investigating complement component inhibitors.

Conclusion Since inflammation is only one component of most retinal diseases, current anti-inflammatory therapies merely provide palliative treatment. Further investigation of adverse effects and long-term follow-up on the anti-inflammatory medications are warranted.

• 3651

Individual ONH blood flow patterns during changes in perfusion pressure

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Purpose Abnormal optic nerve head (ONH) blood flow autoregulation has been implemented in the pathogenesis of glaucoma since decades. In fact, however, the regulation of ONH blood flow is poorly characterized and the mechanisms of autoregulation remain obscure.

Methods Several studies were performed to investigate the behavior of ONH blood flow during changes in perfusion pressure in healthy subjects. In all these studies laser Doppler flowmetry was used to measure ONH blood flow. Interventions included squatting and handgripping to increase ocular perfusion pressure and use of a sclera suction cup to reduce ocular perfusion pressure.

Results During both an increase and a decrease in perfusion pressure the ONH shows some autoregulatory capacity. Data during combined change in arterial pressure and venous pressure indicate that ONH blood flow is not only dependent on the level of perfusion pressure but also on the absolute levels of pressures in the arterial and venous tree. In addition, there is a wide inter-individual variability in the responses. In some subjects a temporal reduction in ocular perfusion pressure is associated with a pronounced decrease in ONH blood flow.

Conclusion Regulation of ONH blood flow is more complex than previously thought. Some subjects show pronounced ischemia during fluctuations in ocular perfusion pressure. Whether this pre-disposes to ONH disease remains unclear.

• 3652

Metabolism in glaucoma using retinal oximetry

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Collaborative studies between the Ophthalmology departments in Leuven and Reykjavik have shown that in glaucoma patients, venous oxygen saturation increases with increasing severity of disease (i.e. with worsening visual field). Patients with considerable visual field loss show higher venous oxygen saturation than healthy individuals, while glaucoma patients with mild visual field loss have saturation similar to normal. Moreover, severe glaucomatous damage was associated with increased oxygen saturation in the retinal venules and decreased AV-difference in retinal oxygen saturation. Finally, a positive correlation between the changes in AV difference and structural changes at the level of the optic disc and nerve fiber layer was found using HRT parameters (rim area, retinal nerve fiber layer thickness). The increase in venous saturation with increased visual field damage may be a consequence of tissue atrophy and less oxygen consumption. Longitudinal studies of glaucoma patients are needed to determine how retinal venous oxygen saturation is related to progression.

• 3653

Spontaneous venous pulsation revisited - relevance to glaucoma?

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Lisboa

Purpose Purpose: Address the clinical significance of spontaneous venous pulsation (SVP) assessment in glaucoma patients.

Methods Methods: Review of the existing literature on the subject, including own published data. Emphasis on studies that have analyzed this phenomenon using OBF studying technologies.

Results Results: Threshold conditions for SVP detection are different in healthy and in glaucoma patients. The variables involved in SVP generation may have a different threshold in normal tension glaucoma (NTG) than the one seen in primary open-angle glaucoma (POAG) patients. Hemodynamic patterns in POAG reveal a selective venous disturbance in patients lacking SVP, while NTG patients have both arterial and venous changes in their central retinal vessels. Clinically, patients with NTG without a visible SVP have a higher functional damage than their SVP-positive counterparts.

Conclusion Conclusions: The lack of SVP in NTG patients may not only represent a more advanced condition, but also both an arterial and venous dysregulation. More studies are needed to validate these findings.

• 3654

From retinal venous pressure to intra-cranial pressure in glaucoma

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The blood pressure in the central retinal vein is supposed to be at last as high as the orbital cererbospinal fluid pressure (CSF-P) plus a hypothetical trans lamina cribrosa outflow resistance-related pressure. The central retinal vein pressure can non-invasively be estimated by modified ophthalmodynamometry. The talk will present results of clinical studies in which ophthalmodynamometry was used to estimate the orbital (and intracranial) CSF-P and to estimate the orbital tissue poressure. The findings could be helpful for the discussion whether an abnormally low CSF-P is associated with glaucomatous optic neuropathy

• 3661

The LDL receptor in the retina: the missing link in aging, the new target in dietary prevention

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Purpose The discovery of the LDL receptor (LDLR) in 1985 by Brown and Goldstein was awarded by a Nobel Prize. The LDLR has initially been identified for its role in mediating the endocytosis of LDL particles in the vascular endothelium. The deposition of lipids, including cholesterol and cholesteryl esters in Bruch's Membrane in the one hand, and in the vessel intima in the other hand, is one of the common features of age related macular degeneration (AMD) and cardiovascular disease (CVD). Dietary habits with high intakes of omega 3 long chain fatty acids (LCFA) have been associated with AMD prevention. Similar effects have been demonstrated in CVD prevention. The mechanisms behind this association in AMD remain partly unknown.

Methods The present paper highlights our recent findings on the pivotal role of LDLR in aging of the retina, and modulation of LDLR expression by dietary omega 3 LCFA.

Results In a humanized mouse, we have shown that the lack of LDLR was associated with the presence of the main characteristics of aging of the human retina: fundus autofluorescence, deposition of cholesteryl esters in Bruch's Membrane, and impairment of the retinal function. We further questioned whether following the dietary guidelines on omega 3 LCFA would modulate gene expression, including LDLR. Expectedly, we found that increasing the intake in omega 3 LCFA and lowering linoleic acid increased LDLR expression and improved the incorporation of omega 3 LCFA.

Conclusion Altogether, our data are consistent with the crucial importance of LDLR in the aging process in the retina. We also strongly support the idea that the modulation of LDLR expression is one of the mechanisms of the preventive effects of omega 3 LCFA in AMD.

• 3662

Aflibercept in clinical practice: Evaluation of the first 50 patients treated with antiVEGF trap for age-related macular degeneration

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Purpose To evaluate the short-term outcomes after intravitreal aflibercept (Eylea; Regeneron Pharmaceuticals, Inc.) injection in a general clinic population treated for neovascular age-related macular degeneration (AMD).

Methods This is aretrospective chart review of consecutive patients who received intravitreal aflibercept injection for AMD. The main outcome measures were mean visual acuity (VA), central macular thickness, presence of subretinal fluid, cystic changes and pigment epithelial detachment on optical coherence tomography (OCT).

Results Sixty-three eyes of 52 patients (mean age 81.2, range 59-98years) were evaluated. Mean baseline visual acuity was 0.79 LogMar (STDEV 0.43)at baseline and 0.66 at follow-up(STDEV 0.48) ($P = 0.43$). Mean follow-up was 1 to 4 month (average 1.7). Mean baseline central macular thickness was 352 microns and improved to 257 microns at 3 months ($P < 0.001$) in patients who had at least 3 months of follow up. 39 patients (75%) were treated with monthly injections, the remaining patients were treated based on a "treat and extend" protocol. Treatment was well tolerated with no adverse events reported.

Conclusion Short-term results of aflibercept therapy showed encouraging results with improvement in OCT parameters. Patients who underwent antiVEGF treatment with other medications prior the use of aflibercept may stabilize but not further improve after short-term treatment with aflibercept. Further studies are needed to assess the effect of aflibercept in patients who are not treatment naïve.

• 3663

Lutein decreases complement factor D in age-related macular degeneration

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Purpose The complement system plays an important role in the pathogenesis of Age-related Macular Degeneration (AMD). In this study we examined the effect of lutein on circulating levels of Complement Factor D (CFD), a rate limiting component of the alternative pathway of complement activation.

Methods Blood samples were collected from 82 early AMD patients from The Netherlands and the UK that took part in a one year multi centre, double masked, placebo controlled intervention trial with lutein supplementation. CFD was measured by ELISA.

Results We found a significant 0.12 µg/ml monthly decrease in serum CFD concentration in the lutein group ($p<0.001$), resulting in a 61% decrease from 2.33 µg/ml at baseline to 0.91 µg/ml at 12 months. We found no change in the placebo group.

Conclusion Lutein supplementation markedly decreases circulating CFD levels thereby offering a simple method to control the alternative complement pathway.

• 3664

Relevance of complement factor H polymorphisms in the response to intravitreal bevacizumab in exudative age-related macular degeneration

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Purpose There is increasing evidence that the complement system, in particular the complement factor H (CFH) plays a significant role in the pathogenesis of age-related macular degeneration (AMD). Over the last decade the use of antibodies against vascular endothelial growth factor has revolutionized the therapy for exudative AMD. However, about 10 to 15% of the patients seem to be poor- or non responders and do not profit from such treatment. The present study investigated whether treatment outcome of intravitreally administered bevacizumab is dependent on 6 common CFH polymorphisms.

Methods In this prospective cohort study 185 eyes of 141 treatment naïve patients with exudative AMD were included. Study eyes were injected with bevacizumab using the as needed regimen. At each follow up visit a complete ophthalmic examination as well as optical coherence tomography was carried out. CFH polymorphisms for rs1061170, rs393955, rs800292, rs1329428, rs1410996 and rs3753394 were determined using real-time PCR. Visual acuity outcome, number of injections and overall time of treatment were analyzed in dependence of the CFH genotype.

Results Patients received up to 15 injections with bevacizumab and the respective total treatment period ranged from 42 to 1182 days. Neither visual acuity, number of treatments nor duration of treatments correlated with any of the 6 CFH polymorphisms.

Conclusion None of the investigated polymorphisms of the CFH gene seem to play a statistically significant role regarding treatment success of bevacizumab in patients with exudative AMD.

• 3665

A randomized observer and subject masked trial comparing the visual outcome after treatment with ranibizumab or bevacizumab in patients with neovascular age-related macular degeneration

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Purpose The western world health care systems are confronted with an increasing burden of patients suffering from age-related macular degeneration (AMD). Anti-VEGF therapy revolutionized the treatment of exudative AMD, but is associated with high costs. This study seeks to compare the treatment effects of ranibizumab and bevacizumab on best corrected distance visual acuity (BCVA) in Austrian patients with neovascular AMD.

Methods This was a prospective, randomized, double blind, multicenter study. Ten clinical trial centers in Austria participated in this one year lasting study and included 321 treatment naïve patients suffering from neovascular AMD. Patients were randomized for treatment with bevacizumab or ranibizumab receiving a loading dose of three consecutive monthly intravitreal injections, followed by monthly treatment as needed.

Results No significant differences were seen in BCVA between ranibizumab (n = 167) and bevacizumab (n = 154) groups. At one year bevacizumab was equivalent to ranibizumab (p=0.78 between groups). This was also not significant when adjusted for age or baseline BCVA. Also the gain and loss of 5 or 15 letters in BCVA showed no significant difference between treatment groups. Finally the analysis of serious adverse events (SAE) revealed no significant difference between the two groups, although SAEs were slightly more in the bevacizumab group.

Conclusion The findings of this study showed no significant difference at one year between the two drugs used in an as needed manner, which displays todays most widely spread treatment regimen. The drugs showed similar efficacy and safety in the Austrian population.

• 3666

Retrospective analysis of the real-world utilization of ranibizumab in wAMD

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Purpose With monthly ranibizumab treatment for wet AMD (wAMD), optimal functional outcomes are achieved. To reduce management burdens, as-needed dosing regimens have been explored. AURA study examines real-world utilization of ranibizumab.

Methods Retrospective, international (Canada, France, Germany, Ireland, Italy, Netherlands, UK, Venezuela), non-interventional, observational study. Target enrollment is 444 patients per country and will be completed by September 2012. Consecutive AMD patients prescribed ranibizumab by their physicians will be included, with a follow-up period of up to 2.5 years. Primary outcomes are (1) change in visual acuity and (2) resource utilization (number of treatment and monitoring visits, treatment use). Descriptive statistics will be used.

Results Results for Germany are already available: 916 patients from 28 sites were screened. Of these, 462 (50.4%) were not enrolled. The reasons (not mutually exclusive) included no written informed consent (n=349), consent obtained after target patient number reached (n=68), use of non-conventional interventions (n=21), ranibizumab use did not start between January-August 2009 (n=23), and no wAMD diagnosis (n=6). Of the 454 enrolled, 437 (96.3%) received ≥1 ranibizumab dose. Of the 437, most were women (n=260, 59.5%), Caucasian (n=368, 84.2%), and initiated treatment at ≥75 years of age (n=304, 69.6%). Mean age was 79.2±8.1 years.

Conclusion These data will provide valuable insight into resource utilization patterns and their effects on visual outcome in various ranibizumab-treated wAMD patient populations.

Commercial interest

• 3671
Diagnosis and treatment of vernal conjunctivitis

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Purpose Kératoconjunctivitis in children is a rare and severe ocular surface pathology. Two main clinical forms need to be recognized, from mild to severe, however vernal kératoconjunctivitis is the more common of these severe ocular surface impairment. The treatment must be corticoid- sparing to avoid sight-threatening iatrogenic complications.

Methods Diagnosis has to consider onset of the disease with clinical signs. The eyelid and limbal forms occurs in different population. The evolution of the disease usually resolve after adolescence but some severe cases transform into atopic keratoconjunctivitis of the adult.

Results The treatment aims to eyelid hygiene, anti-allergic treatment and topical steroid sparing. Place of topical cyclosporine with analyze of literature and clinical cases, is discussed.

Conclusion Eyelid hygiene, topical and sometimes systemic anti-allergic, topical cyclosporine treatments are essential in vernal keratoconjunctivitis for a better quality of life of the children. The careful following is also essential for a safe ocular surface and vision preservation.

Commercial interest

• 3672
Cutaneous and ocular signs of childhood rosacea

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Purpose To describe the clinical features of cutaneous and ocular manifestations of childhood rosacea, to propose diagnostic criteria, and to emphasize the possible severity of ocular complications in this age group.

Methods Children aged 1 to 15 years who had received a diagnosis of cutaneous and/or ocular rosacea and were seen between January 1, 1996, and December 31, 2011.

Results Of 20 patients, 11 had ocular and cutaneous rosacea, 6 had isolated cutaneous involvement, and 3 had isolated ocular involvement. Dermatologic examination results were sufficient to diagnose rosacea in 12 of the patients (60%). The most common presentation was a papulopustular eruption on a telangiectatic background. In 11 patients (55%), ocular involvement preceded the skin eruption. Among the ophthalmologic manifestations, chalazions and blepharoconjunctivitis were the main presenting symptoms; keratitis was observed in 4 patients and corneal ulcers in 2. Ten patients were treated with oral metronidazole. Intermittent treatment for at least 3 months was used to avoid neurologic toxic effects and to achieve complete remission.

Conclusion Although rare, childhood rosacea should be recognized because of the possible severity of ocular involvement.

• 3673
The indications of cyclosporine A in children's ocular surface diseases

DOAN S
Paris

ABSTRACT NOT PROVIDED

• 3674
Limbal stem cell deficiency in children

YEUNG A
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ABSTRACT NOT PROVIDED

• 3675

Noninvasive assessment of the tear film stability in children

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Purpose To evaluate tear break-up time (BUT) with repeated higher order wavefront aberrations (HOA) measurements in children with Meibomian Gland Dysfunction(MGD).

Methods Wavefront aberrations up to the sixth order for a 4-mm pupil were measured in 10 normal children (Group 1) and 10 children with severe MGD (Group 2) with corneal involvement, using the IRX3 (Imagine Eyes, Orsay, France) Hartmann-Shack (H-S) aberrometer. The aberrometry was performed once every second for up to 20 seconds. HOA measurements were performed 3 times in a row. HOA variations were compared with the BUT by the conventional fluorescein method (CFM°.

Results There was an excellent correlation between the HOA variation and the BUT recorded by the CFM in both groups. There was also an excellent reproducibility of the HOA measurements in all patients. BUT was significantly decreased ($P<0.005$) in all children in Group 2 compared to the normal tests subjects(Group 1).

Conclusion HS aberrometry is a non ivasive method, that has been used for the last decade for the assessment of the quality of vision in patients undergoing refractive surgery and cataract or clear lensextration. Studying the HOA variation is a valuable method for evaluating both the quality visionand the BUT in children with MGD.

• 3681
RUNX2 expression in conjunctival melanocytic proliferations

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Purpose Amplification of RUNX2 (6p21.2), a transcription factor involved in bone formation and in tumor progression of prostate and breast cancer, has previously been identified in 76% (16/21) of primary conjunctival melanoma and in 100% (4/4) of metastatic conjunctival melanoma. The aim of this study was to investigate RUNX2 expression at the protein level in a panel of conjunctival melanocytic proliferations

Methods Expression of RUNX2 was assessed by immunohistochemistry in 26 conjunctival naevi (14 compound naevi, 11 subepithelial naevi and 1 cellular blue naevus), 13 PAM (9 PAM with atypia) and 25 conjunctival melanoma. Statistical analysis was performed with JUMP 8,0 software. Expression was regarded as negative if less than 10% of the tumor cells expressed RUNX2. Examination was independently assessed by two observers.

Results RUNX2 was found in 3 naevi (11,5 %), in one PAM with atypia (7,6%) and in 5 melanoma (20 %) without significant variation between the 3 groups. In the melanoma group, there was no correlation between RUNX2 expression and TNM category, depth of invasion, proliferation index (Ki67), local lymphatic invasion and the presence of metastasis. There was however a significant correlation between RUNX2 expression and death (p=0,0191).

Conclusion RUNX2 is expressed in a limited number of conjunctival melanocytic proliferations without significant differential expression between benign and malignant lesions. The biological significance of RUNX2 in conjunctival melanoma tumor progression requires further functional investigations.

• 3682 / S005
Valproic acid (VPA), a class I and II histone deacetylase (HDAC) inhibitor and conjunctival melanoma

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Purpose To investigate the expression of histone deacetylases (HDACs) in human conjunctival melanoma (CM) cell lines and primary melanocytes, and assess the effects of VPA, a broad Class I and II HDAC inhibitor, on cell viability and growth.

Methods CM cell lines (CRMM1 & 2; CM2005.1) and primary melanocytes were immunolabelled with antibodies to HDACs: Class I (HDAC1, 2 and 3), Class IIA and IIB (HDAC4 and HDAC6), and Class III (SIRT2). Antibody localisation was visualised with immunofluorescence and confocal microscopy. Dose-response and proliferative potential following treatment with VPA was assessed for up to 72hrs using MTT and colony assays, respectively Cell cycle dynamics were also assessed.

Results Differential HDAC expression was observed in CM cells and melanocytes, for both immunolocalisation (nuclear vs cytoplasmic) and cell type. CM2005.1 cells displayed lower level expression of HDACs compared to CRMM1 and 2 cells. VPA IC50 (72hrs) was 3.75mM, 5.42mM and 8.33mM for CRMM1, 2 and CM2005.1 cells, respectively. Colony assays showed similar patterns of response, with surviving fractions 0.2 and 0.5 for CRMM1 (VPA 0.3125mM) and CRMM2 (VPA 2.5mM) respectively. Cell cycle analysis showed dose-related G1 block for CRMM1 and G2 block for CRMM2 cells at 24hrs (0mM to 1.25mM VPA).

Conclusion Overall, CM2005.1 cells are more resistant to VPA compared to CRMM1 and 2 cells. VPA inhibition of CM cell growth and proliferation may be related to the observed differential expression of HDACs between cell lines. Combination therapies using VPA and other HDAC inhibitors may be potentially useful in managing the growth of primary CM. Supported by Sydney Foundation for Medical Research.

• 3683
Macrophage markers and C3d in the central & peripheral choroid of young, aged and amd eyes

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Purpose To investigate the distribution and expression of macrophage phenotypes and the complement activation protein, C3d, in human choroid/retina in young, aged and AMD eyes.

Methods Paraffin sections of central and peripheral choroid/retina from young (<40 years, n=6), aged (>70 years, n=4) and AMD (>70 years, n=8) human post-mortem eyes were co-immunolabelled with antibodies to leukocyte and macrophage markers (CD68, CD163, Iba1 & CD45) and complement activation component, C3d. Localisation and distribution of antibodies was assessed using confocal microscopy. Counts of macrophage sub-populations were compared in central and peripheral choroid for each group.

Results Heterogeneous populations of macrophages were found in the choroid/retina of all groups. Iba1+ and CD45+ retinal microglia and macrophages, and choroidal macrophages were observed in all eyes. In AMD eyes, Iba1+ and CD45+ cells were seen in the subretinal space amongst photoreceptors, as well as in inner retina. Compared to young eyes, aged and AMD specimens showed increased numbers of CD163+ macrophages (M2, proangiogenic) in choroid, and in central vs peripheral retina. Fewer CD68+ cells were seen in all specimens, regardless of age or location. C3d was expressed in young, aged and AMD eyes, localised to Bruch's membrane and choriocapillaris, with more extensive immunostaining in aged and AMD eyes. C3d was also seen in drusen in aged and AMD eyes, and more peripherally, compared to young eyes.

Conclusion Age-related changes in macrophage phenotypes and in complement pathway activation at the choroidal/retinal interface may play a role in development and progression of AMD.Supported by Sydney Foundation for Medical Research.

• 3684
Ophthalmological manifestations of IgG4-related disease

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Purpose Ig4-related disease is a recently defined entity characterized by a mono or multi organ lymphoplasmocytic infiltrate with IgG4+staining (IgG4+/IgG+ cell ratio>40%), associated with fibrosis or sclerosis and elevated IgG4 serum rate over 135mg/dL.Purpose is to determine the ophthalmological and histological features of IgG4-RD, and to analyse the outcome under treatment.

Methods Patients with biopsy-proven IgG4-RD, seen between 2009 and 2011 in a single tertiary center, were retrospectively reviewed. Clinical manifestations, biological and radiological results, histological features and outcome under treatment were analyzed.

Results Three caucasian women were included. Mean age was 58 years (range :50-63). One patient presented with unilateral painful propotosis, associated with third and fifth cranial nerve palsy. One patient had recurrent anterior scleritis, and one patient presented with chronic conjonctival inflitration. None of them had extra-ocular involvement (FDG-PET-scan). Other inflammatory conditions were ruled out. Histopathology demonstrated lymphoplasmocytosic proliferation with expression of IgG4+ plasma cells over 40%. IgG4 serum rate was elevated in one case. All patients primary responded to corticosteroids but 2 of them required the adjunction of an immusuppressive drug(fibrosis or relapse).third one presented with epithelial carcinoma.

Conclusion IgG4-RD is a new and rare entity, challenging to diagnose in case of isolated orbital involvement or in atypical features, such as conjonctivitis and scleritis Histopathology is the gold-standard for diagnosis if appropriate staining is performed. Treatment is controvertial : corticosteroids are the mainstay, but many cases require associated immunosuppressors.

• 3685 / S020
Idiopathic orbital inflammation: a report of 18 cases

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Purpose Idiopathic orbital inflammation is a rare clinical entity which has protean clinical manifestations. It's a diagnosis of exclusion which imposes a biopsy, and which can be made only after a screening to rule out a systemic etiology of inflammation.

Methods Retrospective series of 18 histologically-proven orbital inflammation cases seen in our service between 2006 and 2011.

Results The study encompassed 7 men and 11 women, with a mean age of 47 years old (4-83). Patients complained of a pain (44%), a diplopia (33%), a decreased visual acuity (17%). A swollen eyelid or a palpable mass were presents in 78% of the cases. Less often, we noted proptosis, or a diminished ocular motility. The radiologic analysis (CT-scan, NMR, doppler ultrasound examination) found an inflammation localized to the orbital fat, to the lacrymal gland, and to one or several oculomotor muscle(s) in respectively 89%, 67%, and 39% of the cases. Excisional biopsy was curative for 33% of the cases. 61% of the patients received a corticotherapy, with a relapse or a recurrence in 60% of the cases, making necessary to have recourse to immunosuppressive agents (methotrexate), with a good control rate on the inflammation (75%). Finally, 76% of the patients obtained a complete resolution of their symptoms at the end of the follow-up (mean : 20 months).

Conclusion Treatment lies on surgical exeresis if it is safely. Corticotherapy is frequently not sufficient. Methotrexate seems to be an interesting alternative. Recent works concentrate on Systemic IgG4 Disease, who could be a frequent cause of orbital inflammation, calling the term "idiopathic" into question, and letting us think about targeting treatments.

• 3686 / S021
A patient with eyelid and anterior orbital myeloproliferative hypereosinophilic syndrome

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Purpose the aim of the study is to evaluate the clinical- and histopathological discrepancy of the inflamed eyelid/anterior orbital mass features

Methods case report and literature review

Results the clinical picture revealed an erythemaous eyelid-skin inflamed mass without effect on local and general antibiotic treatments . The histopathological "diagnoses was made as "chalazion material". However the mass was superior located from the tarsus pre- and intraseptal with a lot of eosinophilic cell in the pathological material; where the patient already was known with a pulmonal myoblastic hypereosinophilic disease and treated with hydrea with the extra feature of a red face

Conclusion knowledge of the systemic disease of a patient and the precise location of a pathologic ophthalmic process is important to made the definitive diagnosis. In difficult processes it is always necessary that pathologist and ophthalmologist consulted each other and made together the end conclusion

• 3687 / S022
Congenital orbital teratoma

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(3) Institute of Pathology, Sheba Medical Center, Tel Hashomer
(4) Department of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer

Purpose Congenital orbital teratoma is a rare tumor, composed of all three germ cell layers. The purpose is to present a case with congenital orbital teratoma, and discuss the clinical and histological characteristics of the tumor.

Methods Case report of a newborn girl that had a protrusion of the right globe. Imaging disclosed a big intraorbital lesion and capillary hemangioma was suspected, but treatment with propranolol had no effect during 4 months. At the age of 5 months acute progression of the proptosis developed with enlargement of the orbital mass as seen on MRI, pressing on the optic nerve. She underwent surgery and the lesion was removed completely using a cryo-probe.

Results The pathologic diagnosis was orbital teratoma including cysts filled with keratin, hair follicles, glands, bone, cartilage, epithelium and neuronal-brain tissue. On follow-up examination there was no proptosis but some limitation of ocular movements was seen one month after surgery.

Conclusion In order to diagnose clinically orbital teratoma, a high index of suspicion is needed. Surgical excision is the treatment of choice. Early detection and treatment is important in order to prevent mechanical destruction of adjacent tissues.

• 3811
Role of laser

CONRATH J
Marseille

ABSTRACT NOT PROVIDED

• 3812
Role of corticosteroids

BANDELLO F
Milano

Purpose Diabetic Macular Edema (DME) management has been revolutionized by the advent of intravitreal approach. Ain of the presentation is to describe the results of the most important studies about intravitreal corticosteroid therapy for DME.

Methods Critical analysis of the most recent trials on the use of intravitreal corticosteroids for the treatment of DME.

Results Most promising findings can be obtained from trials employng dexamethasone and fluocinolone acetonide. Nevertheless, complication rates, (especially bearing in mind intraocular pressure rise, and cataract) may limit the practical spread of this approach.

Conclusion Long-term trial will help define the best treatment algorithm for each form of DME.

Commercial interest

• 3813
Role of anti-VEGF

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Purpose To assess safety and efficacy of intraocular injections of anti-VEGF in patients with diabetic macular edema (DME)

Methods The gold standard for treatment has been laser coagulation. Limitations of this therapy are refractive DME, ischemic diabetic maculopathy and complications after laser application. The need for a non-destructive and effective strategy has led to investigations regarding VEGF inhibitors for reduction of vessel leakage and edema formation. Critical analysis of the most recent trials on the use of intravitreal anti-VEGF will be discussed for the treatment of DME.

Results For DME, intravitreal pegaptanib and bevacizumab have shown beneficial short-term effects on both visual acuity and retinal thickness. Most recent datas concern the use of ranibizumab and will be detailled. Incidence of ocular adverse events are consistent with prior clinical trials of ranibizumab across multiple retinal diseases. VEGF-trap study will be reported.

Conclusion New therapeutic approaches based on intravitreal injections of anti-VEGF molecules offer new hope for the management of diabetic macular edema. However, randomized studies are needed in order to attest longterm safety and efficacy profiles.

• 3814
Role of vitrectomy

WOLFENSBERGER T
Lausanne

ABSTRACT NOT PROVIDED

• 3815

Case presentation

MASSIN P
Paris

ABSTRACT NOT PROVIDED

• 3821

Incidence of tears and retinal detachments after macular surgery according to the depression of the vitrectomy cutter

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Purpose To study the incidence of tears and rhegmatogenous retinal detachments (RD) after macular surgery, according to the vacuum settings during vitrectomy.

Methods Comparative retrospective study of rhegmatogenous complications occurring during and after vitrectomy between 2 groups of consecutive patients. Group G400, included 1432 eyes vitrectomized with a maximum flow set at 4 ml / min and a maximum vacuum at 400 mm Hg. Group G230 included 434 eyes operated with the same flow rate with vacuum limited at 230 mm Hg. All patients were operated between November 2000 and June 2010, by two experienced surgeons.

Results The incidence of tears observed during surgery was 5.1 % for G400, versus 3 % for G230 (p = 0.01). The incidence of postoperative RD was 3.2 % for G400, versus 1.2 % for G230 (p = 0.02). The mean duration before the occurrence of RD was 73.3 + 98.5 days in G400, versus 21.6 + 16.3 days in G230 (p = 0.004).

Conclusion The incidence of tears observed during surgery was 5.1 % for G400, versus 3 % for G230 (p = 0.01). The incidence of postoperative RD was 3.2 % for G400, versus 1.2 % for G230 (p = 0.02). The mean duration before the occurrence of RD was 73.3 + 98.5 days in G400, versus 21.6 + 16.3 days in G230 (p = 0.004).

• 3822

Outcomes of macular hole surgery in highly myopic eyes : a case-control study

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Purpose To evaluate the outcomes of macular hole (MH) surgery in highly myopic eyes and to compare these results with controls.

Methods The study design was a matched, case-control, retrospective chart review. Ninety-four eyes who underwent vitrectomy with internal limiting membrane removal for a MH without retinal detachment were included. Group 1 included 47 consecutive eyes with high myopia and group 2 included 47 control eyes operated on the same period and matched for MH size. The main outcomes were preoperative and postoperative best-corrected visual acuity (BCVA), MH closure rates and complications.

Results The mean axial length was 28,5 mm in high myopic eyes and 23,3 mm in the controls (p<0,001). There was no significant difference in the mean duration of symptoms, size of the MH and preoperative BCVA between the two groups. Closure of the MH was achieved in only 39/47 eyes (83%) with high myopia versus to 45/47 eyes (96%) in the controls (p=0,04). Mean BCVA improved in both groups (0,41 versus 0,68 logMAR) but was significantly lower in myopic eyes (p<0,001). Anatomical outcomes tended to decrease when axial length increased (p=0,06).

Conclusion MH surgery in high myopic eyes results in satisfactory anatomical and visual improvement but not as good as in the controls. Longer axial length may increase the risk of anatomic failure.

• 3823

Macular sensitivity and structure in epiretinal membranes 6 months after surgical treatment

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Purpose To evaluate the evolution of macular sensitivity (MS) and its correlation with visual acuity (VA) and Spectral-Domain Optical Coherence Tomography (SD-OCT) in patients with idiopathic epiretinal membrane (ERM) at 3 and 6 months after surgical treatment.

Methods In this prospective, monocenter, interventional case series, we included 49 patients (49 eyes) with an idiopathic ERM scheduled for a surgical treatment. Among these patients, 34 were evaluated at 3 months (M3) and 32 at 6 months (M6) after ERM and internal limiting membrane removal. At each visit a measurement of ETDRS best-corrected visual acuity, microperimetry and SD-OCT were performed for all patients.

Results The MS was improved significantly from 11.7±2.1 dB preoperatively to 12.9±1.8 dB (p=0.001) and 13.3±1.9 dB (p=0.001) at M3 and M6 postop respectively. In the same time we observed an improvement of VA from 70.0±10.2 letters ETDRS at inclusion to 80.1±6.9 letters at M3 (p<0.0001) and 80.8±6.5 letters at M6 (p<0.0001). Macular thickness decreased significantly from 412.6±53.1 µm to 340.5±29.6 µm and 332.9±26.9 µm at M3 and M6 respectively. We found a significant correlation between pre and post operative MS at M3 (r=0.565; p=0.0002) and M6 (r=0.584; p=0.0001). A significant correlation between pre and post operative VA was also found at M6 (r=0.558; p=0.0003) but not at M3 (r=0.229; p=0.097). We did not find any significant correlation between the increase in MS and VA (r=0.286; p=0.112) and between MS improvement and macular thickness decrease (r=-0.196; p=0.283).

Conclusion Complementary aspects of macular function were given by VA and MS measurements after ERM surgery.

• 3824

Implication of functional and anatomical preoperative characteristics in the outcomes of epiretinal membrane (ERM) surgery

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Purpose To study the implication and meaning of preoperative functional and anatomical characteristics (based on the parameters Best Corrected Visual Acuity, BCVA, and foveal central thickness, measured by Optical Coherence Tomography, OCT) in the evolution after ERM surgery.

Methods In this longitudinal, prospective study we reviewed 88 eyes (of 86 patients), on whom we had performed vitrectomy or faco-vitrectomy due to ERM, with a follow-up period of three years.We analyzed: ERM etiology, BCVA, metamorphopsia, lens status, and central foveal thickness measured by OCT. We collected the following data during the follow-up: type of surgery (isolated vitrectomy or combined surgery), local complications, changes in BCVA, and changes in foveal central thickness.

Results We observed an improvement in BCVA, and also a decreasement in foveal thickness, being both statistically significant (p<0.01). However, most of the patients showed different grades of oedema and/or macular thickening in the postoperative period. We found significant correlation between preoperative and postoperative BCVA (p=0,001), and also between preoperative and postoperative central foveal thickness (p=0,004), but not between BCVA and foveal thickness.

Conclusion A functional recuperation occurs (based on BCVA) in more of 80% of the patients, after ERM surgery. Most of the eyes show persistent macular thickening, but this does not seem to have influence on the final BCVA. The best determinant of postoperative functional recuperation is, in our experience, the preoperative BCVA, and not the macular thickness.

• 3825

Content-based MPEG-4 video stream retrieval for video-guided eye surgery

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Purpose This work introduces ongoing research on computer-aided retinal surgery. A content-based video retrieval system is presented: given a video stream captured by a digital camera monitoring the current surgery, the system retrieves similar videos in video archives. These informations could guide the surgery steps or generate surgical alerts if the current surgery shares complications with archived videos.

Methods We propose to use data compression to extract video features. 1: motion vectors are derived from MPEG-4 stream. 2: image sequence segmentation is performed by a k-means clustering. 3: we used Kalman filter to track region displacements between consecutive frames and therefore characterize region trajectories. Finally, we combined this motion information with residual consisting of the difference between original input images and predicted images. To compare videos, we adopted an extension of fast dynamic time warping.

Results The system was applied to a small dataset of 24 video-recorded retinal surgeries (621s +- 299s). Images have a definition of 720x576 pixels. An ophthalmic surgeon has divided each video into three new videos, each corresponding to one step of the membrane peeling procedure: Injection, Coat, Vitrectomy. The effectiveness of the proposed method, measured by ROC curve, is interesting (Az ≈ 0.73).

Conclusion A novel CBVR system, allowing retrieval of medical video, has been presented. Experiments on the dataset of retinal surgery steps validate the semantic relevance of retrieved results in ophthalmic applications.

• 3826

Cytopathological findings in the vitreous of patients with retinal detachment

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Purpose Proliferative vitreoretinopathy (PVR) is the leading cause of failure in retinal detachment surgery. The migration of retinal pigment epithelial cells and the occurrence of extracellular matrix changes have been associated with PVR. The purpose of this prospective study was to analyze the cellular contents of the vitreous in patients with retinal detachment.

Methods The vitreous samples of patients with epiretinal membrane and rhegmatogenous retinal detachment were obtained at the initial phase of surgery without previous intraocular infusion. A cytopathological analysis and staining of the vitreous was performed in all cases. The vitreous of 40 patients with retinal detachment and 49 patients undergoing epiretinal membrane peeling (control group) were included.

Results The preparations displayed a variable cellularity. A higher amount of epithelial cell clumping was observed in retinal detachment specimens compared with controls. Furthermore, in the retinal detachment group, more free pigments were encountered and a higher degree of reticulation of the extracellular matrix was noted. In the vitreous of patients with retinal detachment, there is some cytopathological evidence for a higher concentration and an increased activity of retinal pigment epithelial cells compared with controls.

Conclusion The predictive value of cytopathological changes for the occurrence of postoperative proliferative vitreoretinopathy in patients undergoing retinal detachment surgery remains to be demonstrated.

• 3831
Ocular surfaces in the treatment of glaucoma

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The ultimate goal of glaucoma therapy is to prevent ganglion cell death and progression of glaucoma. So far glaucoma has been treated by lowering the intraocular pressure. Although this strategy has been successful in many cases there is a great need to understand the overall benefits, risk factors and adverse reactions of the various existing and new treatment modalities to further improve the success of medical and surgical glaucoma therapies. Ocular surfaces are the most important pathway for the topical glaucoma drugs and thus most vulnerable to the topical adverse reactions. In the aging population the risk for the topical adverse reactions is high and they may jeopardize the success of glaucoma therapy by decreasing the adherence to the treatment or by affecting the outcome of the glaucoma surgery. The cause of these problems might lie in the individual vulnerability, in the active or adjunctive compounds of the medical drugs, in the surgical techniques or biomaterial used in the glaucoma surgery. Therefore the identification of the existing risk factors for these reactions are of great importance for the successful glaucoma therapy.

• 3832
Post-surgical intra-ocular inflammation in a mouse model and high mobility group box protein 1

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Purpose Postsurgical intraocular inflammation is an expected consequence of surgery or trauma. The purpose of this study was to examine new methods for preventing postsurgical inflammation that might avert the problems associated with the use of steroids. An important step was to identify a new molecule that has a leading role in the promotion of inflammation, high mobility group box protein 1, HMGB1.

Methods Surgery was carried on one eye of C57/BL6 mice and the other eye served as control. A scleral incision was created approximately 0.4 mm from the limbus with a 1mm DBL edge sapphire blade inserted at a 3 o'clock position. The incision was closed by 2 interrupted 10-0 nylon monofilament nonabsorbable sutures. In vivo confocal imaging was performed in a preplanned fashion to analyze cell infiltration into the cornea, anterior chamber and iris at PO days 1, 3, 5 and 7. Tissues were collected on the same schedule. Immunofluorescent staining was conducted to examine S100A8, S100A9 and high-mobility-group box-1 (HMGB1) expression, which was confirmed by quantitative real-time polymerase chain reaction (RT-PCR).

Results mRNA levels of S100A8/9 in the cornea, HMGB1 in the cornea and iris increased significantly ($p<0.05$) at PO day 1 and decreased over time. Immunostaining for S100A8/9 and HMGB1 corroborated the RT-PCR results. There was no detectable S100A8/9 or HMGB1 in the unwounded iris. The expression of S100A8/9 and HMGB1 was stimulated in the cornea stroma and iris, with a peak at PO day 3, and decreasing over time. Staining of S100A8/9 and HMGB1 in the cornea epithelium was present at low levels and did not appear to increase after surgery.

Conclusion HMGB1 is a critical early phase regulator of inflammatory events after surgery. The release of HMGB1 can not be avoided as it is released from the nuclei of damagend cells and is therefore always a part of surgical outcomes.

• 3833
Retinal neuroprotection: the path from cell-based high content screening, to animal models, and hopefully to the clinic

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Purpose Vision loss in glaucoma is due to the loss of retinal ganglion cells. Current therapies all act by lowering IOP. However, IOP reduction can be difficult to achieve, and even with significant lowering, RGC loss can continue. Efforts have therefore been made to develop "neuroprotective" agents that would complement IOP-lowering by directly interfering with the RGC cell death process.

Results Using a novel primary RGC-based, high-content phenotypic screen, in which we have tested over 10,000 compounds, we found that the FDA-approved drug sunitinib, a broad-spectrum receptor tyrosine kinase inhibitor, strongly promotes RGC survival. In rodent models of optic neuropathy, including a rat laser glaucoma model, an intravitreally administered slow-release microparticle formulation of sunitinib protects RGCs from cell death. Unfortunately, at its neuroprotective concentration, sunitinib is reported to inhibit nearly 200 kinases, making it a challenge to determine the kinase(s) whose inhibition promotes survival. In order identify the biologically relevant kinase(s) whose inhibition by sunitinib promotes RGC survival, we developed a magnetic nanoparticle-based high throughput siRNA-based assay capable of knocking-down individual genes in cultures of primary murine RGCs. We screened a library of 1869 siRNAs against 623 kinases for siRNAs that increased RGC survival. The top hits were dual-leucine zipper kinase (DLK) and its substrate, mitogen activated protein kinase kinase 7 (MKK7).

Conclusion Our results suggest that a major part of sunitinib's neuroprotective activity is mediated through inhibition of DLK. As a next step, the challenges of bringing a neuroprotective molecule such as sunitinib to clinic will be discussed.

Commercial interest

• 3834
Changes in retinal ganglion cell morphology after optic nerve crush and experimental glaucoma

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Kuopio

Purpose To study sequential changes in retinal ganglion cell (RGC) morphology in mice after induction of experimental glaucoma.

Methods Experimental glaucoma was induced in mice that selectively express yellow fluorescent protein (YFP) in RGCs. Mice were sacrificed 1, 3 and 6 weeks after induction of glaucoma by bead injection. All YFP-RGCs were identified in retinal whole-mounts. Confocal images of randomly selected RGCs were quantified for somal fluorescence brightness, soma size, neurite outgrowth, and dendritic complexity (Sholl analysis).

Results After 6 weeks of glaucoma, 31% of axons died, but there was no loss of YFP-RGC bodies. In combined data from all timepoints, the RGC soma area was larger than control ($P = 0.04$, generalized estimating equation model). At 3 weeks, glaucoma RGCs had significantly larger values for dendritic structure and complexity than controls ($P = 0.044$), but no statistical difference was found at 6 weeks.

Conclusion Despite the moderate loss of axons, significant changes in YFP-RGC morphology were not observed after 6 weeks of follow-up.

• 3841
Progressive serpiginous choroidopathy – what to do?

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A 52 year-old Caucasian female, diagnosed at the age of 11 with tuberculosis presented years later with a picture of serpiginous choroidopathy initially affecting one eye, but later both. She lost vision in her right eye as a consequence of a CNV. She received three courses of anti-TBc treatment but the disease continue to progress. Conventional immunosuppressive therapy was also added with minimal impact on recurrences. Currently in the process of receiving anti-TNF therapy. Infection versus immune response, or a bit of both?

• 3842
Primum non nocere et non occidere

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Purpose "Primum non nocere, "first do no harm", is one of the essential princoples taught to medical students and should accompany us throughout our medical practice.

Methods Case presentations

Results Illustrative example of some "killer cases induced by inappropriate therapeutic interventions will show how important it is to diagnose appropriately our uveitis cases before resorting to a treatment. In particular infectious causes should be excluded before reaching out to immunosuppressive therapies and once powerful potentially dangerous are going to be used, their side-effects should be considered and explained to the patient.

Conclusion A meticulous work-up is necessary before potentially harmful treatments are going to be used but on the other hand exaggerated fear should not prevent us from using necessary corticosteroid and/or immunosuppressive therapeutic intervention as long as the appraisal of the patient has allowed to rule out infectious causes and as far as proper monitoring of side-effects is taken care of.

• 3843
Killer cases due to occult choroidal inflammation : how to prevent them

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Purpose Inflammation of the choroid evolves mostly unnoticed when only clinical examination and/or only classical investigational methods are used. In some cases such occult inflammation, when it is finally noted has already caused irremediable damage.

Methods Inflammatory cases are presented that showed minimal or no signs on clinical examination/investigational tests, where significant occult choroïdal inflammation was detected by ICGA and that responded to therapy initiated on the base of ICGA findings. In parallel, patients that were treated with delay or received no therapy and suffered irremediable damage will be presented.

Results Primary inflammatory choriocapillaropathies PICCPs (MEWDS, APMPPE, multifocal choroiditis) known to be caused by inflammatory choriocapillaris non perfusion can only be meaningfully investigated for activity by ICGA as non-perfused areas are not seen otherwise. If active disease (non-perfusion) is suspected, PICCPs have to be evaluated and followed by ICGA and in case of persistence of non-perfusion and worsening of function, therapy has to be introduced to avoid irremediable damage. For stromal choroiditis such as Vogt-Koyanagi-Harada (VKH) disease, persisting choroiditis after alleged clinical recovery needing continued therapy can only be shown by ICGA, so avoiding complications due to smouldering occult disease.

Conclusion ICGA in the work-up of posterior uveitis should be part of a routine investigation for those case where angiographic work-up is deemed necessary.

• 3844
How a benign granulomatous uveitis can become a killer case

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Purpose To show how failure to diagnose correctly uveitis with micro-granulomatous keratic precipitates and vitritis can have potentially severe and even deadly consequences.

Methods Case presentations.

Results Illustrative cases will show how important it is to diagnose an ubiquitously occurring granulomatous uveitis and crucial elements will be given to avoid to miss the diagnosis.

Conclusion A meticulous clinical examination is the key to a successful uveitis practice.

• 3845
TB or not TB...or what else?!

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(2) The Eye Clinic, Polytechnic University of Marche, Ancona

Purpose To present the clinical pattern of a complex case with atypical clinical features and controversial laboratory results.

Methods Case report

Results Infectious diseases represent always a challenge both for the clinical presentation and the management. The advent of new laboratory tests has lead to diagnosis of certain diseases which were undetectable in the recent past. These techniques have changed the way of treating several diseases, even though the gold standard still represents a chimera. Infact, it is not uncommon to face diseases which present themselves atypically and with laboratory tests which can be controversial. We want to present an anecdotal case that was defined a "killer case" in our tertiary referral centre.

Conclusion The clinical presentation and the laboratory results of certain diseases can often be a tricky challenge even for highly specialized centres. The scientific "methodic doubt" is mandatory in cases which do not present typical clinical features.

• 3846
Infectious driven autoimmunity - how to treat?

DICK A
Bristol

Purpose The question of infectious drive to autoimmunity is highlighted in cases. The debate is when or how to treat with specific anti-infectious agents versus immunosuppression and above all when does malignant transformation occur.

Methods Highlight controversy with cases

Results The outcome of such cases is disappointing given the difficulty in how best to control to progressive degeneration that occurs.

Conclusion To date we are left with delayed diagnosis and poor outcome for such cases. We will discuss how best in future to curtail such outcomes.

• 3851

The association between myopia and glaucoma - causality or classification?

KHAWAJA A
London

Myopia is frequently cited as a risk factor for glaucoma, based on findings from many epidemiological studies. However, these studies are potentially subject to misclassification bias. Glaucoma is largely diagnosed based on optic disc cupping together with a visual field defect. Myopic patients may also have anomalous (or difficult to assess) optic discs together with visual field defects. This talk will examine the epidemiological link between myopia and glaucoma, and address the question whether the observed association between myopia and glaucoma is causal. Published evidence will be critically reviewed and supplemented with the findings from the EPIC-Norfolk Eye Study (European Prospective Investigation of Cancer).

• 3852

Refractive surgery in myopic, glaucomatous patient

CHAVES A
Cliniques Universitaires Saint Luc, Brussels

Purpose This lecture will focus on preoperative examination, IOP changes and postoperative considerations, identifying the patients at higher risk for developing glaucoma and selecting an appropriate and personalized approach.

Conclusion Most refractive surgeries are performed between the 3th and the 5th decade of a patients' life. The prevalence of glaucoma increases with age and the life duration expectancy increases with progress in medicine. Although myopia and increasing age are known risk factors for developing glaucoma, it is impossible to predict which patients undergoing refractive surgery will develop glaucoma later in their life.

• 3853

Glaucoma surgery in high myopia

LIM K
London

This lecture will describe the special pre- and post-operative considerations require for glaucoma drainage surgeries in this group of patient. There are special anatomical features that predisposed this group of patient to have potentially higher complication risk; thin sclera and subsequent difficulty in scleral closure. Once they developed hypotony, these eyes are also more likely to develop hypotonous maculopathy.Therefore, pre-operative assessment must include axial length measurement and carful slit-lamp examination, looking for localised thinning in and around the surgical sites.There is no evidence to choose tube over trabeculectomy with mitomycin-C but it is recommended that surgery should be performed with an anterior chamber maintainer in-situ.

• 3854

Interesting case-reports

POURJAVAN S
Cliniques Universitaires Saint-Luc, Brussels

Purpose The aim of this lecture is to explore and gather all the topics explained in this SIS in some real case-reports.

Methods The diagnosis of glaucoma in high myopic patients can be very bothersome because of the variability of optic disc morphology and the difficulty in visual fields' interpretation caused by the large peripapillary atrophy and the progressive retinal myopic changes. The management, treatment and the follow-up of glaucoma in these patients needs more elaboration than the average, not-myopic POAG patients. The intraocular pressure measurements in patients with a previous refractive surgery demands an especial attention not only inasmuch of the reduced corneal thickness but also because of the postoperative changes in the corneal biomechanical properties.The choice of a target pressure and a target pressure range is highly related with the degree of the myopia.

• 3861

Anatomic and physiologic considerations of the intrinsically-photosensitive retinal ganglion cells

LUCAS R
Faculty of Life Sciences, Manchester

I will provide an overview of the physiology and function of intrinsically photosensitive, melanopsin-expressing, retinal ganglion cells. Originally discovered during the search for photoreceptors regulating the circadian clock, it is now established that these receptors influence a wide array of accessory visual responses. Most recent data indicates that they also can contribute to perceptual vision.

• 3862

Rod, cone and melanopsin contributions to the pupil light reflex

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Purpose To define the relative contributions of rod, cone, and melanopsin to the human pupillary light reflex (PLR) and to determine the optimal conditions for assessing their status in patients with retinal and optic nerve disorders.

Methods The pupil light reflex was measured with an eye tracker, and stimuliwere precisely controlled with a Ganzfeld ERG computerized system. For rod mediated transient pupil responses, a low intensity 1-second duration blue light was given under dark adaptation. For cone mediated transient pupil responses, a red, high intensity 1-second duration light was given on a blue background to suppress rod contributions. For melanopsin mediated sustained pupil responses, a bright 1-second bright blue light was given without background.

Results Rod mediated transient pupil responses were present in normal eyes but not in patients with moderate to advanced retinitis pigmentosa. A blue background suppressed rod and melanopsin responses, enabling assessment of cone contributions with a red flash. Robust melanopsin sustained pupil responses could be seen in patients with lack of contributions from the rods and cones.

Conclusion The rod, cone, and melanopsin contributions to the PLR can be assessed with a simple clinical protocol with blue flashes at two or three intensity levels in the dark and one red flash on a blue background, allowing for diagnosis and differentiation of retinal and optic nerve diseases.

• 3863

Chromatic pupillometry as a novel means to assess outer retinal function in health and disease states

KAWASAKI A
Lausanne

Quantified pupil responses to colored light stimuli is a non-invasive means to monitor melanopsin function as well as rod and cone activity. Understanding the trivariate contributions to the pupil light reflex has led to renewed interest in using the pupil response to monitor a variety of diseases. The characteristic pupillographic feature of intrinsic, melanopsin-mediated ganglion cell activity is persistent contraction after light offset. This post-illumination response is abnormal in patients with glaucoma. In patients with retinal degenerative disease, the retinal sensitivity to blue light as measured by pupillometry is reduced. This correlates with loss of rod function but also hints at reduced melanopsin activity. Clinical examples showing pupil response to red and blue light in patients with neuroretinal visual loss will be discussed.

Commercial interest

• 3864

The importance of blue light exposure to circadian integrity and general health

LUCAS R
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Melanopsin-expressing retinal ganglion cells are capable of supporting an array of visual responses even after complete degeneration of rods and cones. Among their most important roles is the synchronisation (entrainment) of endogenous circadian clocks to local time. Action spectrum studies reveal that these new photoreceptors are maximally sensitive in the 'blue' portion of the spectrum. This has led to the assumption that blue light is especially important for eliciting entrainment and other accessory visual responses. I will discuss how good practice in light measurement and application might be influenced by discovery of these new photoreceptors.

• 3865

Melanopsin and its role in photophobia

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Purpose Photosensitivity is common in patients known to have migraine headaches, in patients following traumatic brain injury, in patients with certain CNS pathology and in inflammatory disorders of the eye. However, it is a subjective complaint and difficult to substantiate and treat. Recently, we have taken advantage of a primitive reflex, the photic blink reflex, to objectively quantify the eye's sensitivity to light.

Methods Patients with light sensitivity and normal subjects were tested using red (640nm) and blue (485nm) Ganzfeld, full field light, one second in duration, over a 6 log unit range of intensity (0.5 log unit steps). Time-stamped, computerized recording of the orbicularis and procerus/corrugator muscle EMG were quantified using the maximum root mean squared (RMS).

Results The photic blink reflex appeared to show similar response characteristics as the pupil light reflex, having both a transient response to photopic red and blue light and a sustained response to high intensity blue light. Patients with light sensitivity showed an exaggerated EMG response to light compared to normals.

Conclusion The sustained EMG response to bright blue light provides evidence for a melanopsin mediated photic blink reflex. The photic blink reflex, as measured by the electromyogram, appears useful for quantifying light sensitivity and its response to treatment.

• 3871

Study of stromal femtosecond laser ablation for deep corneal cut optimization

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Purpose Anterior and posterior stroma of human cornea present different biophysical characteristics, the later being more hydrated and collagen fibers less tightly packed. Our aim was to investigate interactions between femtosecond laser (FL) and stroma according to the depth of cut in order to optimize FL endothelial graft preparation

Methods organ cultured human corneas were prepared with a mechanical microkeratome (Moria, France) by a lamellar cut from anterior side at two different depths: 50µm for the study of anterior stroma and 350µm for the study of posterior stroma. Grooves were then performed in the remaining anterior or posterior stroma with a 800nm, 150fs FL (Thales, France) with different processing configurations (Speed: 1900 to 10000µm/s; Power: 0.8 to 6mW). After treatment, corneas were observed by light and second harmonic generation (SHG) microscopy to compare ablation rates (AR) (in µm/pulse) and cut quality in anterior and posterior stroma

Results Preliminary results (n=4 corneas) showed no significant differences between posterior stroma AR (1.97±0.91µm/pulse) and anterior stroma AR (1.73±0.50µm/pulse). Using SHG microscopy, two different cutting types (with or without disruption) occurred, depending on processing configurations and independently of depth in the stroma

Conclusion These results suggest that there is no significant difference of AR between anterior and posterior stroma. Consequently, difficulties usually encountered to cut endothelial grafts with FL may not directly depend on a particular ablation rate of the posterior human corneal stroma, but rather on the optical scattering when FL passes through the stromal layers, already identify as a limiting factor

• 3872

Large optico-reconstructive corneal grafts in complicated cases

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Purpose Demonstration of different procedures for eye surface reconstruction and visual rehabilitation in complicated conditions.

Methods Case 1: LASIK photokeratomileusis is demonstrated in a case previously operated for penetrating keratoplasty. Case 2: Optico-reconstructive penetrating 11 mm keratoplasty performed in a case of bilateral keratoconus-keratoglobus. The fellow eye had been operated for 11 mm penetrating keratoplasty 20 years earlier, with good result. Two years after the operation of the second eye opacification of the graft developed in the second eye due to irreversible homograft reaction. A second penetrating graft, 7.6 mm in diameter was performed in the center of the previous, opaque, graft. The procedure was combined with simultaneous extracapsular lens removal and IOL implantation.

Results The excellent results of these three examples of complicated large penetrating corneal grafts are demonstrated in all three cases with video and slides.

Conclusion The prognosis of large diameter optico-reconstructive penetrating keratoplasties in apparently unfavourable situations can be definitely improved selecting appropriate surgical indications, combined with a meticoulus surgical technique, adequate postoperative medication (local and systemic corticosteroids, cyclosporine A eye drops 2 %, immunosuppressors, topical cycloplegics, etc.)and rigurous postoperative follow-up control.

• 3873

Spectral domain OCT-assisted "big bubble" deep anterior lamellar keratoplasty in keratoconus patients

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Purpose To visualize intraoperative changes of corneal thickness and bubble creation process using spectral domain OCT.

Methods 15 patients underwent DALK performed using "big bubble" technique. Surgeries were assisted with intraoperative spectral domain OCT imaging (The iVue from Optovue Fremont Calfornia USA). Corneal thickness was measured preoperatively, after manual pre-cutting and after the big-bubble creation.

Results Manual pre-cutting of corneal stroma revealed residual bed thickness of 240-270 µm (mean 256 µm). When residual corneal bad was thicker than 250 µm, the 27G needle was used for big-bubble creation, when it was thinner than 250 µm, 30G needle was used. After injection of an air bubble, in 11 eyes Descemet's membrane was completely separated from stroma, that was shown on OCT scans. In 4 eyes the separation was incomplete that was also clearly visible on OCT images. In one eye OCT imaging showed completely unseparated Descemet's membrane and the additional injection of air bubble was necessary to effectively create the air space between the corneal layers.

Conclusion Intraoperative imaging with Spectral domain OCT provides high-resolution imaging of cornea bed thickness including visualization of the air-bubble formation. This technique could provide enhanced information for the corneal surgeon during lamellar procedures such a DALK.

• 3874

New improvements in Boston Keratoprosthesis (KPro): titanium surface modifications

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(2) Department of Anesthesiology, Children's Hospital Boston, Harvard Medical School, Boston

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Purpose Improve biointegration and esthetics of Boston KPro through Ti coating.

Methods Polydopamine (PDA) was used to form a Ti oxide (TiO2) film on polymethylmethacrylate (PMMA) rods through liquid phase deposition. The rods were inserted in porcine corneas and kept in culture for two weeks. Biointegration was assessed by measuring the force required to pull the rods out of the corneas with an Instron 5542 tensiometer, followed by SEM examination of their surface. Color modification (blue or brown) of Ti backplates of the Boston KPro was achieved using oxide formation in an anodization setup, and biocompatibility was studied using human corneal limbal epithelial cells.

Results Mechanical pull-out showed that TiO2 significantly increased the force required to separate the rods from the corneas (0.354 N), compared to bare PMMA (0.039 N) and PDA (0.098 N). SEM images showed residual cellular and extracellular materials only on TiO2-coated rods. Ti oxidation produced blue or brown-coated backplates. No difference was observed in proliferation, migration or cytotoxicity between coated and uncoated groups in cell culture ($p>0.745$).

Conclusion TiO2 coating enhanced corneal tissue integration with PMMA rods. Oxidation also improved the esthetics of the Ti backplates of the Boston KPro, without compromising its safety or biocompatibility.

• 3875
Stromal alteration in post-lasik ectasia cornea

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Purpose Post-LASIK corneal ectasia is a serious late postoperative complication. After LASIK, the corneal stroma is structurally weakened. Patients with this complication present with an increase in myopia and astigmatism. Here we report the stromal alteration in the post-LASIK cornea.

Methods Two Saudi male patients were diagnosed post-LASIK ectasia. Patient 1, had ectasia six years after LASIK in both eyes. Patient 2, had ectasia four years after LASIK in right eye. Both patients had undergone penetrating keratoplasty in the right eye. The corneas were processed for light (LM) and electron microscopy (EM).

Results The LASIK flap was detached from the residual stromal bed. The posterior end of the flap which had separated from the stromal bed lacked collagen fibrils and instead contained numerous very fine microfilaments. The proteoglycans were absent. There were large keratocytes containing a large nucleus in the stroma. The stromal lamellae were thin and disorganized. The collagen fibrils were running randomly and their distribution was not uniform. There were aggregates of micro-filaments, which replaced some parts of the Bowman's layer and stroma.

Conclusion The present study showed the disorganisation of the lamellae collagen fibrils. A large number of microfilaments were present at the detachment end of the flap and the residual stroma. Numerous aggregates of micro-fibrils replaced some parts of the Bowman's layer and stroma.Acknowledgement: Supported by National Plan for Science and Technology, KSU, Riyadh.

• 3876 / T040
Investigation of bacterial contamination of corneal donors using molecular biology

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Purpose transmission of infectious agents is a major concern for every graft process. Corneal transplantation has been associated to transmission of virus and non conventional agents, but bacterial hazard remains possible in eyebanks. In this prospective study, we investigated the presence of resistant bacteriae in contact with the cornea throughout the whole preservation process.

Methods Samples were taken from donor aqueous humor, conjonctival cul-de-sac and limbus, and from Corneaprep®, Corneamax® and Corneajet® media. Scleral rim was harvested as well after surgery. Bacterial contamination was investigated using direct exam, culture and 16S RNA detection.

Results 164 corneas of 83 donors were included. Cul-de-sacs conjonctivaux (CS). 131 cul-de-sac (79,9%) and 119 limbus (72,6%) were contaminated, from S. epidermidis in 50%. 7 aqueous humors (4%) were positive, 5 with S. epidermidis and 2 with Bacillus. We encountered 34 hemocultures (41%), 6 Corneaprep (4%), 6 Corneamax (4%), 0 Corneajet (0%) and 0 scleral rim (0%) positive.

Conclusion 16S RNA detection did not increase the number of positive samples. 92% of Coag. Neg. Staphylococcus, 19% of S. Aureus, 33% of enterobacteriae, 49% of streptococcus and 75% of enterococcus had an acquired phenotype of resistance to antibiotics. No link between blood contamination and corneal contamination is evidenced. Routine eyebank procedures achieve efficient antimicrobial security.

• 3877 / T068
Surgical approach in corneal perforations and deep ulcers

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(2) Department of Ophthalmology, St. Barbara Hospital, Sosnowiec

Purpose Outcomes of patch grafts in corneal perforations and deep ulcers.

Methods For the study 184 patients (follow-up at least 6 months) were qualified: 57men and 127 women, mean age 61,7,±19,1 years. 198 procedures (112 in corneal perforations and 86 in deep ulcers) were performed. We applied grafts with diameter from 2,5 to 5 mm with oversize of 0,5 – 1 mm. Visual outcomes and corneal surface stability were analysed

Results In 175 eyes we achieved stabile corneal surface, 23 grafts were failed due to graft melting. Among 175 eyes improvement of VA was achieved in 89 eyes, 58 required further procedures of penetrating keratoplasty or cataract surgery. The best visual outcomes were achieved in peripheral ulcers or perforations, central changes usually required further management or were connected with poor prognosis for good vision. 28 eyes due to dry eye, no light localization or retinal detachment (3 eyes) were disqualified to other procedures

Conclusion Patch grafts are useful to restore vision and maintain corneal integrity.

• 3881

EBU - European Blind Union - The voice of blind and partially sighted people in Europe

ANGERMANN W
Hannover

ABSTRACT NOT PROVIDED

• 3882

DBSV – A success story in forming a patient organization for blind and partially sighted people

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German Federation of the Blind and Partially Sighted (DBSV), Berlin

Purpose To develop a support and service system in form of counseling centers or mobile units to address the needs of the increasing number of partially sighted people, especially those who experience sight loss at a later stage in life, as well as their relatives and formal carers.

Methods The situation of support systems in Germany was analyzed. Predominantly partially sighted people were trained and instructed to create a network to other partners, like ophthalmologists, optometrists and rehabilitation specialists. With the support of the organization "Aktion Mensch!" and the "Bernd Mettmann Foundation" pilot projects were created. These new regional centers have been working since the beginning of 2012.

Results Meanwhile consultation centers, mobile units or working groups are running in five regions in Germany. The number of consultations is increasing. The centers are establishing a network of different experts, their organizations and other self-help groups and patient organizations. Project workers assist the regional groups of the German Federation of the Blind and Partially Sighted (DBSV) in creating an area-wide structure to support partially sighted people and their relatives. They have published various information material and papers to raise awareness of the issue of visual impairment.

Conclusion Patients as experts to support partially sighted people, relatives and formal carers in a network of support centers is a successful way to respond efficiently to the increasing number of partially sighted people. Starting in 2013, therefore the regional projects will be extended nationwide. Our positive experiences suggest that the concept of support centers where patients support patients could be transferred to other countries too.

• 3883

Deutsche Uveitis Arbeitsgemeinschaft (DUAG) - How patients can support research

ZIERHUT M
Centre of OPhthalmology, Tübingen

This presentation will summarize how the DUAG (Deutsche Uveitis Arbeitsgemienschaft) was founded and developed. The reasons for the group, having an umbrella position over the local patient groups, will become explained, and how this concept may become adapted to other ocular diseases.

• 3884

Initiating a glaucoma interest group in Belgium

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The Belgian Association for Glaucoma Patients was founded in 2010. Its goals are to inform about glaucoma, to improve early detection and follow-up of glaucoma, to promote interaction between the members and others, to promote the interests of the Belgian glaucoma patients and to enforce their position in the Belgian society. During this lecture, the experiences and activities during the start-up phase will be shared with the audience, followed by an open discussion with the participants.

• 3885

Visual impairment, blindness in an aging society

SUTTIE A
Kirkcaldy

Purpose We face a global growth in the prevalence of age related sight loss and yet services even in well developed countries in Europe, do not currently meet the rehabilitation needs of elderly blind. Nearly 25% of people in the European Union will be over the age of 65 by 2030. It is currently estimated that there are 12 million visually impaired older people in Europe and this is set to grow. The prevalence of serious sight loss increases exponentially with age, from 3.27% between 60 and 69 years up to 15% between 80 and 89 years. We need to think about how we meet the needs of the older old.

Methods Both the European and World Blind Union's have supported expert groups looking to bring together knowledge and expertise in this area. Collaborative working across member countries has both raised the profile of age related sight loss and led to a better understanding of service design.

Results Current practice in the field of vision rehabilitation is primarily geared to meeting the needs of younger blind and partially sighted people. The vast majority of blind and partially sighted people in Europe are: female, over the age of 85 years, living alone and with useful residual sight. They often live with co-morbid conditions such as memory loss, impaired hearing and other frailties of older age.

Conclusion Services firstly need to be designed around an understanding of co-morbidity and partnership with those having expertise in the care of older people. They should encourage and facilitate maximum use of residual vision working on the key principles of size, lighting and tonal contrast. Above all they should help to address the major challenge of social isolation, resulting from living alone with a serious sight loss.

• 4211
Prevention of AMD

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Purpose The prevention of Age Related Macular Degeneration (ARMD) depends on the identification of the main risk factors of the disease.

Methods Clinicians will have to consider genetic and environmental risk factors like smoking habits and obesity. Nowadays, the identification of genetic risk factors mainly depends on the familial past history of the patient. However, an individual identification of the main genetic risk markers will probably have to be considered in the future.

Results Patients without any risk factors are mainly concerned by primary prevention based on nutritional advices based on the intake of macular pigments and polyunsaturated fatty acids. Patients with either genetic or environmental risk factors can benefit from nutritional advices based on the results given by epidemiological studies with higher dietary intake of antioxidants,macular pigments and polyunsaturated fatty acids.

Conclusion Clinicians should give dietary advices to post pone the consequences of ARMD in all patients especially those at high genetic risk.

• 4212
Geographic atrophy

STAURENGHI G
Ponte Lambro

ABSTRACT NOT PROVIDED

• 4213
Genetic retinal diseases

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Purpose To describe the current status of treatment for inherited retinal disease, and illustrate the challenges that lie ahead.

Methods An overview of current treatment trials for inherited retinal disease in humans and animals will be used to illustrate where success has been achieved, but also where challenges remain. These include gene therapy trials in RPE65-related Leber congenital amaurosis, Stargardt macular dystrophy and choroideraemia.

Results Albeit that encouraging breakthroughs have been made with regard to treating inherited retinal diseases, such as in the gene therapy trials in RPE65-related Leber congenital amaurosis, challenges lie ahead, such as gene-specificity of gene therapy, intravitreal as opposed to subretinal injections, stem cell control, and cost.

Conclusion Despite initial success of trials in inherited retinal diseases, quite a number of obstacles remain.

• 4214
Reccurence of vasculitis

BODAGHI B
DHU ViewMaintain, Ophthalmology, Pitie-Salpetriere Hospital, Paris

Retinal vasculitis (RV) is a sight-threatening disease associated with different infectious or auto-immune conditions. RV may be isolated or revealing a systemic disease such as Behçet's disease, sarcoidosis, SLE or multiple sclerosis. Recurrence rate depends on multiple factors such as demographics, etiology, type and extension of vasculitis and most importantly, the therapeutic strategy.The Optimal use of immunosuppressive and biologic agents block recurrences in mots of the cases and decrease the rate of complications. Long-term remission may be achieved in specific entities, after treatment discontinuation.

• 4215
Non diabetic CME

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Purpose Cystoid macular edema (CME) occurs in a variety of pathological conditions beside diabetic retinopathy, such as retinal vein occlusion, pseudophakia, penetrating ocular injury and uveitis. CME is a major cause of vision loss following cataract and vitreoretinal surgery. This presentation overviews the major developments in the treatment of CME, and the contribution of recent clinical trials to the understanding of the pathophysiology and factors that play a role in non-diabetic CME and outcomes of treatment, as well as the problems that remain to be solved by both the basic and clinical researchers.

Methods Differential diagnosis is essential for management and distinction between diabetic, age-related macular degeneration, and other causes of CME. Pseudophakic CME is characterized by poor visual acuity following surgery. Clinically significant CME generally develops 4-12 weeks after surgery. The workup of CME is performed with fluorescein angiography and optical coherence tomography. While pseudophakic CME can resolve spontaneously, some cases of CME require treatment.Refined surgical techniques contribute to reducing the incidence of CME. Intraoperative complications may elevate the risk of developing postoperative CME.

Results Peri- or intraocular corticosteroids can be useful in persistent cases. Topical non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids show the highest success rate for post-surgical CME.

Conclusion While the etiology of CME remains to be elucidated, the recent years have been the framework of major advances in treatment of CME. The response to antiangiogenic treatment is currently under evaluation, with some reported improvements from bevacizumab monotherapy, and combination therapies with NSAIDs and corticosteroids. Surgical treatment is considered in severe case.

Commercial interest

• 4216
Targeted delivery

BEHAR-COHEN F
Paris

ABSTRACT NOT PROVIDED

• 4221

Clinical study results with new wireless electronic subretinal implant alpha-ims

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(3) Mobility Training, Tübingen
(4) Klinikum Friedrichstadt, Dresden
(5) Steinbeis Transfer Centre Eyetrial, Tübingen

Purpose Restitution of vision in blind Retinitis Pigmentosa patients by the new wireless implant Alpha-IMS (Retina Implant AG, Tübingen, Germany).

Methods Each of the 1500 subfoveal photodiodes within an 11 by 11 deg field controls an amplifier that ejects light evoked currents onto bipolar cells via TiN electrodes (Zrenner et al. Proc. R. Soc. B 2011, 278: 1489ff). Power and control signals are transmitted transdermally via retroauricular inductive coils connected to a subdermal cable to the eye.

Results Ten patients received implants since 2010 (average age 46±84). In 8 patients the chip was at the desired subfoveal position; in 2 patients slightly parafoveal. All patients were able to perform the function tests except one due to loss of inner retina function after surgery. Results in all other patients were: light perception 9/9; light localization 8/9; motion recognition 5/9; grating resolution 8/9 (up to 3,3 cycle/degree); Landolt C rings 3/9 (up to 0,036); recognition of geometric objects 8/9; recognition of objects in table setup 8/9; letter reading 4/9; clock hands reading 3/9; grey scale differentiation 6/9; improved outdoor mobility 5/9. Patients` experiences: recognition of unknown objects, facial or clothes' characteristics, moving objects in nature and traffic, small objects (glasses, telephone, doors, door handles, washing basin, dices).

Conclusion The wireless Alpha-IMS implant can restore useful visual abilities in blind RP-patients. Subretinal surgery for positioning chips subfoveally is safe and the multicenter part of the study has been started in Oxford, London and Hongkong.

Commercial interest

• 4222

ARHGEF26/SGEF controls fovea formation, immunity, neurodevelopment and arteriosclerosis

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Purpose Identify cause of congenital syndrome with macular dystrophy, absent fovea in consanguineous family 6 yo girl with congenital nystagmus,low vision after informed consent.

Methods Family had complete ophthalmologic, neurologic examination, brain MRI, genetic tests, array CGH, lipid profiles, vascular Doppler US.Mouse,human fetal ISH

Results Proband had congenital nystagmus and corpus callosum agenesis.Vision was 20/200 w/o photophobia,night blindness. Fundus showed macular atrophy, normal vessels w/o pigment, small papilla. ERG, OP were normal, absent pattern VEP points to macular bundle defect.OCT showed absent fovea, thin retina (102 µm OD and 92 OS) interruption of the photoreceptor layer. MRI showed hippocampi hypoplasia. ABCA4 testing was negative as 18 ARRP genes. Parents have normal vision,ERG,VEP,OCT, angio and brain MRI. Array CGH showed 114kb homozygous 3q23 deletion up to 6th intron of SGEF gene in 3 sibs. Sister had absent fovea on OCT, low vision and macular dystrophy, brother had decreased foveal function on multifocal ERG with normal vision. Girls have repeated infections: EBV hepatitis,dental abcesses..Well parents harbor same heterozygous deletion. Mouse antibody In situ hybridisatio mapped to retina. Human Fetal brain cortex ISH wss positive. SGEF controls leukocyte trans-endothelial migration,1st phase of atherosclerosis. Mother with high cholesterol 212mg/dl and hyper-triglyceridemia had normal cervical arteries doppler US normal examination w/o atherosclerosis at 42yo

Conclusion Data suggests ARHGEF26/SGEF gene controls arteriosclerosis, macular cone development, immune function, axon midline crossing with recessive inheritance. Deletion possibly has protective effect against arteriosclerosis

• 4223

Efficacy and safety of gene therapy with AAV4 in childhood blindness due to rpe65 mutations

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(3) INSERM UMR 1089, Nantes

Purpose To assess the safety and efficiency of an subretinal injection of an AAV2/4. rpe65.hrpe65 in subjects with LCA due to mutations rpe65 genes.

Methods A phase I/II clinical trial assessed the safety and the efficiency of one subretinal injection with AAV2/4.rpe65.hrep65 vector in the worse eye of patient with rpe65-/- retinal dystrophy. Patients of the first cohort received up to 400 µL and patients of the second cohort up to 800 µL of a vector solution at 6.1010 vector genome/mL. The primary safety endpoints are evaluated by biomicroscopy, laser flare meter, fundus photography, fluorescein angiography, OCT and a tolerance questionnaire. Secondary efficacy endpoints are evaluated by global ERG, multifocal ERG, visual field, near and far visual acuity, color vision test, pupillometry, microperimetry, visual mobility, functional MRI and fundus autofluorescence.

Results We will present results of the first six patients included in an ongoing study. Patients are 21 to 42 years old. The three first patients were included in the first cohort and three other were included in the second cohort. No adverse effects or ocular inflammation are noticed one year to 2 months after subretinal injection. Visual acuity is limited to light perception to 1/12 and remained stable after subretinal injection. Visual field modifications in the subretinal treated area are noticed in all patients.

Conclusion subretinal injection of a serotype 4 AAV vector for gene therapy treatment of rpe65-/- retinal degeneration is safe. Visual field improvement found in our adult patients want us to treat 3 childrens scheduled in the third cohort.

• 4224

Etiologic distribution of necrotizing retinopathies : a nine-year experience at a university referral centre

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Purpose To assess the etiologic distribution of necrotizing retinopathies based on an extensive work-up including molecular tools applied to ocular fluids

Methods All patients referred for the diagnostic and therapeutic management of an atypical posterior or panuveitis underwent an extensive work-up to exclude an infectious condition. All patients underwent anterior chamber paracentesis or vitrectomy for diagnostic purposes. PCR and cytology were performed in order to confirm an infectious entity or a masquerade syndrome

Results The clinical findings of 218 patients were analyzed in this retrospective study. The sex-ratio (M/F) was 1.44 including 129 men and 89 women. The mean age was 46.6 years (range from 7 To 90 yo). A viral infection was confirmed in 146 cases (67,5%). Viral distribution determined 55 CMV retinitis, 48 VZV retinitis, 34 HSV 1 or 2 retinitis and 9 EBV panuveitis. Nonviral causes of infectious or inflammatory retinopathies were determined in 66 cases, masquerading as a viral retinopathy. Most of the cases were due to a parasitic infection (59%) followed by a primary intraocular lymphoma (12,1%), a bacterial uveitis (7,5%), Behçet's disease (7,5%), endogenous endophthalmitis (3%), sarcoidosis (1,5%) and others (9,4%). Six cases remained idiopathic

Conclusion All patients with an atypical retinopathy and a suspicion of infectious etiology deserve an extensive work-up, including ocular fluid analysis. The yield of PCR technology remains excellent for viral retinopathies. Even though most of the cases are viral-induced, other entities may present with similar clinical findings. Therefore, prompt diagnosis remains the best strategy to avoid further sight and rarely life-threatening complications

• 4225 / S101

Ocular prognosis of congenital toxoplasmosis (genotypes II and III)

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Purpose There are in France 3 main strains of T. gondii (genotypes I, II and III). Ocular lesions of congenital toxoplasmosis have been reported in 80% of untreated, infected children. But no data were available in Europe on the genotype, on the prevalence of the different strains of T. gondii and on their virulence. Our purpose was to investigate the genotype of strains and the outcome of babies born with congenital toxoplasmosis in our university hospital.

Methods From 1980, every newborn with congenital toxoplasmosis was prospectively referred to the Parasitology Department. Date of birth, sex, time of congenital contamination, pre- and post-natal treatment were recorded. We designed a retrospective follow-up of all these children. Fetal infection was detected using serologic analysis and parasitologic investigations, such as mice inoculation and PCR from samples of amniotic fluid or placenta. For 43 newborns, genotyping of T. gondii strains was performed, using multilocus analysis.

Results The median follow-up was 38.6 months. 28,2% of 78 infected children were treated in-utero upon detection of the maternal infection. 66.1% of 71 alive new borns underwent a post-natal treatment.Genotype of T. gondii was analysed for 55% of infected children. 41 strains were identified as genotype II and 2 strains as genotype III. Among the 10 children with at least 1 retinochoroidal lesion, 5 strains were analyzed: 4 were genotype II (2 peripheral lesions, 1 macular, 1 peripapillar) and 1 was genotype III (1 macular lesion).

Conclusion Genotype II is confirmed to be the most common strain in France. Percentages of ophthalmological lesions accorded to the literature. No prognostic factor was identified for the occurrence or the seriousness of retinal lesions.

• 4226 / S102

Circadien cycle and chronic central serous chorioretinopathy

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Purpose Chronic central serous chorioretinopathy (CSCR) is a multifactorial disease. The present study was designed to evaluate the prevalence of circadian disturbance and corticosteroid treatment in patients treated with chronic CSCR.

Methods Patients presenting with chronic CSCR between 01/01/2009 and 30/11/2011 were prospectively enrolled. A history of corticosteroid treatment, sleep disturbances and irregular working hours was noted. Two questionnaires (PSQI and Epworth) regarding sleeping distrurbancies were applied. After a follow up of 3 months, the patients with persisting fluid and visual acuity below 20/40 were treated with photodynamic therapy (PDT).

Results During the period of inclusion, among 26 included patients, 19 were treated with PDT (73%). A history of corticosteroid tretment was found in 12 patients (19%), 4 currently used psychopharmacologic drugs (15%) and 8 had irregular working hours (30%). The analysis of the Epworth questionnaire enabled to record moderate sleeping disturbances in 11 patients (42%), none of the patients were classified as having severe sleeping disturbances.

Conclusion It is likely that general factors such as the existence of a corticosteroid treatment or a disruption of the circadian cycle are involved in the occurrence of patients with CSCR.

• 4227 / S103

Comparative study of post-natal retinal vascular development in mice models of iPLA2 inhibition and plasmalogen deficiency

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Purpose Plasmalogens are particular phospholipids characterized by the presence of a polyunsaturated fatty acid (PUFA) at sn-2 position of glycerol. Plasmalogen deficiency in mouse leads to developmental abnormalities in retinal vasculature. We propose that liberation of PUFA by the specific calcium-independent phospholipase A2 (iPLA2), is involved in the mechanism by which plasmalogens control retinal vascular development. To confirm this hypothesis, we performed a comparative study of retinal vascular development in a mouse model of retinal iPLA2 inhibition and a model of plasmalogen deficiency.

Methods Vessel and astrocyte networks were visualized on flat-mounted retinas through immunostaining methods.

Results Similar abnormalities were observed in retina of both mouse models. They consisted in an increased number of vessel ramifications at PN14, and in an abnormal glial cells migration from the optic nerve, at PN14 and at PN21. An activation of microglial cells was also observed at adult age.

Conclusion These results confirm the implication of plasmalogen in the control of retinal vessel development through PUFA release from their sn-2 position.

• 4231

Genetics of keratoconus

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Keratoconus (KC) is a vision-threatening condition characterized by thinning and deformation of the cornea. It is one of the most common indications for corneal grafting in industrialized countries. The disease prevalence is approximately 1 in 2000. Familial aggregation, together with increased familial risk, suggests important genetic influences on its pathogenesis. To date, it has been shown that several genomic regions are linked to KC rare familial forms but no genes have been identified as responsible for common KC. Aside from genetic determinants, environmental stresses such as eye rubbing or atopy have been suggested as possible causes or aggravating factors in KC. The interaction of genetics and environmental factors in diseases occurrence contributes to the development of complex and multifactorial trait, such as KC. And, despite the many attempts to reveal KC pathophysiology, the mechanisms leading to its corneal characteristics and vision impairment are still poorly understood.In this presentation, we will discuss all works that have been achieved on keratoconus pathophysiology and we will consider future directions on this topic.

• 4232

Biomechanics in keratoconus

TOUBOUL D
Bordeaux

ABSTRACT NOT PROVIDED

• 4233

Inflammation in the pathogenesis of keratoconus

JUN A
Baltimore

ABSTRACT NOT PROVIDED

• 4234

Oxidative stress in keratoconus

MENEZO ROZALEN JL, PERIS-MARTINEZ C
Fundacion Oftalmologica del Mediterraneo, Valencia

ABSTRACT NOT PROVIDED

• 4235

Endocrinology and keratoconus

GATZIOUFAS Z
Homburg/Saar

ABSTRACT NOT PROVIDED

• 4241

Chromatic pupillometry as highly sensitive testing method of photoreceptor function in retinal dystrophies

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Purpose Objective methods for the characterization of photosensitive cells are highly needed in patients with retinal dystrophies. The pupil light reflex is driven by rod, cone, and intrinsic photosensitive retinal ganglion cell (ipRGC) input. The aim of this study is to analyze two protocols of chromatic pupillometry with differing stimulus paradigms to gather isolated functional information of the three cell populations in patients with different forms of retinal dystrophies.

Methods The study group comprised 60 patients with different forms of retinal dystrophies, and 32 healthy probands. Patients were grouped according to their electroretinography (ERG) data. A custom made binocular chromatic pupillometer (Bino I, AMTech) connected to the Colordome Ganzfeld stimulator (Diagnosys LLC) was used to assess changes in pupil diameter in response to red (640nm) and blue (462nm) light stimuli.

Results Patients who had no measurable scotopic ERG also had the most reduced yet often still measurable rod-weighted pupil responses (PR), while patients with abnormal or normal scotopic ERG had reduced or normal rod-weighted PR. Similarly, patients with no measurable photopic ERG had reduced but still measurable cone-weighted PR, while patients with abnormal of normal photopic ERG had mostly normal cone-weighted PR. Reduced ipRGC-weighted PR could not be correlated with the ERG classification.

Conclusion In the absence of a measurable ERG, chromatic pupillometry generates important functional and quantifiable data on residual rod and cone activity. These data show that this technique should be added to the panel of examination tools for the characterisation of retinal dystrophies and for quantifying the clinical benefit of experimental treatment protocols.

• 4242

Boleslaw Wicherkiewicz: interesting contributor to European ophthalmology

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Purpose Boleslaw Wicherkiewicz (1847–1915) was the most prominent Polish ophthalmologist at the end of the 19th century and beginning of the 20th century. Between 1877 and 1895, he founded in Poznan and developed the largest and internationally best known 19th century ophthalmic hospital in Poland. In 1895, the hospital had a total of 80 beds. With his extensive experience gained abroad, Wicherkiewicz was well prepared to become in 1895 the head of the most important university ophthalmology centre in Poland – the Department of Ophthalmology at the Jagiellonian University in Cracow. In 1899, Wicherkiewicz founded the first Polish ophthalmic journal 'Progress in Ophthalmology'.

Methods The study is based on analysis of all papers written by Wicherkiewicz, mainly in Polish and German. The biographical details were verified in National Archives in Poznan and Cracow, cities where he lived and worked. The secondary sources, including review articles and other reports about his life and activities, were also collected and analyzed.

Results Original contributions on oculoplastic surgery (epicanthus, lid coloboma, ectropion and enctropion, trichiasis, distichiasis, lid replacement, free skin transplantation), cornea transplants (first in Poland), glaucoma surgery (sclerotomia cruciata posterior superficialis), cataract surgery (cataract irrigation technique), clear lens surgery in myopia (before Fukala).

Conclusion Wicherkiewicz played a crucial role in the development of Polish ophthalmology. He was internationally recognized due to his surgery innovations and scientific activities. He was a member of majority of ophthalmic European societies (including many honorary memberships), and he was given honorary doctorate by Leuven University in 1909.

• 4243

Apoplexy in pituitary tumors, clinical and MRI analyses

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Purpose The aim of the study is to evaluate the different types and incidence of pituitary tumors with apoplexy between 1988-2009.

Methods Retrospective data analysis from the notes of the neuro-endocrine multidiciplinary workgroup and medical records of these patients treated by neurosurgeon or conservatively.

Results complete notes were found from 5 years. Different ways of detection were found: the classic tumor pituitary apoplexy, accidental during MRI analyses and during surgery for an pituitary adenoma.Of the 82 macroadenomas, found in the notes over 5 years, in 17 cases an apoplexy was found, which is a higher incidency than described in the literature. From the in total 27 cases found during the 20 years period analysis, 15 cases had the classic pattern, with- at most- eyemovements disorders ; 10 cases had a subclinical pattern and were diagnosed by MRI, and or histopathological or biochemical; in 2 patients the mass was without tumor, and only hemorrhage.

Conclusion Headache, eye motility disturbances and +/- chiasmal syndrome may pronounce in 20 % of the pituirary masses to an apoplexy.Because a pituirary mass frequently is managed with surgery, but conservative treatment is possible without complications, this differential diagnosis is important in neuro-ophthalmological clinical practice. The different MRI patterns will demonstrated during the presentation.

• 4244

Four-year- old child with optic nerve glioma revealed by a proptosis

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(4) Cytogenetic Department, University Hospital of Amiens, Picardie Jules Verne University, Amiens
(5) INSERM UMRS 968, Vision Institute, Paris VI University, Paris

Purpose Optic pathway gliomas are rare tumors accounting for 3-5% of brain tumors in children. Our case aims to understand surgical options.

Methods We report the case of a 4-year-old child with a single optic pathway glioma revealed by a non esthetical proptosis and blindness. Association with NF1 was not found. The MRI showed a tortuous enlargement of the left optic nerve, the glioma extended into the optic canal with a scleral invasion. Considering those results, a treatment consisting of a double team surgery, ophthalmologists and neurosurgeons was performed with enucleation and complete section of the nerve at its optic chiasm root.

Results Histology confirmed the diagnosis of glioma, as a pilocytic astrocytoma, with safety margins. Cytogenetic analysis showed an unspecific chromosome 8 deletion. Chemotherapy was avoided because of systemic toxicity and tumor localization.

Conclusion Association with NF1 is classical and the incidence of optic nerve glioma is estimated at 15%. In young children the glioma can be the first manifestation of NF1 and the disease should be kept in mind. Cytogenetic mutation must be searched with surgical sample in culture. In children, surgical treatment can be preferred to chemotherapy when excision of the total tumor removal can be performed.

• 4245

Strabismus and visual acuity in children with ocular coloboma

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Purpose to report visual acuity and strabismus frequency in children with ocular coloboma.

Methods We retrospectively analysed 43 children diagnosed as having ocular coloboma (18 boys and 25 girls). Median patient age at diagnosis was 30 months. We studied: visual acuity, binocular status, and refractive errors. We ranked different coloboma as anterior, posterior and antero-posterior with a whole ophthalmological examination and were divided in two groups: with (I) or without (II) strabismus.

Results 43 children were included, 25 (58.1 %) had strabismus, 18 with esotropia (72 %) and 7 with exotropia (28 %). Groups I and II were similar on social issues. 23 children had bilateral coloboma and 20 unilateral coloboma. A total of 66 eyes were studied: we found 5 anterior coloboma, 33 posterior and 28 antero-posterior. 13 were associated with microphtalmia. There was no significant difference between children in group I and II. 29 Colobomatous anomalies were found in group I and 37 in group II. Children in group I had a worse visual acuity than in group II ($p< 0.001$). Severe coloboma frequency (posterior or antero-posterior with macular involution) was higher in group I than in group II.

Conclusion These results are comparable to those found in literature. There is a worse visual acuity for strabismus-associated coloboma.Strabismus more often occurs in coloboma-diagnosed children than in general population and is often associated with amblyopia.

• 4246

Evaluation of the retinal fiber layer thickness as a biomarker for sleep apnea syndrome

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Purpose To evaluate the peripapillary retinal nerve fiber layer (RNFL) thickness measured with spectral-domain optical coherence tomography (OCT) in obstructive sleep apnea syndrome (OSA) patients, as a biological marker of neuronal damage.

Methods Sixty-four OSA patients and one hundred twenty-nine healthy controls were consecutive and prospectively selected. Only one eye per subject was randomly chosen. AOS patients were classified in three groups according to apnea/hipopnea index: mild, moderate and severe. All participants performed a comprehensive ophthalmologic examination and at least a reliable standard automated perimetry (SAP). Peripapillary RNFL thicknesses were measured with the Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany). After checking for a normal distribution of variables, differences between both groups were tested by Student t test.

Results Age was 50.6 ± 9.3 years in control eyes and 47.8 ± 11.5 years in AOS patients ($p = 0.09$). Mean deviation of SAP was -0.50 ± 1.0 dB and -1.4± 2.3 dB, in control and AOS patients, respectively ($p<0.001$). Pattern standard deviation and Visual Field Index (VFI) of SAP were also different between both groups. The RNFL thickness at temporal superior segment and the superior segment had lower thicknesses in AOS patients compared to healthy individuals.

Conclusion OCT detected a mild reduction of RNFL thickness in AOS patients compared with healthy subjects. Visual field indices were also different between both groups.

• 4251

Cataract and glaucoma surgery, combined or staged: where do we stand?

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Purpose Glaucoma surgery in presence of a cataract is a challenging problem. Are patients better served by combined glaucoma and cataract surgery, or would cataract extraction alone be sufficient or is it best to establish a bleb before performing cataract surgery? As the techniques have evolved during the past years, the literature has enriched with new evidences and new suggestions. During this part of the course we will review in detail the past and actual literature in this field as well as more recent data from meta-analysis studies.

Methods literature review

Results discussion of the most pertinent studies

Conclusion see above

• 4252

Combined approach, the yield of microincisions for cataract surgery

BRON A
Dijon

Cataract extraction combined with glaucoma surgery remains a matter of debate. Some authors advocate consecutive surgeries arguing that the expected lower inflammation will allow a better outcome of the filtering surgery. However cataract extraction after a filter may impair the long term efficacy of glaucoma surgery. Conversely the combined approach is more convenient for the patient with one operation and generally a better visual result. However it is generally considered that the IOP-lowering effect is less effective in combined procedures. Rather than opposing these two approaches, it is probable than according to the characteristics of the patient and the type and the stage of glaucoma, a consecutive or a combined surgery is more appropriate. Therefore the surgeon must be prepared to perform the two types of surgery. Micro incisions for cataract surgery (MICS) offer some substantial advantages vs conventional corneal incisions; a better tightness of the surgical wound allows a better control of IOP during the surgery. Therefore glaucoma surgeries (penetrating or not) are much easier to perform without changing your technique. In this presentation some surgical tips will be given in order to facilitate your combined procedures.

• 4253

Staging the surgeries: glaucoma first or cataract first?

ZEYEN T
Leuven

A combined Phaco-Trabeculectomy will often not have the same result as both procedures separately. The IOP lowering effect of a combined procedure is usually less than that of Trabeculectomy alone. Likewise, post-operative fluctuations of the anterior chamber depth after a combined procedure will influence the post-operative refraction, especially in the early post-operative period and/or if additional procedures (e.g. needling) are necessary to rescue a failing bleb.Therefore, most surgeons will prefer to stage both procedures. Since cataract surgery might compromise an existing filtering bleb, it is recommended to perform Phaco first if the IOP is not too elevated. If the glaucoma is at risk to deteriorate in the short term, filtering surgery should be performed first. It is advisable to wait 6 months between the cataract and glaucoma surgery.

• 4254

Combined approach: practical tips

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Purpose The presentation will feature practical advice on undertaking combined phacoemulsification/IOL insertion with trabeculectomy. The specific indications, and particular advantages of this combined technique in groups of patients will be highlighted, and the techniques covered will include:

Methods 1) Approach to the case: whether a combined approach is optimal in the individual patient, contraindications, and choice of antimetabolite 2) Technical details: including ajustable suture techniques3) Postoperative management

Results Video examples will be used to illustrate the surgical techniques discussed

• 4261

An ex vivo assay to measure the intravitreal mobility of nanomedicines for retinal gene therapy

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Purpose In retinal gene therapy, intravitreal injection is a promising technique for administering nanomedicines, granted they remain mobile in the vitreous humour. Here, we optimized an ex vivo assay to measure this mobility in intact bovine vitreous. The results from this work and the newly developed methodology are expected to aid in the rational design of nanomedicines for retinal drug delivery.

Methods Excised bovine eyes were prepared in such a way to preserve the fragile structure of the vitreous humour, while permitting fluorescence microscopy inside the bovine vitreous. This assay was used to determine by single particle tracking analysis the intravitreal mobility of both model polystyrene beads with different sizes and surface groups, as well as gene nanomedicines composed of poly(amido amine)s and plasmid DNA.

Results Cationic nanoparticles were readily immobilized in the vitreous humour, while anionic polystyrene beads remained mobile. Surface modification with the hydrophilic polymer polyethylene glycol (PEG) resulted in the best mobility of the polystyrene beads. In correspondence with these results, the cationic gene nanomedicines were immobilized in the vitreous humour, while modification with PEG resulted in a drastic improvement of their mobility.

Conclusion Here an ex vivo assay is presented to study nanoparticle mobility in intact vitreous humour by single particle tracking microscopy, which showed that cationic surface charge limits intravitreal diffusion of nanoparticles by binding to biopolymer structures, while anionic and PEGylated nanoparticles remain mobile. These results should help in the rational design of nanomedicines used for intravitreal drug delivery.

• 4262

Drug delivery by ionic hydrogel contact lenses in preoperative prophylaxis of intraocular infections

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Purpose To evaluate the efficiency of ophthalmic drug delivery through ionic hydrogel soft contact lenses (SCL) in comparison with eye drops in preoperative prophylaxis of intraocular infections.

Methods The efficiency of moxifloxacin and levofloxacin delivered via SCL was compared to eye drops in patients having cataract surgery. Investigations were conducted with 1-DAY ACUVUE® TruEye® hydrogel SCL, saturated with moxifloxacin solution 0.16 % (Avelox) and levofloxacin solution 0.5% (Tavanic), which were put on the cornea (Group 1). Another group of patients were given five times the dosage of these drugs (Group 2). These manipulations were made one hour before phacoemulsification in both groups. Aqueous samples (0.1 mL) were collected at the beginning of the surgery. The antibiotic concentration in aqueous aliquots was determined using spectrofluorimetry and liquid chromatography.

Results Maximum therapeutic concentrations (TC) of moxifloxacin and levofloxacin in the aqueous humor were achieved after 4 hours 18.0 ± 2.0 and 9.0 ± 1.2 μg/mL (Group 1), followed by gradual decrease of them ($p<0.05$). TC lasted no less than 6 hours. The minimum inhibitory concentrations were only achieved by eye drops of the same drugs (Group 2). Moxifloxacin and levofloxacin delivered via SCL in 10 and 5 times respectively increased the relative bioavailability in comparison with the eye drops of these antibiotics.

Conclusion 1. The application of ionic hydrogel soft contact lenses is an effective drug delivery method.2. Ionic hydrogel soft contact lenses, saturated with moxifloxacin and levofloxacin, provide a therapeutic antibiotic concentration in the aqueous humor.3. Ophthalmic drug delivery through contact lenses increases bioavailability.

• 4263

Ghrelin's expression in the eye and its implication in the reduction of intraocular pressure

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Purpose To investigate ghrelin's and GHSR-1 distribution in the rat's ocular tissue and ghrelin's role in the modulation of IOP in animal models of acute glaucoma.

Methods Immunolocalization of ghrelin and GHSR-1 was performed in male Wistar rats (200–300g). Acute glaucoma was induced in male New Zealand white rabbits (2,0-3,0Kg) and male Wistar rats (200–300g) through an intravitreous injection of 20% NaCl. Afterwards either ghrelin or des-acyl ghrelin was subconjunctivaly injected. In the rabbit, ghrelin's effect in the presence of L-NAME or ketorolac.

Results Ghrelin and GHSR-1 were detected in the rat's eye, being ghrelin expressed in the ciliary processes, having co-localization with lectin, an endothelial cell marker, been also verified. GHSR-1 expression was detected in the base of the ciliary body and in the choroid, presenting focal co-localization with α-smooth muscle actin. Ghrelin, but not des-acyl ghrelin, decreased the IOP in rabbit's and rat's glaucomatous eyes (maximal percentual decrease relative to peak versus control in rabbit: 65,9±12,4%; maximal percentual decrease relative to peak versus control in rat:27,45±4,8%). In the rabbit, this effect was blunted in the presence of L-NAME and ketorolac.

Conclusion Ghrelin and GHSR-1 are expressed in the rat's eye. Ghrelin promoted a decrease in the IOP of rat's and rabbit's glaucomatous eyes. These data suggest a role for ghrelin in the pathophysiology of glaucoma.

Commercial interest

• 4264

Polyunsaturated fatty acids and Plasmalogens in diabetics

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Purpose Plasmalogens (PLS) are phospholipids characterized by a vinyl ether bond and a preferential esterification of polyunsaturated fatty acids (PUFA). We have previously shown that the lack of PLS leads to retinal hyper-capillarization. We hypothesize that PLS are negative regulators of vascular development, and aimed to check their circulating levels in diabetic patients.

Methods Blood samples were collected from 88 patients and 14 control subjects. Among diabetics we had 14 patients without diabetic retinopathy (DR), 12 with a mild non proliferative DR, 12 with a moderate non proliferative DR, 22 with a severe non proliferative DR and 24 with a proliferative DR (PDR). Erythrocytes were isolated from total blood samples. The PLS content and the fatty acid composition of erythrocyte phospholipids were determined using capillary column gas chromatography. Individual species of phospholipids, including PLS, were quantified by liquid chromatography coupled with a triple quadrupole mass spectrometry instrument (HPLC-ESI+MS/MS).

Results Gas chromatographic analyzes showed significant reduced levels of omega-3 PUFAs including docosahexaenoic acid (DHA) and omega-6 PUFAs including arachidonic acid in diabetic patients without DR and in patients with DR at any stage. The analysis of individual species of phospholipids by HPLC-ESI+MS/MS showed reduced levels of choline-phospholipids esterified with DHA in PRD patients and ethanolamine-phospholipids esterified with DHA at the mild, moderate, severe stages of DR but not in PRD. Levels of cholin and ethanolamine-PLS remained stable in all the diabetic patients when compared to controls.

Conclusion Our results suggest that omega-6 and omega-3 PUFAs from conventional phospholipids but not PLS may be involved in the pathogenesis of DR.

• 4265

Cicrulating markers of retinal and optic nerve lipids

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Purpose Blood lipids are frequently used as a surrogate of lipid composition of peripheral tissues. Even if it is well accepted such a relationship has never been clearly demonstrated for the eye. The aim of this study was to determine in human samples whether a lipidomic approach based on red blood cells could reveal associations between circulating and ocular lipid profiles.

Methods Red blood cells, retinas and optic nerves were collected from 9 human donors. The lipidomic analyses on these tissues consisted in gas chromatography and liquid chromatography coupled to an electrospray ionization source-mass spectrometer (LC-ESI-MS).

Results Gas chromatographic approach did not shpw any relevant association between circulating and ocular lipids except for arachidonic acid whose circulating amounts were positively associated with its retinal and optic nerve levels. However, significant associations emerged from LC-ESI-MS analyses. Indeed, phospholipid species in red blood cells were positively or negatively associated with representative pools of retinal DHA (docosahexaenoic acid), retinal VLC-PUFA (very-long chain polyunsaturated fatty acids) or optic nerve plasmalogens.

Conclusion First, our results show that LC-ESI-MS methodology is more appropriate than gas chromatography for lipidomics on red blood cells, and further extrapolation to ocular lipids. Second, this study has identified several individual lipid species as good candidates to represent circulating biomarkers of ocular lipids.

• 4266 / F122

Oxidative stress in retinal pigment epithelial cells: protective effect of wood-derived phenolic compounds

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Purpose Oxidative stress is related to chronic diseases including age-related macular degeneration (AMD), which is the leading cause of blindness in the elderly worldwide. Functional roles of wood-derived phenolic compounds such as flavonoids, phenolic acids, tannins and stilbenes are not well known, but some of them are effective antioxidants capable of providing defence against oxidative stress. Besides reducing ROS production by their antioxidant activity, phenolics can also activate the expression of phase II genes via the activation of transcription factors, such as Nfr2.

Methods In this work, the protective effect of wood phenolics against oxidative stress were determined by pre-incubating ARPE-19 cells in medium containing wood compounds (pinosylvin, piceatannol, trans-resveratrol or pinosylvin monomethyl ether) at different concentrations. After pre-incubation with phenolics, cells were treated with oxidative stress causing agent, hydroquinone, for 24 hours. The viability of cells was determined by using MTT assay. To elucidate the mechanisms behind the phenolics-mediated protection against oxidative stress and inflammation, the activity of genes such as Nrf2, IL-6 and p62 was determined.

Results Wood-derived phenols were well tolerated by the cells and some of the compounds such as pinosylvin were able to increase the viability of cells in response to induced oxidative stress.

Conclusion These results suggest that wood-derived phenolic compounds can provide additional protection against oxidative stress in retinal cells.

• 4271

Anatomy, physiology and pathophysiology of the meibomian gland

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Purpose The sebaceous meibomian glands (MG) in the eyelids, that secrete lipids for the superficial tear film layer, are of increased scientific and clinical interest. The recent MGD report of the non-profit organization Tear Film and Ocular Surface Society (TFOS, www.tearfilm.org) revealed that MG Dysfunction (MGD) with lack of tear film lipids and the resultant evaporative type of dry eye is the main underlying reason for the wide-spread dry eye disease that affects millions of patients world wide

Methods A literature review based on the TFOS MGD Report together with own findings is discussed in order to explain the anatomy, physiology, pathophysiology and clinics of MGD.

Results MGD is a multifactorial disease based on endogeneous and exogeneous factors that interact in self propagating vicious circles. Advancing age, female sex, environmental factors such as topical medication, bacterial influences and probably subclinical inflammatory pathways as well as contact lens wear are some main factors lead to the onset and propagation of MGD. These result in hyperkeratinization of the gland epithelium as well as increased viscosity of the secretum. Together this results in the obstructive type of MGD. Two effector arms of obstruction lead to a primary lack of oil on the tear film with downstream evaporative dry eye but also to a secondary hidden degeneration of the glandular tissue inside the lids that results in gland atrophy.

Conclusion Obstructive MGD with downstream lipid deficiency is now recognized as the main cause for dry eye disease and this achievement of the TFOS MGD Workshop has already changed/revolutionized our view on dry eye disease as well as lead to several new developments for diagnosis and treatment that specifically address MGD.Support DFG KN 317-11

• 4272

Obvious, non-obvious MGD and new therapy options & the German perspective on MGD

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Purpose The concept of meibomian gland dysfunction (MGD) has drastically changed during the last century. Obstructive MGD has often few or no symptoms although an atrophic process proceeds inside the gland tissue. This conceivably most frequent form of MGD is called non-obvious MGD or NOMGD.

Methods A literature review on MGD together with own findings is discussed in order to explain the different types of MGD and new options for their diagnosis and treatment.

Results Historically, MGD was thought to have purulent hypersecretion with ouvert inflammation. Since a few decades it has occurred that MGD also includes obstructive, hyposecretory forms, that had escaped attention because of less obvious symptoms. In fact this represents the vast majority of disease and results from stasis due to hyperkeratinization of the ducts and hardened secretum. It often leads to a still borderline normal tear film and hence symptoms only occur due to environmental stress like air condition, video terminal work or contact lenses. The term MGD was coined only 30 years ago when apparently normal patients became symptomatic after fitting of a contact lens. The diagnosis of tear film lipid deficiencies and the removal of hardened secretum by physical measures require new diagnostic and therapeutic approaches and instruments but may offer, for the first time, a causative approach to dry eye disease

Conclusion Recognition of MGD with tear film instability due to lipid deficiency and with atropic gland destruction has lead to a paradigm shift in the understanding of dry eye disease and to new developments in diagnostics and therapy. This requires new sophisticated forms of lipid layer diagnostics and physical therapy together with addition of lipids to tear substitutions.

• 4273

Physical therapy in MGD as a cornerstone for improvement of signs and symptoms & The British perspective on MGD

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Purpose This talk will present the typical management of meibomian gland dysfunction (MGD) that is currently implemented in British primary eye care, and where the current focus lies in newer diagnostic techniques and therapies.

Methods Recent focus on MGD has highlighted this condition as one that is under-estimated and under-managed, particularly amongst contact lens wearers. This renewed appreciation for the major cause of dry eye has resulted in parallel interest amongst eye care practitioners for an evidence-based approach to management. The most common approaches are reviewed, alongside some emerging popular choices.

Results There is robust evidence to support modern approaches, and to discourage some of the old-fashioned management strategies.

Conclusion Whilst there is still a lot to understand about MGD, there is no doubt that eye care practitioners can do more to help patients manage this highly prevalent problem.

• 4274

Identification of MGD in dry eye patients and its treatment in the practical clinical setting & The Austrian perspective on MGD

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MGD can be found in about 70% of patients with ocular discomfort as evaluated in a large clinic-based population of Austria. It is characterized by a continuum of clinical severity. Especially discrete cases are often underestimated und receive not enough attention. In patients with ocular discomfort it is important to investigate the blinking action, the lid margins (crusts, vascularisation, Marx line, meibomian orifices) and also to perform the expression of the meibomian glands. Tear deficiency is often accompanied with MGD therefore the function of the lacrimal glands should be tested. To evaluate the damage of the ocular surface, staining with fluorescein and lissamine green are recommended. Further important diagnostic measures are the evaluation of the lipid layer and the examination of the meibomian glands with meibography. Although there is an overlap between different subtypes of dry eye, proper diagnostic evaluation is important to identify adequate therapeutic treatments that would best target the underlying dysfunctions. The most commonly recommended treatment option for every stage of MGD remains eyelid hygiene that should be performed on a regular basis. Eyelid warming to melt the meibum and eyelid massage to express secretion shall prevent obstruction of the terminal ducts. To improve compliance special devices that are more convenient for the patients can be used. Instillation of artificial lubricants, especially with lipid containing components may stabilize the tear film. Essential fatty acids, topical and systemic antibiotics and other anti-inflammatory medication are further important therapeutic options.

• 4275

Special features of MGD in children: how to diagnose how to treat and the French perspective on MGD

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Purpose MGD in children is a common pathology. Many clinical forms need to be recognized, from mild to severe, with classical features of chalazia and blepharitis or more unusual the sight-threatening ocular rosacea.

Methods Ocular rosacea in children, secondary to severe MGD, is probably underdiagnosed meanwhile it induces major ocular discomfort. The treatment aims to eyelid hygiene, anti-inflammatory treatment and topical steroid sparing.

Results Place of heat therapy with innovative steamed goggles, topical azithromycin and topical cyclosporine with analyze of literature and clinical cases, is discussed. The French prospective clinical study performed was useful to evaluate the interest of each treatment.

Conclusion Further studies with more patients are needed to a better understanding of the severe MGD. Ocular rosacea in children should be recognized early and to avoid steroid dependence and complications. Eyelid hygiene, topical anti-inflammatory and topical cyclosporin are essential in MGD treatment for a better quality of life of the children and their parents.

Commercial interest

• 4281
Can scattered light improve visual performance?

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Purpose Light scattered by the media within the eye reduces object contrast and can also cause visual discomfort, in the presence of bright light sources. The addition of uniform veiling light over the retina can, however, change retinal sensitivity by increasing retinal illuminance. The extent to which reduction of target contrast and changes in retinal sensitivity caused by the presence of a glare source affect contrast acuity (CA) thresholds remains to be established. We investigate how CA is affected by glare source intensity, surround luminance and test target location on the retina. The aim is to determine the range of glare source intensity and background adaptation level that can improve visual performance.

Methods 45 subjects with normal vision were investigated. A psychophysical flicker-cancellation test (Ophthalmic & Physiological Optics, 17, 171, 1997) was used to measure the amount and angular distribution of scattered light in the eye. CA thresholds were measured using the Contrast Acuity Assessment test (ASEM, 74, 551-559, 2003). Three glare source intensities (i.e., 0, 1.35 and 19.21 lm/m^2 in the pupil plane), three eccentricities (5, 10 and 15 degrees), and three background luminances (1, 2.6 and 26 cd/m^2) were investigated.

Results CA thresholds were measured for the test target / glare source parameters listed above. In addition, the scatter function of the eye was assessed for each subject and the measured parameters were used to predict the effect of veiling glare on CA thresholds.

Conclusion Low intensity glare can improve CA in the high mesopic range. High intensity glare yields increased thresholds, but this loss of contrast sensitivity is, in general, smaller than predictions based on veiling glare luminance caused by forward light scatter in the eye.

• 4282
Effect of light source size on discomfort glare thresholds

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Purpose Bright light sources, such as car headlamps or residential street lights, can cause visual discomfort. The origins of discomfort glare (DG) or the factors that contribute to it remain poorly understood, even after 50 years of multidisciplinary research [American Journal of Ophthalmology, 153(4):587-593(2012)]. This study examined the effect of the light-source intensity, size, surround luminance and pupil size on DG thresholds.

Methods The pupil was measured in real time to calculate retinal illuminance, a more pertinent parameter in studies of DG. DG thresholds were estimated with a staircase procedure: the retinal illuminance was increased or decreased based on whether the participant indicated the absence or presence of DG, respectively. The subjects were required to view a source of light presented against a simulated residential street background. The size of the disc source was selected randomly under computer control. Five different source sizes were used to produce a 40 fold variation in stimulus area. The light source behind the aperture disc was designed to produce uniform flashes of light of varying intensity, while the surround light level remained unchanged.

Results It was found that at the threshold for DG, the retinal illuminance is approximately constant and independent of source size. On the other hand, pupil plane illuminance increases as source size increases.

Conclusion These findings suggest that DG depends mostly on localised retinal illuminance, rather than the total amount of light entering the eye. DG therefore appears to be largely related to saturation of photoreceptor signals. The results also suggest that higher levels of street illumination can be achieved by increasing the size of light source without causing any increase in DG.

• 4283
The effect of discomfort glare on parallel processing of visual information

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Purpose When a person is confronted with a bright light source against a dim background, scattered light can cause visual discomfort in addition to reducing object contrast on the retina. Previous work addressing the effect of glare on visual performance has focused mainly on the reduction in retinal image contrast (known as disability glare) rather than the often accompanying experience of discomfort glare. This study examines how parallel processing of visual information is affected under conditions of discomfort glare.

Methods Light scatter sources surrounded a monitor on which the subject carried out standard contrast acuity (CA) tasks. All CA tasks were carried out with and without discomfort glare (estimated in a prior experiment). In the parallel task, a fovea target (Landolt C) and four peripheral stimuli (three distractors and one target) were presented concurrently; the subject had to indicate both the orientation of the gap for the foveal target and the quadrant containing the peripheral target. The size of the peripheral target was increased relative to the foveal target to ensure that all targets were equally detectable. This was done separately with and without discomfort glare, thus negating any influence of disability glare.

Results The presence of discomfort glare degrades visual performance in the parallel processing task even when adjustments are made to cancel out the effects of disability glare.

Conclusion Studies that have focused only on disability glare may be underestimating the adverse effect glaring light sources can have on visual performance, particularly in real world scenarios where attention to objects in both the fovea and periphery is often required.

• 4284
Characterization of human corneal grafts' transparency by optical coherence tomography and scattering measurements

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Purpose In clinical and graft sorting applications, cornea's transparency is only subjectively qualified. The aim of this study is to bring tools to achieve transparency quantification regarding the evolution of edema within the tissue.

Methods The samples are human corneal grafts rejected from bank of tissue due to physiologic issues, which are submitted to swelling protocol to study their properties with edema.A multiscale analysis of the microstructure imaged by 1 µm resolved Optical Coherence Tomography (OCT) combined with a detailed characterization of backscattering properties is performed.Electromagnetical modelization is used to numerically link scattering measurements with structural defects observed with OCT.

Results Backscattered intensity measurements enable corneal grafts' transparency evaluation (backscattering level increases with swelling). Moreover, microstructural tissue modifications occurring during swelling (microstructure disorganization and heterogeneities) are highlighted by OCT imagery. We show that the observed heterogeneities imply higher scattering levels and explain the experimental results.

Conclusion Combining both techniques allows linking the scattering behavior with the evolution of microstructures within the tissue and permits to quantify corneal grafts transparency.This study has to be extended to tissues eligible for graft but this characterization in the backscattered space could directly be applied to future study of tissues before removal or to in vivo diagnosis.

• 4285

Characterization of visual impairment in a Wfs1 mouse model of Wolfram syndrome

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Purpose Wolfram syndrome is a childhood onset rare genetic disease (1/180,000) featuring diabetes mellitus and optic neuropathy progressing towards legal blindness before the age of 20. A Wfs1-/- mouse model has been generated showing pancreatic beta cell atrophy. Nothing is known about the visual function of Wfs1-/- mouse. We have studied the visual impairment of these mice by electrophysiology and histopathology.

Methods Electroretinogram testing (ERG) and visual evoked potentials (VEP) were performed in Wfs1-/- and Wfs1+/+ mice at 3, 6, 9, and 12 months of age. Total nuclei and retinal ganglion cell (RGC) populations of nerve fiber layer were quantified from Brn3a immunolabeling of retinal sections. RGC axonal loss was also quantified by electron microscopy.Grating acuity and contrast sensitivity were measured based on the optomotor tracking responses on a virtual apparatus.

Results Visual evaked potentials showed progressive decrease of N+P amplitudes in Wfs1-/- by 30, 40 and 50% at 6, 9 and 12 months, respectively while both a- and b-wave ERG amplitudes were slightly reduced at 12 months.Brn3a positive RGC and total nuclei in RGC layer were not significantly lost in Wfs1-/- genotype. Transmission electron microscopy analysis of 10 month-old Wfs1-/- mice determined little reduction in axonal density. Frequency and contrast thresholds of optokinetic tracking reflex remained normal in Wfs1-/- mice.

Conclusion Progressive VEPs alteration with minimal cell loss suggests functional defect of the signal conduction in the optic pathway. However, visual acuity is preserved and immunohistology didn't show any alteration of RGC layer in the retina. We conclude of a mild visual phenotype in the exon 2 deleted Wfs1 mice.

• 4286 / F075

Adjuvant stem cell-based therapy in acute retinal injury after sodium iodate administration in mice

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Purpose The aim of this study was to determine and optimize a new strategy of SC-based therapy of selectively damaged retina after sodium iodate (NaIO3) administration in C57BL/6J mice.

Methods To address this issue, we investigated the effects of NaIO3 administrated in two different concentrations, i.e. 40 and 20 mg per kg of the body mass. Electrophysiological function of the retina using dark-and light-adapted full field flash ERG as well as morphological characteristics, were determined at several time points after each dose administration. Next, we performed intravitreal transplantation of murine GFP+Lin- cells on the 1st day since NaIO3 administration. We analyzed the retinal functional changes as well as the number, localization and phenotype of intravitreally injected GFP+Lin- cells within recipients' retinas.

Results Our findings revealed that massive destruction of the tissue was associated with irreversible retinal dysfunction, whereas moderate retinal injury triggered regenerative mechanisms that restore bioelectrical function of the damaged retina. By employing SC-based therapy we achieved noticeable improvement of the retinal function, particularly in the short-term observation. We observed the presence and proliferation of the injected cells at the site of RPE injury.

Conclusion Our study provides evidence that NaIO3-induced retinal damage triggers a sequence of pathophysiological events dedicated to supporting the self-regeneration of injured tissue. Our results indicate that if the scope of retinal destruction is profound, endogenous regeneration is ineffective and may ultimately require therapeutic transplantation of specific stem cell subpopulations and other adjuvant therapies.

• 4287 / F076

Fructose diet induced short-term impairment of cone sensitivity and gene expression in rat retina

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Purpose A high fructose diet has been widely used to trigger insulin resistance in rodent; insulin resistance is one of the major risk factor for the development of type 2 diabetes. Thirty to 40% of diabetic patients develop diabetic retinopathy. In this study, we aimed to evaluate the short-term effect, at 1, 3, 5, 8 days, of a 60% fructose diet, on photoreceptor sensitivity and gene expression in the retina of Brown Norway rats.

Methods Flicker electroretinograms (8Hz) were recorded under anesthesia, from both eyes simultaneously in order to study sensitivity of photoreceptors. Then, rats were euthanized and enucleated. Retinae and posterior poles were collected to analyze gene expression by RT-PCR. We specifically focused on 45 genes involved in cholesterol homeostasis, lipid trafficking, vascular changes and inflammation.

Results Our data showed that a short period of fructose feeding induced early changes in retinal functionality and homeostasis. Interestingly, we reported a partial loss of cone sensitivity after 8 days of feeding rats with the high-fructose diet. No effect was found in rod sensitivity.

Conclusion These findings are consistent with the sensibility and susceptibility of cones to dietary changes. These data deserve further investigations on the cross-talk between cones and rods upon metabolic changes associated with aging.

• 4411

In vitro studies on the mechanism of action of VEGF and its inhibitors on blood-retina barrier

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Purpose VEGF-induced permeability of immortalized endothelial cells of the bovine retina (iBREC) can be completely restored by the VEGF-binding Fab-fragment ranibizumab, but expression of other growth factors like bFGF, IGF-1 or PLGF is also elevated in diabetic macular edema (DME). Therefore, we investigated whether combination of these growth factors enhance or diminish the long-term effect of VEGF and whether combined effects can be restored by VEGF-inhibition alone. We also studied potential uptake and accumulation of ranibizumab or the humanized VEGF-binding antibody bevacizumab.

Methods Measured transendothelial resistance (TER) of iBREC (+/- growth factors or inhibitors) showed effects on permeability, indicated also by Western blot-determined tight junction protein Claudin-1. Uptake of VEGF inhibitors by iBREC was visualised by immunofluorescence staining and Western blot analyses.

Results VEGF decreased TER and Claudin-1 in a concentration dependent manner whereas bFGF, IGF-1 or PLGF as single agent did not influence these processes during treatment for 2 days. In contrast to PLGF, bFGF and IGF-1 maintained the effect of VEGF especially at low VEGF concentrations. Reduction of TER or Claudin-1 induced by combination of all growth factors was completely restored by addition of ranibizumab. Both VEGF inhibitors were internalised but bevacizumab accumulated further. Ranibizumab was found in the membrane/organelle fraction, whereas bevacizumab associated with the cytoskeleton. Both inhibitors did not disturb the barrier of iBREC.

Conclusion VEGF is mainly responsible for disrupting the barrier function of REC. This supports VEGF targeting as a therapeutic concept.Independent research grant by Novartis Pharma, Germany

• 4412

Role of retinal glial cells in pathogenesis of macular oedema

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Purpose Macular edema is a complex nonspecific reaction that results in intraretinal fluid accumulation and leads to a decrease of retinal transparency and visual impairment. Virtually all retinal disorders associated with ischemia, inflammation and/or mechanical traction may be accompanied by the development of macular edema. The pathogenic mechanisms underlying the development of macular edema are largely unresolved. Most studies favor vasogenic edema as key mechanism in the development of macular edema. However there are indications that a swelling of retinal Müller cells may also contribute to the development of macular edema.

Methods Immunohistochemical staining as well as recording of Müller cells behavior was investigated under normal conditions, under osmotic stress and under different pathological processes, e.g., retinal ischemia, ocular inflammation, and diabetes.

Results The Müller cells are responsible for the maintenance of the retinal homeostasis including intraretinal osmolyte and water homeostasis through coupling of transglial water fluxes (via aquaporins) to potassium currents clearance. Functional alterations of Müller cells in course of ischemia and/or inflammation contribute to the downregulation of potassium conductance and intracellular overload of potassium ions. This results in osmotically driven water movements from the blood and vitreous into the glial cells and causes neuronal hyperexcitability and glial cell

Conclusion An impairment of ion and water movements through Müller cells (in addition to vascular leakage) may contribute to the development of macular edema. A better understanding of the mechanisms of cellular ion and water homeostasis will facilitate the development of efficient edema-resolving drugs.

• 4413

Combination of ranibizumab and laser photocoagulation in CRVO

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Purpose In a model of CRVO upregulation of VEGF was strongest in the ischemic areas. Therefore initiated a proof of concept study to evaluate the efficacy of intraocular ranibizumab injections combined with laser photocoagulation of the non perfused areas in patients with CRVO.

Methods 22 patients with areas of non-perfusion were randomized into two groups. In the treatment arm patients received the ranibizumab injections with additional selective laser photocoagulation. The controls were treated with ranibizumab only. All patients received an upload and were re-injected in a PRN regimen. The results at month 6 were evaluated. The change in BCVA compared with baseline as well as the amount of ranibizumab injections and the percentage of patients progressing to neovascularization (retina and/or anterior segment) were analyzed in the both arms.

Results BCVA increased at month 6 compared with baseline in the treatment arm from 61.6±12.7 to 68.9±13.7 ETDRS letters and in the control arm from 59.25±10.9 to 64.1±16.5 letters. One control patient developed retinal neovascularisation and required panretinal aser photocoagulation. Due to the small number of patients the differences between experimental and control arm are not statistically significant. The sample size calculation showed, that 100 patients are required to achieve the statistical power of 90%.

Conclusion The preliminary results of the study showed a positive effect of the additional selective laser photocoagulation in patients with CRVO. The laser treatment seems to lead to faster and substantial resolution of the macular edema. A multicenter trial is currently prepared to confirm the results of this proof of concept study.

• 4414

Vasomotor reaction of retinal arterioles in hypoxic and ischemic conditions

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Purpose Retinal blood flow is autoregulated by the adaptation ofthe vascular tone of resistance vessels (arterioles, capillaries) to changes in the perfusion pressure (PP) or metabolic needs of the tissue. The purpose of this study was to evaluate the disturbance of arteriolar reactivity, and thus of blood flow regulation, during the evolution of ischemic retinal microangiopathies.

Methods Much of our basic knowledge of retinal arteriolar reactivity is based on data obtained from animal experiments through the use of invasive techniques. However, a variety of non-invasive techniques has been applied to the human eye for the investigation of retinal hemo-dynamics and, more specifically, the reactivity of the retinal arterioles in response to a number of physiologic and pharmacologic stimuli, under normal, hypoxic and ischemic conditions.

Results In patients with non-proliferative diabetic retinopathy (DR), isocapnic hypoxia induces a significant increase in Vleuk in the perifoveal circulation, whereas in patients with proliferative DR, the diameter of the retinal vessels remains unchanged, indicating that blood flow regulation in response to a hypoxic challenge is blunted,consequent to the hypoxic retinal conditions. In those patients a hyperoxia-induced blunted vasoconstriction of the retinal arterioles is also observed.The ability of the retinal arterioles to respond to changes in ocular PP is altered in diabetes, while the response of retinal vessels to diffuse luminance flicker is blunted, particularly in patients suffering from insulin-dependent diabetes.

Conclusion During the evolution of retinal ischemic microangiopathies, impairment of various mechanisms of retinal arteriolar reactivity leads to disturbed retinal blood flow regulation.

• 4415

Treatment of macular oedema due to branch retinal vein occlusion with laser induced arterial constriction. Twenty years results of retrospective interventional study

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Purpose To evaluate the final visual acuity (VA) in patients with Branch Retinal Vein Occlusion (BRVO) treated with either laser arteriolar constriction (ACo) or grid laser photocoagulation (GLP).

Methods 265 BRVOs were treated with 3 different approaches: early ACo performed ≤ 9 weeks after onset of BRVO, late ACo performed > 9 weeks after onset and GLP. The groups were divided into 3 subgroups according to initial VA: ≤ 0.1; 0.16-0.3; and ≥ 0.4. The data were analyzed using univariate and multivariate logistic regression and, Receiver Operating Characteristics analysis. Factors which could have influenced final VA such as age, sex, localization of occlusion (major temporal or macular BRVO) and the presence of retinal ischemia were taken into account. In the group of early and late ACo, patients with VA ≤ 0.5 and a ME persisting over three months, underwent additional macular GLP.

Results Based on the proportion of 1 year VA ≤ 0.1 as a risk category, the results of early ACo (3.8%) were significantly better than either GLP (29.6%, $p < 0.001$) or late ACo (16.1%, p=0.006). In the subgroup of intermediate initial VA 0.16-0.3, a significant difference was only found between the early ACo group and GLP (p=0.004). The effect of the treatments on the prevalence of final VA ≤ 0.1 was not significantly different for patients with an initial VA ≥ 0.4. In patients treated by ACo, residual chronic ME requiring additional GLP was present in 35% of early and 44% of late ACo cases.

Conclusion ACo performed in the first 9 weeks after onset of BRVO significantly reduces the prevalence of a final VA ≤ 0.1 in patients with an initial VA < 0.3.

• 4416

Neurodegeneration in retinal diseases and new strategies in its inhibition

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Purpose Recent studies showed the role of toll-like receptors (e.g.TLR4) in the generation of inflammatory cytokines, initiation of oxidative DNA damage, and induction of mitochondrial oxidative stress.

Methods Several retinal diseases result in photoreceptor mitochondrial oxidative damage. The oxidative-stress-induced nitration of photoreceptor mitochondrial proteins and peroxidation of membrane lipids led to activation and migration of microglia toward the photoreceptors. These observations suggest oxidative stress could be an initial pathologic event leading to amplification of inflammation inducing photoreceptor damage. Molecules that prevent mitochondrial oxidative stress and photoreceptor apoptosis may help prevent retinal damage and preserve vision in patients with different retinal disease.

Results Several different agents were investigated to reduce the mitochondrial oxidative stress. The small heat shock protein alpha-A crystallin prevents photoreceptor mitochondrial oxidative stress-mediated apoptosis in inflammatory disease such an experimental autoimmune uveitis (EAU). Interestingly, only alpha-A and not alpha-B-crystallin, a closely related small heat shock protein works, pointing to molecular specificity in the observed retinal protection. based on modulation of the systemic B and T cell immunity.

Conclusion In the ischemic retinal diseases the neuroprotective role of neuroglobin has been shown. Neuroglobin overexpression plays a protective role against retinal ischemia reperfusion injury due to decreasing of mitochondrial oxidative stress-mediated apoptosis.

• 4421

ICGA: why I think that it is still relevant today

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Purpose To discuss the role of indocyanine green angiography (ICGA) in ophthalmology and the breaking news on this methodology.

Methods The current literature is reviewed and the experience of a tertiary referral centre is reported.

Results ICGA is an essential method used to explore the posterior pole in several sight-threatening diseases. Although this technique has been proven effective in detecting anomalies which were unappreciable with the traditional methods, there is still reluctancy in making use of such method. In the recent past months the topic of ICGA has again moved to the forefront of angiographic actuality with two editorial articles in largely diffused ophthalmological journals. The scientific dignity of ICGA is discussed and advocated by the western World, mostly by highly specialized ophthalmic centres in Europe. We will discuss the state of the art of the clinical use and the evidences in the medical literature of the ICGA.

Conclusion ICGA is a validated method for the evaluation of the posterior pole, which can provide essential informations for the clinical assessment and management of several diseases. Albeit the validity of such technique has been proven, there is still some unjustified reluctancy in accepting its pivotal role in ophthalmology: the evidences suggest its use for every single disease that can affect the choroid and cannot be appreciated by the traditional tests.

• 4422

ICGA in inflammatory diseases

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Purpose Choroidal involvement in uveitis is present at least as often if not more often than retinal involvement. Imaging of the different choroidal compartments is only possible using indocyanine green angiography (ICGA). The trend presently seems to shift away from ICGA for diseases of the fundus. Unlike other fundus conditions where use of ICGA is debated, this imaging technique is crucial for inflammatory conditions in order not to miss choroidal involvement especially in diseases where the primary lesion process is exclusively situated either in the choroidal stroma as for Vogt-Koyanagi-Harada (VKH)disease or at the level of the choriocapillaris as for MEWDS or APMPPE.

Methods ICGA is ideal to explore the choroid as the ICG molecule has two crucial properties : (1)it fluoresces in the infrared, allowing to "see" through the RPE into the choroid; linked to proteins it forms a macromolecular complex that is trapped in the choroidal stroma so outlining inflammatory foci. Hence, different lesion processi were identified by ICGA which allowed a classification of choroiditis into choriocapillaritis and stromal choroiditis according to the anatomic location of the disease. Mostly these lesions are occult and can only be identified by ICGA.

Results Primary choroidal diseases (choriocapillaritis, stromal choroiditis) could only meaningfully be investigated and followed by ICGA. It was found to be diagnostic in a substantial proportion of cases. In those entities such as VKH where the inflammatory insult is exclusively limited to the choroid, ICGA is the only mean to monitor subclinical disease and adjust therapy.

Conclusion In inflammatory diseases, unlike in other fields where opinions diverge, ICGA is not only relevant but essential for global appraisal and follow-up.

• 4423

Advances in central serous chorioretinopathy: from diagnosis to treatment

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Purpose To discuss the role of indocyanine green angiography (ICGA) in central serous chorioretinopathy (CSC)

Methods Review of the current literature and the experience of a tertiary referral centre is reported.

Results ICGA is an essential method used to diagnose, treat and follow patient affected by central serous chorioretinopathy. This technique enabled ophthalmologists to have more insight in the pathogenesis of CSC. Recently the utility of ICGA in CSC has been re-discussed again in relation to the different patterns of choroidal permeability, distribution of the fluid and the reponse to photodynami therapy. We will discuss the state of the art of clinical use and the evidences in the medical literature of the ICGA.

Conclusion ICGA is an validated method for the evaluation of CSC, which can provide essential informations for the clinical assessment and management of this disease. The evidences suggest its use in every case of CSC in order to make diagnosis and guide photodynamic therapy.

• 4424

Anatomical location of polypoidal choroidal vasculopathy lesions inferred from simultaneous ICGA-OCT

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Purpose To identify the spatial location of polypoidal choroidal vasculopathy (PCV) lesions including branching vascular network (BVN) and late geographic hyperfluorescence (LGH).

Methods This retrospective study involved 15 eyes (15 subjects) affected by active PCV. Utilizing innate software for simultaneous indocyanine green angiography (ICGA) and optical coherence tomography (OCT), we identified the corresponding tomographic locations of BVN and LGH on ICGA.

Results LGH was noted in 9 eyes, and the extent of LGH was the same (5 eyes) as or larger (4 eyes) than the extent of BVN. The extent of 'double layer sign' on OCT coincided exactly with the extent of LGH on ICGA. Image analysis revealed that larger vessels of BVN located not in-between retinal pigment epithelium and Bruch's membrane but within choroidal layer.

Conclusion This study indicates that, at least, a part of BVN locates within choroidal layer. And the tomographic location of the lesion corresponding to LGH lies above Bruch's membrane. The origin of LGH would be fluorescein staining of the lesion above Bruch' membrane, possibly due to exudation from BVN.

• 4425

Anatomic response of occult choroidal neovascularization to intravitreal ranibizumab: a study by indocyanine green angiography

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Purpose To investigate changes in indocyanine green angiography (ICGA) features of occult choroidal neo-vascularization (CNV) after intravitreal ranibizumab injections.

Methods We reviewed the charts of all consecutive patients with newly diagnosed occult CNV secondary to age-related macular degeneration (AMD) treated by intravitreal ranibizumab. In all patients, optical coherence tomography(OCT) and ICGA were performed at baseline, after 3 months and 12 months.

Results Fifty-one eyes of 44 patients (ten males, 34 females, mean age 77.8±7.3 years) were included. Mean follow-up was 20.3±6.2 months. During the first 12 months, patients received 5.5±2.7 intravitreal ranibizumab injections.When compared with baseline, best-corrected visual acuity(BCVA) significantly improved at the 3-month follow-up visit(60.5 ±22.0 vs 50.9 ±20.7 letters, p=0.04), and stabilized at 12-month visit (55.7 ±18.2 letters; p=0.05). Central macular thickness (CMT) significantly improved during follow-up (229±54.7µm vs 281±61.3 µm at baseline, p=0.003). An overall stabilization was observed on ICGA in both the lesion area (5.27±3.9 mm2 at baseline vs 4.60±3.5 mm2 at month 12, p=0.4), and greatest linear dimension (GLD 2.66±1.2 mm at baseline vs 2.55±1.0 mm at month 12, p=0.3). Eight eyes (15.7%) showed CNV growth on ICGA (lesion area 3.98±3.2 mm2 at baseline vs 4.3±2.7 mm2 at month-12,p=0.6; GLD 2.11±1.0 mm at baseline vs 2.70±0.8 mm at month-12, p=0.05).

Conclusion ICGA suggests that functional outcomes after intravitreal ranibizumab is related to CMT reduction rather than CNV regression

• 4426

Integrated imaging approach in RAP diagnosis

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Purpose to explore the inter-observer agreement in the diagnosis of retinal angiomatous proliferation (RAP) using fluorescein (FA) and indocyanine green angiographies (ICGA) and to detect which morphological features of the neovascular lesion are associated with RAP diagnosis.

Methods cross-sectional study. Consecutive patients with newly diagnosed neovascular AMD evaluated in 8 Retina Centres have been considered. FA and ICGA were obtained in all centres according to a standard protocol, both performed either as a static or as a dynamic examination. All images were graded by two observers from different institutions.

Results 201 eyes with neovascular AMD of 155 consecutive patients (mean age: 76±8 years) have been considered. Overall RAP prevalence was 30% using FA and 26% using ICGA. Patients studied with dynamic angiography were twice more likely to be diagnosed RAP as those using static angiography. Inter-observer agreement for the overall detection of RAP was high using FA (kappa: 0.868; 95%CI: 0.793-0.944) and very high using ICGA (kappa: 0.905; 95%CI: 0.836-0.974). The agreement between the two observers tended to be higher for the truncated vessel than for the anastomosis in FA as wells as in ICGA, but no comparison yielded statistical significance (p=0.258 and p=0.584, respectively).

Conclusion the inter-observer agreement for RAP detection was very good both using FA and ICGA, but the overall detection of RAP was higher for dynamic strategy compared with static one.

• 4431

Keratoconus and keratectasia

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ABSTRACT NOT PROVIDED

• 4432

Long-term results of deep anterior lamellar keratoplasty in patients with keratoconus

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Purpose Long-term endothelial cell density changes and visual and refractive outcomes after descemetic (d) and predescemetic (pd) deep anterior lamellar keratoplasty (DALK) using the big-bubble technique in eyes with keratoconus.

Methods Retrospective, consecutive, non-comparative, case series analysis of 95 eyes that have undergone DALK for keratoconus using the big-bubble technique with at least 1 year of follow-up. Big-bubble was achieved in 74 (77.9%) eyes (dDALK), whereas 21 (22.1%) eyes underwent manual lamellar dissection (pdDALK) because of failed big-bubble.

Results Descemet ruptures occurred in 13 of 95 cases (13.7%). Five ruptures (5.3%) were converted to penetrating keratoplasty. Mean length of follow-up was 5.3 years (range, 1-8 years). Postoperative best spectacle-corrected visual acuity was significantly better in dDALK group than in pdDALK group at years 1 and 2. But, at the final examinations, there was no significant difference between the study groups (0.25 ± 0.22 logarithm of the minimum angle of resolution in dDALK group and 0.33 ± 0.15 logarithm of the minimum angle of resolution in pdDALK group; p = 0.12). The 2 groups were comparable regarding astigmatism and spherical equivalent refractive error throughout the follow-up period. Mean endothelial cell loss was 22.5 ± 17.9% at last follow-up with most of the loss occurring in the first year (8.7% ± 5.6%). Stromal graft rejection episodes occurred in 3 eyes (3.2%), which resolved with appropriate therapy.

Conclusion DALK using the big-bubble technique is effective in patients with keratoconus. In DALK, manual lamellar dissection is a reasonable alternative when big-bubble separation of the Descemet membrane is not achieved.

• 4433

Keratoconus patterns and intrastromal segments

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Purpose Intrastromal corneal segments (ICS) are a popular alternative for the treatment of keratoconus. However, its variability makes difficult a simple approach to ICS implantation. The SA.ANA classification of ICS implant modalities was developed to enable comparability between case series, with implications on the best ICS combinations for the different keratoconus patterns.

Methods A multicenter database was established including ICS implanted during the 2004 to 2011 period. Based on 1097 cases, a simple classification of ICS implantation modalities was devised using 2 basic criteria: symmetry and axiality, whose combination results in 4 major types. The observed series was fitted into this framework.

Results 2 equal ICS facing each other define symmetrical (S) implantation. Asymmetrical (A) means only 1 or 2 different ICS. Axial (A) implants are those placed with their center at the flatter astigmatism axis, while non-axial (NA) refers to those at an axis differing ≥30° from that of astigmatism. This results in 4 main types (SA, AA, SNA, ANA), while the asymmetric types can include 1 or 2 ICS (AA1, AA2, ANA1, ANA2). The most frequent modality was asymmetrical-axial (AA) totaling almost 70% of the implants. Symmetric-axial (SA) represent about 10%. The non-axial groups account for the remaining minority (20%).

Conclusion The SAANA classification employs simple criteria for a comprehensive description of the ICS implantation types. Identifying these types is a prerequisite for a meaningful comparison of the clinical results. This classification is also useful as a guideline to select the best ICS combinations for a particular keratoconus case. While axial implantation constitutes 80% of the cases, the non-axial types may address special problems as non-coincident astigmatism & coma.

Commercial interest

• 4434

Visual and refractive outcomes of intracorneal ring segments in the treatment of keratoconus: the RETICS multicentrical study

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Purpose Analyze the outcomes of intracorneal ring segment (ICRS) implantation for the treatment of Keratoconus based on preoperative visual impairment.Design: Multicenter, retrospective, nonrandomized study.

Methods 611 eyes of 361 keratoconic patients were evaluated. Subjects were classified according to their preoperative corrected distance visual acuity (CDVA) into five different groups: Grade I, CDVA of 0.90 or better, Grade II, CDVA equal or better than 0.60 and worse than 0.90, Grade III, CDVA equal or better than 0.40 and worse than 0.60, Grade IV CDVA equal or better than 0.20 and worse than 0.40 and Grade Plus, CDVA worse than 0.20. Success and failure indexes were defined based on visual, refractive, corneal topographic and aberrometric data and evaluated in each group six months after ICRS implantation.

Results Significant improvement after the procedure was observed regarding uncorrected distance visual acuity in all grades ($p<0.05$). CDVA significantly decrease in Grade I ($p<0.01$), but significantly increases in all other grades ($p<0.05$). 37.9% of patients with preoperative CDVA 0.6 or better gained 1 or more lines of CDVA, while 82.8% of patients with preoperative CDVA 0.4 or worse gained 1 or more lines of CDVA ($p<0.01$). Spherical equivalent and keratometry readings showed a significant reduction in all Grades ($p\leq0.02$). Corneal higher order aberrations did not change after the procedure ($p\geq0.05$).

Conclusion Based on preoperative visual impairment, ICRS implantation provides significantly better results in patients with a severe form of the disease. A notably lost of CDVA lines can be expected in patients with a milder form of Keratoconus.

• 4435

Cross linking for keratoconus - clinical results comparing epithelium removal versus no removal

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Purpose Comparative prospective mid-term 24 months functional analysis after Epi-off and Epi-on Riboflavin UV A corneal cross-linking (CXL) in patients affected by progressive keratoconus (KC).

Methods Functional analysis comprised 30 eyes of 24 patients (15 - 26 years) treated by epi-on trans-epithelial CXL procedure and 30 eyes of 24 patients (10 - 26 years) treated by standard epi-off CXL. Therapy was performed according to the Siena protocol by using the Vega CBM (Caporossi-Baiocchi-Mazzotta) X linker (CSO, Florence, Italy) at Siena University.

Results At 24 months follow-up patients showed a mean gain in UCVA of +0.2, +Snellen lines in the epi-off group while in the epi-on group after a mean improvement of 1 Snellen Line at 3 months, uncorrected visual acuity gradually returned to baseline. BSCVA gained by a mean of +0.2 Snellen lines in the epi-off procedure while in the epi-on patients no significant improvement was recorded at 24 moths follow-up. Kmax was reduced by a mean value of –0.6D, and Coma values improved by a mean of –0.45 µm in the epi-off group. No significant variation in K readings and coma values were recorded in the epi-on treatment.

Conclusion Epi-off CXL showed a constant improvement of functional data while the epi-on procedure showed a relative instability with a regression of functional outcomes returning to baseline at 24 months of follow-up. In patients with progressive keratoconus under 26 years with corneal thickness over 400 microns epi-off cross-linking should be the first choice therapy. According to actual limitations epi-on procedure should be reserved in patients over 26 years with low KC progression or in patients with thinnest point under 400 microns.

• 4441

Assessment of dry eye after LASIK by real-time measurement of higher order aberrations variation

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Purpose To evaluate tear break-up time (BUT) with real-time (RT) higher order wavefront aberrations (HOA) measurements in myopic patients after Laser-Assisted In Situ Keratomileusis (LASIK) surgery.

Methods HOA up to the sixth order for a 4-mm pupil were measured in 20 normal subjects (Group 1) and in 20 myopic patients, with no history of dry eye (DE), before and after LASIK surgery (Group 2), using the IRX3 (Imagine Eyes, Orsay, France) Hartmann-Shack (H-S) aberrometer. The HOA measurements were performed (in triplicate) with a new dedicated software, once every second for up to 20 seconds. HOA variations were compared with the BUT by the conventional fluorescein method (CFM).

Results Twenty percent of the patients from Group 2 were complaining from DE symptoms. There was an excellent correlation between the HOA variation and the BUT recorded by the CFM in both groups. Reproducibility of the HOA measurements in all subjects and patients was excellent. BUT was significantly decreased ($P<0.005$) in 30% of the patients in Group 2 when compared to the normal tests subjects (Group 1).

Conclusion HS aberrometry is a non invasive method that has been used for the last decade for the assessment of the quality of vision, in patients undergoing refractive surgery and cataract or clear lens extraction. Studying the HOA variation is a new interesting method for evaluating both the quality vision and the BUT in patients after LASIK surgery.

• 4442

Pathogenetic evaluation of the ocular surface drug correction in patients before LASIK

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Purpose Development and evaluation of the method of optimizing the ocular surface before the refractive intervention.

Methods Overall, 485 patients were enrolled in this case-control study. Assessed the ocular surface, tear film and tear production before and after optimization of preoperative LASIK patients in 4 groups. Group 1 (A) - high myopia - (97), aged 18 to 35 years, group 2 (B) - medium myopia – (145), aged 18 to 35 years, group 3 (C) - myopia medium or high – (73), older than 35 years, group 4 (D) - hypermetropia medium or high - (49), older than 35 years. The criteria for preoperative drug correction of refractive surgery to the stage were the following diagnostic blocks: clinical data in diagnosis of dry eye and corneal status, corneal thickness, the definition of clinical refraction, including patient age, antioxidant and immune activity of tears.

Results The use of a preparation containing hydroxypropylguar and sorbitol in groups A and D, and a preparation containing hydroxyproylguar in groups B and C before LASIK reduces the number of complications refractive surgery.

Conclusion The correlation between the choice of ocular surface drug correction and the evaluation of the Norn, Lipkof, cornea vital coloring tests, cornea thickness (mm), the type of refractive error and degree of change (and its degree of myopia), the patient's age (35 and older than 35 years of age), antioxidant and immune activity of tears (the concentration of peroxyredoxin 6 (PRDX6), the presence or absence of gamma globulin).

• 4443

Keratocyte density after microkeratome LASIK versus femtosecond laser-assisted LASIK

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Purpose to compare the keratocyte density after microkeratome LASIK (MK-LASIK) and femtosecond-laser assisted LASIK (FS-LASIK)

Methods We performed a prospective study of myopic patients that underwent MK-LASIK or FS-LASIK. We measured keratocyte density 3 and 15 months, and 3-5 years after the surgery using confocal microscopy

Results we included 31 eyes in LASIK (FS-LASIK) and 30 eyes MK-LASIK, we detected an initial increase in the keratocyte population of the whole cornea, due to an increase in the stromal bed and mid and posterior stromal layers, followed by a normalisation of those deeper layers, and a decrease of the cell density in the stromal flap and stromal bed 3-5 years postoperatively. The average cell density throughout the cornea was not decreased compared to controls.

Conclusion : we found a reorganization of keratocytes in the cornea up to 5 years after LASIK, with a decrease in the stromal flap and bed, but maintaining normal average cell densities, and with no significant differences between MK and FS-LASIK.

• 4444

Evaluation of intraocular pressure according to corneal thickness before and after Excimer laser corneal ablation for myopia

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Purpose Intraocular pressure is affected by corneal thickness and biomechanics. Following ablative corneal refractive surgery, corneal structural changes occur. Our aim in this study was to determine the relation between the mean central corneal thickness and the change in intraocular pressure measurements following various corneal ablation techniques, using different measurement methods.

Methods This is a prospective, nonrandomized study.200 myopic eyes undergoing laser in situ keratomileusis or photorefractive keratectomy were enrolled. Corneal parameters examined included, full ocular examination, measurement of central corneal thickness, corneal topography, corneal curvature and ocular refractivity. Intraocular pressure measurements were obtained using three different instruments: Non Contact Tonometer, Goldmann Applanation Tonometer and TonoPen XL (TonoPen-Central, and TonoPen-Peripheral). All measurements were performed preoperatively and 4 months postoperatively. differences in inter-device intraocular pressure measurements were done using ANOVA test.

Results Postoperative intraocular pressure was significantly lower than preoperative values, with all instruments (p value <0.001, Student's t-test). The postoperative intraocular pressure decrease was smallest using the Tonopen-XL compared to the Goldmann applanation tonometer and Non-contact tonometer (p value <0.001,ANOVA).

Conclusion Intraocular pressure readings are significantly reduced following corneal ablation surgery. We determined in our myopic patient cohort that the TonoPen XL intraocular pressure measurement method is the least affected following photorefractive keratectomy and laser in situ keratomileusis as compared to other techniques.

• 4445
Effects of subconjunctival bevacizumab on corneal neovascularization: results of a prospective study

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Purpose To evaluate the effect of subconjunctival bevacizumab injections in patients with corneal neovascularization resulting from different ocular surface disorders.

Methods Prospective case series. Fourteen eyes of 13 patients with corneal neovascularization caused by different ocular surface disorders, such as healed corneal ulcers, long-standing chronic inflammatory diseases and corneal ischaemia secondary to burn were included. All eyes received a single subconjunctival injection of 2.5 mg (0.1 ml) bevacizumab. Morphological changes in neovascularization were evaluated during 3 months using slit-lamp biomicroscopy, corneal digital photography, and computed-assisted semi-automatic analysis of corneal neovascularization area.

Results Recession of corneal vessels was observed in all eyes at 1 week post-injection. The surface of the neovascular tree continued to decrease noticeably for one month and then increased again for the remainder of the follow-up period. The corneal neovascularization area amounted to 12.14± 4.38% of the corneal surface pre-injection, compared with 9.10± 3.16% post-injection (p=0.02), reflecting a mean decrease in corneal neovascularization of 25 %. No local or systemic adverse events possibly related to subconjunctival bevacizumab injection were observed.

Conclusion Short-term results suggest that subconjunctival bevacizumab can be used safely and effectively for corneal neovascularization resulting from different ocular surface disorders, providing an additional strategy to improve success of corneal grafts.

• 4446 / T036
Comparison of the anti-inflammatory effects of artificial tears in a rat model of corneal scraping

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Purpose The aim of the present study was to evaluate the safety and tolerance of cationic oil-in-water emulsion on debrided cornea, and to characterize its benefits on the corneal epithelium healing process.

Methods A rat model of corneal scraping was used to characterize the effects of four commercially available artificial tears (Cationorm®, Vismed®, Optive® and Systane Balance®) on the recovery process of the debrided corneas. The upper part of the corneal epithelium was scraped mechanically prior to a 5-day treatment with different artificial tears. At the end of the treatment, the ocular surface was evaluated clinically (corneal fluorescein staining, CFS) and by in vivo confocal microscopy (IVCM). Conjunctival function was assessed by goblet cell count and MUC5AC immunostaining.

Results The four artificial tears were all well tolerated by the debrided cornea. By restoring an adequately hydrated ocular surface environment they promote corneal healing, as evidenced by CFS measurements of the scraped area. In contrast 0.02% BAK solution inhibits the healing process. IVCM analysis of the different layers of the cornea confirmed the benefits of the cationic emulsion (Cationorm®). Interestingly inflammatory cells infiltration in the stroma was at its lower following Cationorm® treatment, while 0.02% BAK treatment resulted in marked inflammation. The different treatments were all able to protect goblet cells function and MUC5AC expression.

Conclusion BAK-free cationic emulsion (Cationorm®) is well tolerated by debrided cornea and allow for a safe healing of the cornea. The findings suggest that Cationorm® have the potential to benefit patients with corneal epithelium disorder.

Commercial interest

• 4447 / T039
Secreted frizzled proteins in control and keratoconus (KC) tears and corneas

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Purpose To investigate the expression and distribution of Wnt pathway antagonists, secreted frizzled-related proteins (SFRPs), in tears and corneas from control and keratoconus (KC) patients.

Methods Immunofluorescence and confocal microscopy were used to examine the expression patterns of SFRP1, 2, 3, and 5 in paraffin sections of KC (n=11) and control (n=7) corneas. A custom SFRP1 ELISA was developed and used to quantify SFRP1 concentration in basal tear samples collected from KC (n=10) and control patients (n=10). The percentage SFRP1 of total tear protein concentration (%SFRP1) was calculated and compared between KC and control groups.

Results Immunofluorescence showed heterogeneous epithelial SFRP1 expression in all KC corneas compared to low expression in controls. SFRP3 and SFRP5 showed unique patterns of immunolabelling. SFRP3 was localised to epithelial cell membranes and limbal vessels in control corneas; cell membrane and cytoplasmic immunolabelling, and increased expression centrally, was seen in KC. SFRP5 was expressed strongly in the corneal stroma (KC and control). SFRP2 immunoreactivity not obvious in either control or KC corneas. ELISA results showed that tear SFRP1 levels were lower in KC compared to control tears.

Conclusion The pathogenesis of KC remains poorly understood. Our current study shows that SFRP1, 2, 3 and 5 are differentially expressed in control and KC corneas, consistent with previous work, suggesting Wnt signalling involvement in KC. The decreased levels of KC tear SFRP1 contrasts with increased expression in KC corneal epithelium, and may suggest KC-associated differences in tear secretion or tear protein breakdown.Funded in part by Sydney Eye Hospital Foundation

• 4451

Diagnostic ability for glaucoma of imaging technologies based on optic nerve head parameters

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Purpose To assess the ability of optic nerve head (ONH) parameters measured with 2 different imaging technologies to discriminate between normal and glaucoma patients with visual field losses.

Methods Sixty-seven normal eyes and 43 glaucoma patients were consecutive and prospectively selected. Participants were classified depending on the results of standard automated perimetry (SAP) and intraocular pressure. All of them underwent a comprehensive ophthalmic examination, at least 2 reliable SAP tests, and imaging of the ONH with the Heidelberg Retina Tomograph 3 (HRT; Heidelberg Engineering, Heidelberg, Germany) and with Cirrus OCT (Carl Zeiss Meditec, Dublin, Ca). Only one eye per subject was randomly included in the statistical analysis. The areas under the receiver operating characteristic curve (AUCs) were plotted and sensitivity-specificity pairs compared.

Results The mean age was 55.7+/-13.6 years for the normal group and 59.1+/-6.2 years for the glaucoma group (p=0.133). The mean deviation of SAP was -0.7+/-1.2 dB and -5.9+/-6.1 dB (p<0.001) for the normal and glaucoma groups, respectively. The largest AUCs were observed for the rim area of Cirrus (0.954; 95% confidence interval [CI]: 0.919-0.989), and the vertical cup/disk ratio of HRT3 (0.924; 95% CI: 0.890-0.959). There was not a significant difference between them. Sensitivity at 85% fixed specificity was 86% for the rim area of Cirrus and 83.7% for the cup/disk area ratio of HRT3.

Conclusion ONH parameters measured with spectral-domain OCT and HRT3 have similar diagnostic performance. OCT, however, does not require prior manual outlining of disc boundaries, reducing the dependency on operator skill.

• 4452

Parapapillary atrophy: histological gamma zone and delta zone

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Purpose To examine histomorphometrically the parapapillary region in human eyes

Methods The histomorphometric study included 65 human globes (axial length:21-37mm). On anterior-posterior histological sections, we measured the distance Bruch´s membrane end (BME)-optic nerve margin ("Gamma zone"), BME-retinal pigment epithelium (RPE) ("Beta zone"), BME-beginning of non-occluded choriocapillaris, and BME-beginning of photoreceptor layer. "Delta zone" was defined as part of gamma zone in which blood vessels of at least 50µm diameter were not present over a length of >300µm.

Results Beta zone (mean length:0.34±0.52mm) was significantly (P=0.046) larger in the glaucoma group than in the non-glaucomatous group. It was not significantly (P=0.28) associated with axial length. Beta zone was significantly (P=0.03) larger than the region with occluded choriocapillaris. Gamma zone (mean length:0.63±1.15mm) was associated with axial length (P<0.001;r2=0.72) with an increase starting at an axial length of 26.5mm. It was not significantly (P=0.24) associated with glaucomatous optic neuropathy. Delta zone (present only in eyes with axial length of ≥27mm) was associated with axial length (P=0.04) but not with glaucoma (P=0.18).

Conclusion Parapapillary gamma zone was related with axial globe elongation and was independent of glaucoma. Beta zone (Bruch´s membrane without RPE) was correlated with glaucoma but not with globe elongation. Since the region with occluded choriocapillaris was smaller than beta zone, complete loss of RPE may have occurred before complete choriocapillaris closure. Delta zone was present only in highly axially elongated globes.

• 4453 / F015

Biomechanical response of lamina cribrosa and prelaminar tissue to an acute induced IOP elevati

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Purpose We decided to investigate the effects of an acute induced IOP elevation on the prelaminar tissue and on the lamina cribrosa in glaucomatous eyes and in healthy eyes by means of an high resolution Spectral Domain (SD) OCT.

Methods We enrolled 10 patients (mean age 70.2 years) affected by primary open angle glaucoma (POAG) and 10 healthy subjects (mean age 70.8 years) as controls. All the subjects were scanned with a SD-OCT with real-time eye tracking at baseline and in the same exact position during IOP elevation performed with an ophthalmodynamometer. The IOP was measured with a Tono-Pen at baseline and during IOP elevation. The SD-OCT images acquired were processed with a computer graphical suite to determine the prelaminar tissue displacement (PTD) and the laminar displacement in the two groups. An analysis of variance was used for evaluating group differences considering statistically significant a $P < 0.05$.

Results Baseline IOP was significantly different in the two groups, with higher values in patients compared to controls: 18.9(4.3) vs. 15.7(2.6) mmHg (P<0.037). Mean PTD was significantly lower in glaucomatous eyes compared to healthy eyes: 6.8(13.7) vs. 20.8(17.5) micron (P<0.039); whereas LD was similar in the two groups: -0.5(3.7) vs. 0.2(2.0) micron (P=0.366), and not statistically different from 0 (P=0.366).

Conclusion The study shows that an acute induced elevation of IOP does not induce a detectable movement of the lamina cribrosa anterior surface both in glaucomatous and healthy eyes.On the other hand the displacement of the prelaminar tissue is lower in patients with POAG than in controls.

• 4454

Advanced open angle glaucoma with controlled intraocular pressure and cataract: one-year predictive model of glaucoma progression after surgical treatment.

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Purpose To identify the predictive factors of midterm postoperative course in patients with visually significant cataract and advanced open angle glaucoma with intraocular pressure controlled on topical medications.

Methods 55 patients with visually significant cataract and advanced open angle glaucoma (visual field Mean Deviation (MD)≤-12dB) and intraocular pressure(IOP)≤21mmHg on topical medications were prospectively studied(longitudinal data analysis).32 patients undergone phacoemulsification alone versus 23 patients undergoing combined phaco-trabeculectomy. Main outcome measures: IOP(mmHg), visual acuity(VA)(logMAR), MD(dB), number of antiglaucoma medications needed postoperatively. Follow-up 1 year.

Results The combined surgery provided more IOP reduction (-5.76(-7 to -4.5) mmHg) (p<0.001) and allowed the reduction of antiglaucoma medications postop by 2.2(2.7 to 1.8) (p<0.001). VA improvement was more by the time elapsed (p=0.014) and preoperative MD (p=0.006) and less by the presence of relative afferent pupillary defect(RAPD)(p<0.001). The MD change was related to the preoperative MD (p<0.001) while Cup-Disc Ratio had a negative effect on postoperative MD change (p=0.001). The presence of RAPD reduced the MD change (p=0.052) while patients with pseudoexfoliation syndrome and women showed improvement in their MD postoperatively (p=0.038 and p=0.021, respectively).

Conclusion type of operation is the main predictive factor of the IOP change and number of antiglaucoma medication reduction. VA improvement is related to severe damage of the optic nerve and visual field change is related to the degree of glaucomatous damage of the optic nerve.

• 4455

Therapeutic options for narrow angle glaucoma

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Purpose To explain into detail the different therapeutic options present today for the treatment of narrow angles with and without glaucoma. Since not much is understood yet from narrow angle glaucoma; for instance why do some patients develop acute glaucoma and others don't?

Methods Patients files of patients with narrow angles (classified by Visante OCT readings with an angle depth of less than 10°) were retrospectively investigated and subdivided into different groups based on the treatment they received. The first group received a bilateral Argon laser iridoplasty followed a bilateral yag iridotomy; whereas the second group of patients received a primary phacoemulsification.Primary outcome was the intraocular pressure, secondary outcome the effect on the Visante OCT and thereby the influence of the angle structure on progression of glaucoma.

Results Both methods same to be effective in lowering the intraocular pressure. Of great importance is the selection of patients. Patients with a huge lens rise will obviously benefit more from a phacoemulsification, whereas hypermetropic patients will have a sufficient effect from the Argon-Yag combination. Complications, repeatability, effectiveness of the therapies will be further compared in a prospective trial.

Conclusion Both methods same to be effective in lowering the intraocular pressure. Randomized, prospective clinical trials are further necessary to solve this horrific type of narrow angle glaucoma.

• 4456

STARfloTM, a new suprachoroidal drainage implant for glaucoma: 3 months clinical results

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Purpose STARfloTM is a silicone implant for IOP reduction in POAG. STARfloTM is made with STAR® Biomaterial, a flexible tissue-friendly, micro-porous structure designed to reduce fibrotic response and maximize long-term performance.The safety and performance endpoints of the study were; 1. Feasibility of STARfloTM device implantation; 2. Incidence of device and procedure related-complication and unanticipated adverse device effects; 3. Reduction in IOP; 4. Reduction in number of glaucoma medications.

Methods 4 patients with advanced POAG and preop IOP>21 mmHg underwent STARfloTM implantation in suprachoroidal space. Outcome measures were IOP, biomicroscopy, ophthalmoscopy and the number of anti-glaucomatous drugs on D1, W1, M1 and M3 postop.

Results Mean preop IOP was 37.0±8.4 mmHg and mean preop glaucoma medication was 2.5±1 intake/day. 1m postop (4 cases), mean IOP decreased to 21.8±9.7 mmHg (38.4% reduction/patient) and mean glaucoma medication decreased to 1.0±1.2 intake/day. At 3 m (3 cases), mean IOP was 25±11.3 mmHg (33.1% reduction/patient) and mean glaucoma medication was 1±1 intake/day. No adverse events were reported during or immediately postop and no device-related serious adverse events were reported during follow-up. Early complications were: transient hypotony for 2 cases, transient choroidal hemorrhage in 1 case, transient abnormal macula in 1 case. In 3 cases, bleb disappeared at month 1, and in 1 case it disappeared at month 3. 1 patient, with posttraumatic COAG, was dropped 4 m after implantation.

Conclusion Early results for STARflo met the safety and performance endpoints of study. STARflo reduces IOP in refractory glaucoma,

Commercial interest

• 4457 / F037

Marginally controlled open angle glaucoma and cataract: sequential (1st phacoemulsification,2nd trabeculectomy) versus combined (phacotrabeculectomy) surgery

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Purpose glaucoma patients with borderline controlled intraocular pressure (IOP) may benefit from cataract surgery alone. However it is possible that these patients may need glaucoma surgery at some point in the future. Furthermore the risk of postoperative IOP spikes and the inconvenience of two operations (sequential) should be weighed against the complexity of the combined operation. The purpose of the study is to compare the results of phacotrabeculectomy with trabeculectomy in clear corneal incision pseudophacic eyes.

Methods retrospective study of 31 patients with visually significant cataract and open angle glaucoma with IOP 22-25 mmHg on topical medications. The patients were assigned to either surgical treatment according to their glaucoma severity. 20 patients underwent combined phacotrabeculectomy (two-sites) and 11 patients underwent sequential (1st phacoemulsification(temporal clear corneal incision with intraocular lens implantation), 2nd trabeculectomy). Antimetabolites and adjustable sutures were used in all glaucoma operations. IOP measurements were recorded. Follow up time was 6-18 months (median 12 months).

Results the effect of type of surgical treatment on postoperative IOPs was not statistically significant. Combined phacotrabeculectomy resulted in higher IOPs by 0.97(95% Confidence Interval [-1.6 3.59]) mmHg (p=0.47) versus sequential surgery.

Conclusion in patients with clinically significant cataract and glaucoma with borderline control of IOP the choice of combined (phacotrabeculectomy) versus sequential (1st phaco, 2nd trabeculectomy) surgery can be done according to the severity of glaucoma and based on surgeon's preference and experience.

• 4461

Local recurrence after uveal melanoma protontherapy: prognostic consequences

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Purpose To study the prognosis of the different types of uveal melanoma recurrences treated by proton beam therapy

Methods This retrospective study analyzed 61 cases of uveal melanoma local recurrence on a total of 1102 patients treated with protontherapy between June 1991 and December 2010. Survival rates have been determined by using Kaplan-Meier curves. Prognostic factors have been evaluated by using Log-rank test or Cox model.

Results Our local recurrence rate was 5.5%. These recurrences were divided into: 25 patients with marginal recurrences, 18 global recurrences, 12 far recurrences and 6 extra-scleral extensions.4 factors have been identified as statistically significant risk factor of local recurrence in univariate analysis: large tumoral diameter, weak tumoral volume, weak ratio of tumoral volume over eyeball volume and safety margin inferior to 1 mm.In the local recurrence free population, the overall survival rate was 59.8% at 15 years and the specific survival rate was 80.9% at 15 years.In the local recurrence population, the overall survival rate was 34.5% at 15 years and the specific survival rate was 55% at 15 years.Kaplan-Meier survival curves have shown a better prognosis for marginal recurrences compared to the other recurrences.

Conclusion Survival rate of marginal recurrences is highly superior to the other recurrences. The type of recurrence is an important clinical prognostic value to know.

• 4462

When should we retreat choroidal melanomas?

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Purpose Early detection of choroidal melanomas' relapse after conservative treatment is a challenge. Ocular echography is the main exam for the follow up of tumoral thickness, but are all the growths observed after treatment reccurences? We decided to study the regression pattern of uveal melanomas after proton beam therapy to look for an association with local recurrences.

Methods Our study is a retrospective study on all the patients treated by proton beam therapy at the Cyclotron of Nice between june 1991 and july 2010. Our inclusion criterias were a minimum of two echographic eight measurments after treatment and a follow up of a minimum of 6 months, exams were made by the same specialist(JPC).

Results Over the 1155 patients treated, 779 encountered the inclusion criterias. The mean decrease is 8% at 6 months, 20% at 12 months and 35% at 24 months. we observed that 70% of the tumors are stable at 6 months, 50% at 12 months and only 30% at 24 months. An increase of more than 15% is encoutered in 10% of the patients at 6 months, 5 and 2,5% at 12 and 24 months.At 6 and 12 months, tumors which increase is bigger than 15% show no differences for local control. At 24 months,there is a significative difference for local control if the tumor increases(p=0,0003).

Conclusion Analysis of regression pattern allows us to observe that an increase of tumoral thickness is quite usual and isn't statistically linked to local control failure if observed before 12 months. Confirmation of tumor growth is then necessary before an enucleation or a second radiotherapy. After 24 months, we found an association between recurrences and tumor growth and we need new exam to quickly confirm the diagnosis and start treatment.

• 4463

Second course of proton beam therapy for recurrent uveal melanoma

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Purpose To evaluate the outcomes of patients with recurrent uveal melanoma, treated by a second course of fractionated proton beam therapy (PBT) or by enucleation

Methods Tumor recurrence was documented in 54 patients treated with PBT for uveal melanoma.Of these patients, 26 received a second course of PBT and 22 underwent enucleation.The mean patient age was 60,4 years (range, 27–85 years). Among patients with recurrence, the mean followuptime was 5,8 years (range, 6 months–16,4 years). The mean visual acuity was 4,5/10 initially.All patients received 60 cobalt Gray equivalent for both courses.24 recurrences occurred at the margin. The tumor regrowth was within the irradiated area in 17 patients(global recurrence), through the sclera in 4 patients (extra sclera extension), and completely outside theirradiated area in 9 patients.

Results The 5-year cumulative rate of local recurrence after the second treatment was 7,69 % (2 patients among 26 reirradiation).There had 5 enucleations (19,3%) among 26 reirradiations.A third of reirradiated patients maintained useful vision after a second course of PBT : 39% had 20/200 vision or better after the second treatment.The Kaplan-Meier overall survival rate is better with Proton Beam Therapy (PBT) VS Enucleation ($p<0,02$)

Conclusion A second course of PBRT for recurrent uveal melanoma was associated with a relatively good probability oflocal control and a low enucleation rate. This retrospective analysis suggests that survival in reirradiatedpatients is not compromised by administration of a second course of PBT for recurrent uveal melanoma.

• 4464

Pediatric uveal melanoma

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Purpose To study the clinical characteristics, outcome and prognosis of very young patients treated for choroidal melanoma at l' Institut Curie.

Methods Retrospective case-control series.Patients aged ≤16 years were extracted from the database. Patients were treated by enucleation or irradiation depending on tumor size and site. Histology and genomics of the enucleated globes were reviewed. Metastasis and survival were evaluated using the Kaplan-Meier method.

Results From August 1990 to January 2011, 4,857 patients treated for uveal melanoma were prospectively recorded in the database. Fourteen patients (0.3%), 10 girls, 4 boys, mean age 12 years, (median: 14; [range: 2-16 years]) at onset were extracted. Mean basal tumor diameter was 14 mm (median: 14.5; [range: 6 to 22 mm]). Mean tumor thickness was 7.3 mm (median: 6.4 [range: 2.4 to 16 mm]). One half of patients were enucleated, while the other half was treated conservatively by proton beam or iodine plaque radiotherapy. Histopathology of enucleated globes showed epithelioid cellularity in all patients. Genomic analysis by CGH-array was available for 4 patients and showed monosomy 3 for 2 patients and 8q gain for 3 patients. Median follow-up was 91 months [range: 1 to 243 months]. At the end of follow-up, 13 patients (93%) were alive, one presented metastatic disease and one had died. The eye was retained in all patients treated conservatively.

Conclusion Most children had an excellent outcome in terms of survival. An excellent eye retention rate was observed in conservatively treated patients.

• 4465

Uveal melanoma among Finnish children and adolescents

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Purpose To report uveal melanoma (UM) before the age of 25 years in Finland, a high incidence region for this cancer.

Methods A population-based study identified 24 patients (0.3%), aged between 13 and 24 years at diagnosis, treated in our hospital in 1963-2006. They were divided in two groups, the first consisted of 11 patients (9 females, 2 males) enucleated before 1997. The second was treated by irradiation after 1991, consisting of 11 patients (9 females, 2 males). Two other patients underwent local resection (male and female).

Results Tumour height was 4-11 mm (mean, 7) in the first and 4.4-13.7 mm (mean, 8.5) in the second group and largest basal diameter ranged from 5-16 mm (mean, 10) and 2.5- 21 mm (mean, 15), respectively. Four patients died, 3 of UM (after 4, 12 and 21 years). All were female with spindle tumours. In the second group, 2 females died of UM (after 3 and 4 years).

Conclusion UM is rarely seen among young children and adolescents. In this small series, females outnumbered males.

• 4466

Lethal metastatic ciliary body melanoma without hepatic disease in a young girl

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Purpose To illustrate a case report of rapid metastatic death due to a ciliary body melanoma in a a young female of 19 years of age, with no hepatic metastatic disease.

Methods A young algerian girl was send for conservative treatment for a ciliary body tumor of the left eye on the 19th of march 2012.This eye was blind, with a white cataract. Rubeosis iridis was present on the whole iris surface with total angle closure ,ocular pressure was 41 mm and US showed a temporal ciliary body tumor of 3.5 mm in height and 10 mm in diameter .

Results An enucleation was performed on March 20th , but the patient had to be hospitalized on the same afternoon in Intensive Care Unit for drainage of bilateral pleural effusion, purely inflammatory .Full Body CT Scan has shown brain secondary foci of 3 and 5 mm on both frontal lobes.A nodular lesion of 7 mm was also present on the Fowler lung lobe.The liver was not invaded but massive mesenteric necrotic lesions with peritoneal effusion were found.Surgical biopsy of the mesenteric lesions was done in the General Surgery Unit on March 22nd showing melanoma cells.In the same time the ocular pathologists diagnosis was an epithelioid ciliary body melanoma of 10x10 mm.On April 3rd a pleurodesis was created with pleural biopsies in the Thoracic Surgery Unit.Mesothelial pleural hyperplasia without malignancy sign was diagnosed.A chemotherapy with Muphoran has been advised by oncologists and begun soon after she returned in her country where she died at the end of May .

Conclusion Death by metastatic disease can also occur without detectable hepatic lesions by US or CT Scan in case of severe ciliary body melanoma.The mechanism of responsible mesenteric lesions for death in the hepatic vicinity has to be explained.

• 4467

Fine needle aspiration biopsy in uveal melanoma : the Curie experience

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Purpose In order to posssibly include uveal melanoma patients in a randomized trial on adjuvant therapy by Fotemustine we have started in 2009 to propose fine needle aspiration biopsy for genetic studies during clip or plaque positioning

Methods Biopsies were proposed to patients with uveal melanomas of more than 5 mm in thickness.we have used transcleral or transvitreal biopsies depending on the location of the tumor with 25 or 23 gauge needles. Histoacryl glue was used after transcleral biopsies and cryotherapy for transvitreal biopsies.Patients signed an inform consent

Results 108 biopsies were performed between January 2009 and april 2012; 6 patients had transient vitreal hemorrhages (much more frequent with transvitreal p<0,0001)) but no other side effects was observed. A sufficient quantity of DNA for CGH array was present in76% of cases, using whole genome amplification in 60% of cases. The quality of the specimen was strongly correlated with the presence of tumor cells' p<0, 0001). 28, 7% of patients were classified as high genomic risk. No correlation was found between location and size of the tumor or any other clinical factor and the biopsy success rate

Conclusion fine needle aspiration biopsy is a safe procedure to allow genetic testing in uveal melanoma patients

• 4468

A randomized multicentric phase III ongoing study of adjuvant fotemustine versus observation in high risk uveal melanoma patients (FOTEADJ)

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Purpose International guidelines recommend 6 monthly liver US after the local treatment of uveal melanoma (UM), with a constant 20% rate of metastasis, and no impact on the outcome (survival or R0 liver surgery).Clinical risk factors for metastasis include age, largest tumor diameter(LTD),ciliary body involvement, retinal detachment, extra-scleral extension, epithelioid cell type. More recently, genetic alterations of chromosome 3 and 8 have been shown to be highly predictive of a poor prognosis.

Methods We designed a multicentric phase III study with adjuvant Fotemustine versus observation in 302 UM patients with high-risk of recurrence, defined by clinical criteria: LTD≥15 mm with extra scleral extension or retinal detachment or LTD≥18 mm; or genomic high risk signature(a-CGH, NimbleGen 72K microarray) monosomy 3 or partial deletion of 3p associated with 8q gain.The primary objective is to increase the 5-year Metastasis Free Survival from 50 to 70% (5% type I error rate,95 % power). Secondary objectives are overall survival,safety, quality of life.

Results Main inclusion criteria: age ≥18 years, ECOG PS ≤2, no prior chemotherapy or history of invasive cancer,and written informed consent.The genomic analysis is performed by FNA biopsies before the conservative treatment for small UM or after enucleation for large tumors.Schedule: Fotemustine 100 mg/m2, 1 hour IV infusion D1D8D15(induction cycle);5 week rest period; 5 maintenance cycles 100 mg/m2 1 hour IV infusion D1 D21 Follow up period: 3 years (LFTs/3 months, liver MRI or CT/6 months, whole body CT/12 months)

Conclusion June 2009-Jan 2012:70 patients were included in 4 participating centres, extension to other countries is underway.

• 4471

Importance of visual evoked potential in amblyopic children

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Purpose To compare responses to VEP of amblyopic and sound eyes in amblyopic children.

Methods Observational descriptive study of 65 amblyopic children (ages between 20-162 months) with pattern reversal VEPs elicited by checkerboard stimuli with large (120') medium (42') and small (12') checks.

Results No statistically significant difference was revealed concerning P1 amplitude and latencies for any check sizes between the amblyopic and sound eye of amblyopic children.

Conclusion VEP is a very important tool to understand the complex amblyopic mechanism. Although the superior VA of the sound eye, the VEP alterations demonstrate the functional abnormality of the eye considered "good". More studies are necessary to explain why the sound eye in amblyopic children cannot be considered completely normal therefore, special attention should be paid to amblyopic treatment, as patching can have a negative effect on the sound eye.

• 4472

Evaluation of a new technique to evaluate the visual pursuit in infants

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Purpose This study presents a new technique for recording visual pursuit and its evaluation.In infants, visual acuity is usually estimated using behavioral methods. Nowadays, an objective response can be recorded using eye trackers based on the corneal reflex and pupil positions. However, these systems have limitations, such as large eye eccentricity and parasite reflections on tears or eyeglasses. To avoid these constraints, a new technique has been developed and evaluated.

Methods The system is composed of a stimulation monitor equipped with a near infra-red light source and a video camera. A real-time analysis of the video identifies the head position, using a reflective dot placed between the patient's eyes. The gaze orientation is obtained from the relative position of the reflective dot and the eye pupils.Clinical tests were carried out on 90 infants (3 months to 4 years). Gabor type stimuli moving along the horizontal axis were presented while head and eye movements were recorded.

Results Visual pursuit was recorded in 84 infants, some of them with nystagmus or large eye deviation. The visual tracking patterns matched with the literature, i.e. saccadic for the youngest ages and smooth in older normal children.

Conclusion Results show that the new technique is robust and efficient for recording infants' visual pursuit under clinical conditions. Further tests are planned to evaluate if visual acuity estimation agrees with clinical exams.

Commercial interest

• 4473

Quantification of axonal loss in pseudotumor cerebri syndrome using macular thickness measurements with frequency domain-OCT

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Purpose To evaluate the ability of fourier domain-optical coherence tomography (FD-OCT)-measured macular thickness parameters to differentiate between eyes with chronic papilledema from pseudotumor cerebri (PTC) and healthy eyes and its relationship with visual field (VF) loss on standard automated perimetry (SAP).

Methods Fifty-five eyes from 30 patients with PTC syndrome and 70 eyes from 35 normal controls underwent FD-OCT (3D OCT-1000, Topcon) scanning and ophthalmic evaluation including SAP using Humphrey perimetry. All patients had been submitted to previous treatment with clinically resolved papilledema and stable VF for at least 6 months. Macular and peripapillary RNFL thickness measurements were determined. Comparisons were made using Generalized Estimated Equations. Correlations between OCT and VF measurements were also verified.

Results All macular and most RNFL thickness measurements were significantly reduced in eyes with resolved papilledema from PTC syndrome compared to normal controls. Although both OCT-measured macular and RNFL thickness measurements correlated with visual loss on SAP, correlation coefficients were greater for former.

Conclusion Eyes with chronic papilledema show significant macular thinning which is correlated with the severity of VF loss. Macular thickness measurements could potentially estimate the amount of ganglion cell loss during follow-up of patients with pseudotumor cerebri syndrome.

• 4474

Correlation between function and structure of retinal nerve fiber layer in Parkinson disease

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Purpose To determine the capacity of the axonal application for Optical Coherence Tomography (OCT) to detect axonal loss in the retinal nerve fiber layer (RNFL) in Parkinson's disease (PD) and to evaluate the structure/function relationship between OCT measurements and visual function tests.

Methods One hundred patients and 100 controls were included in the study and underwent a complete neuro-ophthalmologic examination consisting in best corrected visual acuity (BCVA), color vision test with Ishihara's pseudoisochromatic charts, automatic perimetry with Strategy SITA standard 30.2 of Humphrey and Spectralis OCT using the new axonal application. Mean and standard deviation of all parameters were calculated and correlation between RNFL, BCVA, Ishihara test's score and the mean and mean standard deviation of the automatic perimetry.

Results Significant differences between controls and patients were found in inferior and temporoinferior RNFL thicknesses (133.18 in controls vs 125.03 µm in PD, p=0.006; 149.53 vs 141.32 µm, p=0.020 respectively) and sector number 8 in papillomacular bundle (306.13 vs 271.19 µm, p= 0.006). Significant differences were also observed in automatic perimetry and Ishihara's score (p<0.001). The RNFL thickness of the papillomacular bundle showed strong correlation (correlation index >0.700) with perimetry values and mild association with Ishihara's score.

Conclusion RNFL loss is detectable by the axonal application of Spectralis OCT in Parkinson disease. Functional parameters obtained by automatic perimetry present strong association with papillomacular bundle measurements.

• 4475

Neuroprotective and regenerative effect of neurotrophin-4 on neuronal degeneration induced by advanced glycation end-products in adult rat retinas

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Purpose To determine the effect of AGEs with or without NT-4 on neuronal cell death and regeneration in isolated rat retinas.

Methods Retinal explants of 4 adult SD rats were three-dimensionally cultured in collagen gel and were incubated either in; 1) serum free control culture media, 2) 10 μg/ml glucose-AGE-BSA media, 3) 10 μg/ml glycolaldehyde-AGE-BSA media, 4) 10 μg/ml glyceraldehyde-AGE-BSA media, 5) glucose-AGE+100ng/ml NT-4 media, 6) glycol-AGE+100ng/ml NT-4 media, or 7) glycer-AGE+100 ng/ml NT-4 supplemented culture media. After 7 days, the number of regenerating neurites from the explants was counted under a phase-contrast microscope. After counting, retinal explants were fixed, cryosectioned, and stained by TUNEL and DAPI. The ratio of TUNEL-positive cells to the number of DAPI-staining nuclei in the ganglion cell layer was calculated. Statistical analysis was performed by one-way ANOVA.

Results In retinas incubated with AGEs (glucose-AGE, glycol-AGE, and glycer-AGE), the numbers of regenerating neurites were fewer than in retinas without AGE ($P=0.0033$, $P=0.0044$, and $P=0.0238$, respectively) and the numbers of TUNEL-positive cells were higher than in control media ($P<0.0001$, respectively). NT-4 supplementation increased, the numbers of regenerating neuritis ($P<0.0001$) and the numbers of TUNEL-positives cells were significantly lower than those in glucose-AGE without NT-4 ($P<0.001$) in glycol-AGE without NT-4 ($P=0.005$) and in glycer-AGE without NT-4 ($P=0.0003$).

Conclusion AGEs induce neuronal cell death and impede neurite regeneration in adult rat retinas. NT-4 significantly enhances neuronal survival and regeneration in retinas exposed to AGEs.

• 4476 / T143

Generating human retinal ganglion cells from human induced pluripotent cells in feeder and feeder-free conditions

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Purpose Glaucoma, and other optic neuropathies, results in the loss of retinal ganglion cells (RGCs) and vision dysfunction. Therefore, cell replacement therapy may offer promising treatments to protect the degenerating retina and potentially restore vision function. Although significant progress has been made to generate photoreceptors from stem cells, there has been little advancement in efficiently generating RGCs. Therefore, we have been investigating the optimal conditions for differentiating RGCs from stem cells for cell replacement therapy.

Methods Human induced pluripotent stem cells (iPSCs) were maintained and expanded on feeder layers using previously published conditions. During embryoid body formation, genes and proteins were tested for effects on increasing RGC differentiation efficiency. Differentiated RGCs were identified and quantified using RGC-specific markers including Brn3. Feeder-free conditions were examined for functional equivalence.

Results iPSCs that express stem cell-specific markers were passaged in proliferative conditions and differentiated into RGCs in vitro. Feeder-free cell culture conditions allowed iPSC maintenance without the presence of mouse immunogenicity. iPSCs were found to respond to pro-RGC differentiation signals in similar fashion to rodent embryonic retinal progenitors.

Conclusion These findings will provide valuable insight in our understanding of RGC differentiation and will pave the way to cure retinal diseases. The transplantation of these cells in vivo will elucidate the integration potential of these cells in degenerating retina.

• 4477 / T142

The use of propranolol in the treatment of periocular infantile hemangiomas

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Purpose Infantile capillary hemangiomas (IH) are the most common tumours of the eyelid and orbit in infants. Despite their self-limited course, IH can impair visual function. Recently, the use of propranolol was found to reduce the size of IH. We will present our own case series of patients with periocular IH treated with propranolol to illustrate these findings.

Methods We conducted a retrospective study on 10 children with IH treated with propranolol. After exclusion of any contra-indication, propranolol was initiated at a dose of 1 mg/kg/d. After 10-14 days, patients were checked again for side-effects. If these were absent, propranolol was increased to 2 mg/kg/d. Further follow-up consists of monthly clinical and photographical evaluations of the IH, monitoring of treatment compliance and tolerance. Success of treatment is defined as stopping growth or reducing size. The response to treatment was rated by 3 blinded, independent observers.

Results The age range at start of treatment with propranolol was between 2 and 19 months (mean 6,8 months). The mean age at stopping propranolol was 14,4 months. The mean duration of treatment was 7,6 months and only 1 patient had to stop treatment because of side effects. Two patients (20%) had a rebound after temporary stop of propranolol. The success rate in our case serie was 100%. Half of the group had excellent results, 30% had a good response and 20% had a fair response. We also obtained objective measures of astigmatism and anisometropia in 6 patients. We report a reduction in anisometropic astigmatism in 5 of these 6 patients.

Conclusion These data support the current perception that propranolol is a highly effective first line treatment for IH with very limited and mild side effects.

• 4481

AICAR induces effectively autophagy clearance in ARPE-19 cells

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Purpose The ubiquitin-proteasome pathway and lysosomal pathway including autophagy are the master clearance systems in cells. The p62/sequestosome 1 (p62) and LC3 have been observed to be key players linking the proteasomal and lysosomal clearance systems. In this study, crosstalk of proteasomes and autophagy was examined.

Methods Effect of autophagy activator (AICAR) and inhibitor (bafilomycin) on protein aggregation and autophagy markers were studied in the ARPE-19 cells treated with proteasome inhibitor (MG-132, 5μM) with or without AICAR (2mM) or bafilomycin (50nM) for 24h hours. Autophagy gene activation was studied by cDNA PCR array. The protein levels of LC3 were evaluated by western blotting. The localization and movement of p62 and LC3 were analyzed by live confocal microscopy. Cellular organelles were visualized by transmission electron microscopy.

Results MG-132 clearly increased perinuclear protein aggregation, while AICAR robustly decreased the amount of aggregates together with LC3 activation. AICAR upregulates the most important autophagy genes. We show that p62 and LC3 colocalizes with the protein aggregates that all are finally degraded in autophagy.

Conclusion Autophagy is effective clearance machine in RPE cells that might be a novel therapy target to prevent cell degeneration.

• 4482

The p62/sequestosome 1 binds irreversibly to protein aggregates prior to autophagy clearance in ARPE-19 cells

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Purpose The pathogenesis of AMD involves impaired protein degradation in RPE cells. The ubiquitin-proteasome pathway and the lysosomal pathway including autophagy are the major proteolytic systems in eukaryotic cells. Recently, p62/sequestosome 1 (p62) has been shown to be a key player linking the proteasomal and lysosomal clearance systems. In this study, expression and trafficking of p62 was examined.

Methods To study the effect of autophagy activator (AICAR) and inhibitor (bafilomycin) on p62 expression levels, the ARPE-19 cells were treated with proteasome inhibitor (MG-132, 5μM) with or without AICAR (2mM) or bafilomycin (50nM) for 24h hours. The protein levels of p62 were evaluated by western blotting. The localization and movement of p62 were analyzed by live confocal microscopy.

Results MG-132 increased the p62 protein levels, while AICAR robustly decreased the p62 levels. When autophagy was inhibited with bafilomycin the p62 was highly accumulated. We show that p62 binds irreversibly to protein aggregates that are finally degraded in autophagy.

Conclusion The p62/sequestosome 1 function as a linker protein between proteasomes and autophagy and can be used as a autophagy flux marker. Autophagy is effective clearance machine that may be disturbed in aged RPE cells.

• 4483

Triamcinolone regulated apopto-phagocytic gene expression patterns in the clearance of dying cells in the retina

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Purpose The clearance of dying cells in the retina has known relevance to development of age-related macular degeneration (AMD). We aimed to investigate the gene expression patterns present during such a clearance process and the effect of triamcinolone (TC) treatment on them.

Methods Primary human retinal pigment epithelium (hRPE) and ARPE-19 cells were induced to undergo cell death by loss of extracellular matrix attachment (anoikis). Phagocytic clearance assays of the engulfment of anoikic cells by human monocyte-derived macrophages (HMDMs) were performed in the presence or absence of TC. Phagocytosis was quantified using a standard double-staining method on flow cytometry. TaqMan low-density array determining the gene expression of known markers of phagocytosis was carried out in HMDMs engulfing anoikic cells. Loss-of-function studies using siRNA were also performed on selected apopto-phagocytic genes.

Results The glucocorticoid TC had a profound phagocytosis-enhancing effect on HMDMs engulfing anoikic hRPE or ARPE-19 cells, causing a selective upregulation of the Mer tyrosine kinase (MERTK) receptor, while decreasing the expression of the AXL receptor tyrosine kinase and THSB-1 (phagocytosis bridging molecule). Similar expression patterns were also observed in the anoikic cells. The key role of the MERTK could be demonstrated in HMDMs engulfing the dying cells using gene silencing as well as blocking antibodies.

Conclusion Specific agonists of the tyrosine kinase receptors may have a potential role as phagocytosis enhancers in the retina and serve as future targets for AMD therapy.

• 4484

Human pluripotent stem cell derived retinal pigment epithelium fulfills requirements of the in vitro functionality

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Purpose Human pluripotent stem cell (hPSC) therapy is a potential approach for the replacement of degenerated retinal pigment epithelium (RPE) cells. For therapeutic use, safety and functionality of the RPE cells needs to be guaranteed. In addition to the basic cell and molecular biological characterizations it is vitally important to assess the differentiation status of acquired cells with functional tests.

Methods We have previously shown that hPSC differentiate into RPE in xeno-free and defined conditions. Recent advances as a culture of hPSC-derived RPE cells sheets on clinically accepted material have led us to investigate the functionality of the RPE epithelium. The tightness of the epithelium was evaluated by measuring transepithelial electrical resistance and cell permeability. The phagocytic properties of hPSC-RPE cells were studied using rat retinal explants.

Results Human PSC-derived putative RPE cells exhibits typical pigmented cobblestone-like morphology and express RPE specific markers at both mRNA and protein level. In addition, cultured cells form a polarized epithelium with high integrity. In addition, co-culturing hPSC-RPE monolayers with rat retinal explants demonstrated that rhodopsin is internalized by cells in vitro.

Conclusion We have demonstrated that hPSC-RPE monolayers acquired RPE-like properties, including characteristic RPE phenotype, expression of RPE markers and barrier functions. In addition, cells were capable of binding and internalizing rat rhodopsin when co-cultured with rat retinal explants. Currently we investigate the correlations of the functions in the Royal College of Surgeons (RCS) rats.

• 4485

Assessment of the retinal pigment epithelial functions-modelling approach

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Purpose Our purpose is to construct mathematical models of functions of retinal pigment epithelium (RPE). Here we show the development and results of two models: 1) a compartmental model of Ca2+ dynamics 2) finite element model of epithelial transport and trans-epithelial resistance.

Methods A model of Ca2+ dynamics of APRE-19 cells based on an experimental data and literature was constructed. Ca+2 dynamics of APRE-19 cells were recorded using fluorescent microscope after mechanical stimulation. Various Ca+2 functional conditions were tested. The computational model constructed (Matlab SimBiology) comprises over 40 cell function parameters and twelve variables ranging from stretch-sensitive ion channels to ryanodine receptor dynamics and sarco/endoplasmic reticulum ATPases. Further, a model of RPE epithelia barrier was developed based on finite element modelling (FEM) of the epithelia and trans-epithelial resistance simulating the spatial distribution of epithelial properties originating of the tight junction distribution on epithelia.

Results The Ca+2 kinetics model of RPE was able to reproduce the Ca+2 dynamics of APRE cells with high accuracy with above 0.97 cross-correlation. Further, including stretch-sensitive ion channels explained the Ca+2 dynamics of the cells close to the mechanically stimulated cell. The epithelial model showed that epithelial inhomogeneity may play a crucial role in epithelial tightness and even very small cellular changes produce large variation on the measures of the epithelial properties.

Conclusion The models constructed provide new insight of the functions of the RPE with applications from drug transport studies to assessment of the functionality of stem cell derived RPE.

• 4486 / T020

CD34 marks angiogenic tip cells in human vascular endothelial cell cultures: a new model to study mechanisms of ocular angiogenesis

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Purpose The functional shift of quiescent endothelial cells into tip cells that migrate and stalk cells that proliferate is a key event during sprouting angiogenesis. Unfortunately, a model of tip cells in vascular endothelial cell cultures is lacking.

Methods We employed the sialomucin CD34 to isolate a small subset of elongated endothelial cells with filopodia from endothelial cell cultures and tested if these cells had properties similar to tip cells in vivo at the functional and molecular level.

Results As predicted by our hypothesis, CD34+ endothelial cells had low proliferation activity. The CD34+ phenotype was upregulated by VEGF-A and downregulated by TNF-alpha and DLL4, three mechanisms known to regulate the tip cell phenotype in vivo. Real-time qPCR and microarray data analysis of the CD34+ cells identified increased expression of all known genes previously associated with tip cells in vivo. Genome-wide mRNA profiling analysis of CD34+ cells demonstrated enrichment for biological functions related to angiogenesis and migration, whereas CD34-negative cells were enriched for functions related to proliferation

Conclusion Our findings suggest that cells with virtually all known properties of tip cells are present in vascular endothelial cell cultures, and that they can be isolated based on expression of CD34. In addition, we characterized the transcriptome of these cells and identified many novel genes with potential significance for angiogenesis. This novel strategy may open alternative avenues of research that may help to understand the molecular processes and functions in angiogenesis in general and of the specialized endothelial tip cell in particular.

• 4511

VEGF Trap-Eye: features of the molecule

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Paris

The role of the vascular endothelial growth factors in neovascular AMD and the features of the VEGF Trap-Eye molecule are presented including binding mechanism, affinity, and predicted biologic activities that support the rationale for every-other-month dosing.

• 4512

The VIEW Studies: clinical results in wet AMD

WEBER M
Vertou

The study design, treatment schedule and the results of the clinical trials VIEW 1 and 2 are shown, including the primary and secondary endpoints. All VEGF Trap-Eye treatment regimens were non-inferior to monthly ranibizumab treatment, and achieved numerically similar outcomes on all endpoints assessed. The results of the follow-up phase at week 96 are presented including safety and efficacy data.

• 4513

VEGF Trap-Eye: update on ongoing clinical trials

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Studies are underway that investigate the safety and efficacy of VEGF Trap-Eye in other indications than neovascular AMD, i.e. central retinal vein occlusion (CALILEO and COPERNICUS trials), diabetic macular edema (GALILEO, VIVID&VISTA trials), myopic choroidal neovascularization (MYRROR).

• 4611

Response of retinal blood flow to systemic hyperoxia as measured with dual-beam bidirectional Doppler Fourier-domain optical coherence tomography

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Purpose Much effort was directed towards the quantification of retinal blood flow in the past decades. In the recent years, optical coherence tomography (OCT) based systems were introduced to measure retinal perfusion. The current study compares a new technique, dual beam bidirectional Doppler Fourier domain OCT (FD-OCT), with laser Doppler velocimeter (LDV), while breathing ambient air and pure oxygen.

Methods 10 healthy volunteers were included into the present study and two study days were scheduled. On one study day assessment of the effect of 100% O2 breathing on retinal blood velocities was performed using FD-OCT. LDV was used to investigate retinal blood velocities on the other study day. In addition to velocity measurements retinal vessel diameters were assessed with Dynamic Vessel Analyzer (DVA, Imedos, Germany). Baseline data as well as hyperoxia data were compared between each study day.

Results Reduced vessel diameters, velocities and blood flow were found while breathing 100% O2 compared to baseline. Our findings showed a high correlation between retinal blood velocities obtained with the OCT system and the LDV during baseline and under hyperoxia ($p<0.01$ each). However, velocities measured with the OCT were slightly higher.

Conclusion Good correlation was found between dual-beam bidirectional Doppler FD-OCT and LDV data. Dual-beam bidirectional Doppler FD-OCT is a promising approach for studying retinal blood flow in vivo.

• 4612

The influence of retinal oxygenation on the clinical outcomes in eyes with epiretinal membrane after successful vitrectomy

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Purpose In the present study patients with epiretinal membrane underwent 23G vitrectomy and ICG membrane peeling. Little information is available about the effects of this treatment on retinal oxygenation. Hence, we set out to investigate the effects of vitrectomy on retinal oxygenation in patients with epiretinal membrane.

Methods In this unmasked, prospective study, patients with macular edema as a result of epiretinal membrane scheduled to undergo vitrectomy without endotamponade, were included. The main outcome measure was oxygenation of the retinal vessels. The measurement of oxygenation in retinal vessels and retinal vessel diameters was performed with the Retinal Vessel Analyzer at baseline, at day 1, day 7, week 4, and week 12 after surgery. At each follow-up visit, a high-definition OCT examination and ETDRS visual acuity were also performed.

Results Retinal venous diameter increased significantly at the first follow-up examination. There was no significant change in oxygen saturation in retinal arteries. Retinal oxygen saturation in retinal veins showed a tendency to decrease at the 3 months follow-up visit. Visual acuity did not change significantly after 3 months. Central retinal thickness was decreased after 3 months as expected but not to a significant level.

Conclusion Vitrectomy for epiretinal membrane may show beneficial short-term effects on retinal oxygenation. In eyes with macular edema due to other pathologies with retinal ischemia, vitrectomy may be performed as an additional treatment modality. Further studies evaluating whether these effects are associated with changes in long-term visual acuity are warranted.

• 4613

Prevention of ocular hypertension in patients receiving intra-vitreal steroids

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Purpose Ocular hypertension is a frequent complication associated with intra-vitreal injection of corticosteroids, in some cases it may require surgery. The present study was designed to evaluate the benefit of a preventive treatment in patients receiving intra-vitreal triamcinolone.

Methods A retrospective study of 90 patients treated with intravitreal triamcinolone in one eye is reported. Injections were performed between 2007 and 2011 in the department of ophthalmology at Reims University Hospital. 77 eyes were treated with brinzolamide in the first three months after the triamcinolone injection. 13 were not treated. Brinzolamide was chosen as it has few systemic side effects and no potential pro-inflammatory action. In both groups, the measurement of the intraocular pressure was performed 7 days, 1,3,6 and 12 months after the injection.

Results A total of 23 cases of ocular hypertension were encountered (25.6%), 14 in the group receiving brinzolamide treatment (18.2%) and 9 in the no treatment group (69.2 %). This difference is statistically significant ($p <0.005$). The peak intraocular pressure was observed 3 months after the injection in both groups.

Conclusion The limited number of patients in the control group and the retrospective design of the study limits the general conclusions which can be drawn. Although there appears to be a measurable effect of brinzolamide in preventing ocular hypertension, a prospective study is necessary to confirm these preliminary findings.

• 4614

Clinical and SD-OCT pattern of retinal venous occlusion with cystoid macular oedema treated with Ozurdex®

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Purpose To report our experience with sustained-release dexamethasone 0.7 mg intravitreal implants (Ozurdex®; Allergan, Inc., Irvine, CA) in first-line treatment of retinal vein occlusion with macular edema.

Methods 26 patients with a minimum follow-up time of 6 months (CRVO n=15, BRVO n=11) make up our study. Complete ophthalmic examination including visual acuity, fundus biomicroscopy, fundus photography, fluorescein angiography and spectral domain optical coherence tomography (Cirrus SD-OCT ; Carl Zeiss Meditec, CA) was performed at baseline and follow-up (1 week, 1 month, 2 months, 3 months, 4 months, 5 months and 6 months) and tolerance of the implant was assessed.

Results Twenty-six eyes of 26 consecutive patients treated with a total of 26 sustained-release dexamethasone 0.7 mg intravitreal implants for macular edema associated with retinal vein occlusion were included. Thirty-three percent of patients gained at least 3 lines of best-corrected visual acuity (BCVA) at 2 months. Forty-four percent of eyes showed SD-OCT significative decrease of the edema following implant placement at 1 week ($p<0.05$). Despite an increase of the macular edema in 57% of the eyes at 4 months, the final best-corrected visual acuity (BCVA) was still better at 6 months than BCVA at baseline. High intraocular pressure (IOP) was mostly controlled with only one medication after OZURDEX. The peak of IOP was noted in 26% of the eyes at 2 months.

Conclusion Sustained-release dexamethasone 0.7 mg intravitreal implant may be an effective treatment option to control macular edema in patients with retinal vein occlusion. Anatomical and functional benefits of OZURDEX are better when the treatment is done at an early stage.

• 4615 / S104

A retrospective data collection study in patients receiving two or more OZURDEX® injections for macular oedema secondary to retinal vein occlusion

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Purpose This retrospective study was designed to investigate the re-injection interval, efficacy and safety of OZURDEX® in routine clinical practice.

Methods This analysis contains data from 87 patients from 10 sites in Germany who had received at least 2 OZURDEX® injections. Data was collected from the time of the patients' first injection until 3 – 6 months following their latest OZURDEX® injection.

Results The mean time to OZURDEX® re-injection between 1st and 2nd treatments was 141 days (5.03 months) in the overall population. Mean time intervals for the BRVO and CRVO sub-populations were 153 days (5.46 months) and 127 days (4.52 months) respectively.In the overall population, a mean LogMAR BCVA improvement from 0.68 to 0.51 was recorded following the last OZURDEX® injection (mean time of 11.0 weeks post-injection). For BRVO, mean improvement was from 0.54 to 0.43 (mean time of 10.5 weeks post injection) and for CRVO, 0.83 to 0.58 (mean time of 11.5 weeks post injection). Reductions in central retinal thickness were also observed.Intraocular pressure measurements over 25mmHg were reported in 19.5% of patients. No glaucoma surgeries were reported. 5 patients underwent cataract surgery during the course of the study (4 had known lens opacity at baseline and opacity status data from the 5th was missing).

Conclusion In this real life study, OZURDEX® was found to be safe and effective with repeat treatments. The mean re-injection interval for RVO patients was 5.0 months.

• 4617 / S106

Pars plana vitrectomy for valsalva retinopathy: a case series

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Purpose To investigate the utility of pars plana vitrectomy in a series of patients with Valsalva retinopathy.

Methods A retrospective, case series study that includes five patients with sudden visual acuity loss owing to Valsalva retinopathy with too dense premacular hemorrhages, treated in our hospital in the last three years. The etiology of the premacular hemorrhage was: vomiting (cases 1, 2 and 3), trauma (case 4) and vigorous dancing (case 5). Mean age was 33±19 years. After a period of observation ranging between three and four weeks, all patients underwent 23-gauge pars plana vitrectomy. The internal limiting membrane (ILM) was released and the hemorrhage was cleaned.The sub-ILM localization was confirmed in all cases during vitrectomy. One patient suffered an accidental break during peribulbar anaesthesia which was resolved successfully with laser photocoagulation. Full clinical examination including best-corrected visual acuity (BCVA) (Snellen chart), intraocular pressure, fundus examination, and Optical Coherence Tomography (OCT) was performed at baseline and at last examination in all patients. The mean follow-up was 16.1 (3-32) months.

Results BCVA was 10/10 in all patients one month after surgery and it remained unchanged during the follow-up period. Funduscopy appearance was excellent in all eyes.No postoperative complications were found.

Conclusion Valsalva retinopathy is a very rare condition that causes sudden visual acuity loss. In those cases with too dense hemorrhages it is necessary to perform vitrectomy, with excellent visual outcomes, as these hemorrhages are highly unlikely to resolve spontaneously.

• 4616 / S105

Dexamethasone drug delivery system (Ozurdex) for the treatment of refractory diabetic macular oedema: retrospective case series analysis

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Purpose The purpose of this study is to report the clinical outcome of the treatment of DME patients with the Dexamethasone Drug Delivery System (Ozurdex) in clinical practice.

Methods This retrospective case series study included 25 consecutive patients (25 eyes) with refractory DME. This preliminary report includes 10 patients who completed a 12 months follow-up. VA (EDTRS), CRT (OCT) and IOP were assessed at baseline, 7 days, and 1, 6 and 12 months after Ozurdex injection. If necessary, a second implant was injected at 6 and/or 12 month.

Results The mean duration of diabetes at baseline was 18.6 years with a mean HbA1c level of 8.97. At baseline the mean VA was 52 letters, mean CRT 467µm and mean IOP 15.9 mmHg. At day 7, the mean VA increased to 62.22 letters (+ 10.22 letters) and the mean CRT decreased to 290.25µm with a mean IOP level of 16.66 mmHg.At month 1: mean VA was maintained to 58.66 letters (+ 6.66 letters) and the CRT continued to decrease to 201µm.The mean IOP slightly increased to 17.83 mmHg (we had 1 case at 24 mmHg)At month 6: mean visual acuity continued to increase to 64.33 letters (+12.33 letters gain). The mean CRT was 281µm with an IOP level of 15.16 mmHg.At month 12: mean visual acuity was maintained to 65.41 letters (2-line gain: + 13.41 letters), mean retinal thickness and IOP level were normal (200µm and 16.81 mmHg respectively). At month 12: 5 patients (50%) had an improvement of more than 15 letters.50% of the patients underwent a second injection, and 33% of them

Conclusion The present clinical study suggests that intravitreal injection of the dexamethasone drug delivery system (Ozurdex) seems to be effective and well tolerated in eyes with refractory DME

• 4618 / S107

Retinal vascular reactivity over extended vessel segments

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Purpose To assess the impact of vessel segment length when analysing retinal vessel responses to flicker light provocation in healthy individuals.

Methods 12 healthy individuals (mean age 30±6) underwent digital sphygmomanometry (UA-767, A&D Instruments, UK), non-contact tonometry (Keeler Pulsair, UK) and dynamic retinal diameter assessment using the retinal vessel analyser (Imedos Systems, Germany) in order to evaluate the influence of segment length on flicker light induced dilation of retinal arterioles and venules. Up to seven segments of each superior artery and vein, were extracted off-line from video recordings of each subject within a minimum distance of 1 disc diameter (DD) from the rim of the optic nerve head and up to a maximum of 4 DD away from the rim.

Results Retinal arteriolar and venular dilation amplitude were independent of segment length, blood pressure and intraocular pressure.

Conclusion Independence of segment length is essential as retinal vessel anatomy is highly variable, some individuals having numerous vessel crossings and bifurcations making it difficult to measure long vessel segments.

• 4631

Infection and inflammation in Boston Type 1 KPro

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Purpose We show possible risk factors for extrusion or endophthalmitis , significance of different clinical features, how to approach them clinically and surgically in order to try to obtain the most successful results in patients who underwent Boston KPro type I surgery.

Methods Review of clinical experience through the last 6½ years dealing with Boston KPro type I surgeries and subsequent possible complications such as melting, thinning, extrusion and endophthalmitis.

Results The main risk factor for KPro failure is inflammation level of the ocular surface. The origin of this inflammation can be diverse: blepharitis, mechanical, immunological. Many inflammatory molecules, through different pathways, can lead to an increase of many metalloproteinases which are involved in the digestion of corneal collagen, producing melting, cornea thinning or even KPro extrusion. Infectious keratitis or endophthalmitis are other dramatic possible complications in KPro patients that can also be associated to collagenolisi

Conclusion Control of ocular surface inflammation is crucial to succeed in the postop of KPro surgeries. In order to achieve this point, management of clinical signs, use of different topical and systemic drugs, and some tricky surgeries should be learned. In case of endophthalmitis, very early surgery consisting of removal of KPro, pars plana vitrectomy and keratoplasty is mandatory.

• 4632

Boston Keratoprosthesis in 2012: preventing complications and optimizing outcomes

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Purpose To provide an update on Boston KPro indications, post-operative care and prevention and management of the complications based upon experience at the MEEI and results presented at the Eighth KPro Study Group Meeting in May 2012.

Methods Clinical records were reviewed to determine outcomes of primary KPro surgery and surgery done using backplates of different materials and design. The origin of retroprosthetic membranes (RPM) from 4 explanted KPro's was determined using immunohistochemistry and light and transmission electron microscopy. Wound anatomy in 6 KPro patients with larger 9.5 mm backplates was evaluated by anterior segment OCT and compared to wound anatomy in patients with standard 8.5 mm backplates.

Results Titanium backplates reduce RPM formation. Histopathologic evaluation showed that RPM are fibrous membranes that originate from activated host stromal cells that migrate through gaps in the graft-host junction, suggesting that better wound apposition may reduce RPM formation. OCT demonstrated that larger backplates clamp the graft-host junction more effectively than standard backplates, resulting in a thinner graft-host junction and better wound apposition. Primary Boston KPro surgery provides good outcomes and device retention in situation such as limbal stem cell deficiency where traditional keratoplasty does poorly.

Conclusion Indications for the Boston KPro continue to expand as complications are reduced. Primary Boston KPro may be considered in certain circumstances. Strategies for prevention of RPM include titanium backplates and complete apposition of the graft-host junction using larger KPro backplates.

• 4633

Advances in imaging of the OOKP lamina

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Purpose The anatomical integrity of an eye bearing an OOKP depends on the integrity and dimensions of the OOKP lamina itself. The lamina is anchored onto the corneo-scleral envelope initially through suturing. Later on, the overlying buccal mucous membrane graft adheres onto the soft tissues invested into the bone of the lamina, retaining it and providing a seal to guard against entry of microbes into the eye. The integrity and dimensions of the lamina is ascertained clinically at each hospital visit, and this is aided by periodic radiological imaging.

Methods We studied the relative merits of volumetric analysis, multislice CT vs Aquilion, and texture analysis. We also studied the feasibility of inserting radioopaque markers into the optical cylinder to aid inter examination orientation thus allowing subtraction radiology.

Results Volumetric analysis has proven useful but cannot detect fractures in the lamina. The Aquilion provides slightly superior images but its major advantages are speed of acquisition and a much lower radiation dosage, allowing more frequent examination in cases where there is a suspicion of rapid dissolution of the lamina. Asymmetric markers placed with an optical cylinder can be imaged successfully.

Conclusion Much work remains to be done to improve imaging of the OOKP lamina. Considerators include image resolution, speed of acquisition, radiation dosage, costs, and repeatibility.

• 4634

Oculoplastic complications of OOKP surgery

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Purpose To report the incidence, types and management of oculoplastic complications following OOKP surgery.

Methods A retrospective review of case records of 60 patients who underwent OOKP surgery was performed between November 1996 and March 2012. Mucous membrane, eyelid and cosmetic complications were studied following each stage in the two stage OOKP procedure.

Results Patients age ranged from 19 to 95 years and the follow up duration varied from 6 months to 15 years. The commonest diagnosis was Stevens-Johnson syndrome followed by chemical or thermal burns and mucous membrane pemphigoid. Forty nine or 82% of these patients had some form of oculoplastic complication. After the Stage 1, 27% of these patients had mucous membrane complications and 15% had eyelid complications. Following the Stage 2, 68% of these patients had mucous membrane complications and 53% had eyelid complications Three patients wore cosmetic shells and all of them had shell fitting problems. Most of the complications were successfully managed with appropriate surgical procedures.

Conclusion Oculoplastic complications are the most common complications after the OOKP surgery. They are most frequently noted following the Stage 2 procedure. The outcome is generally favorable with timely recognition and management and they do not usually have an adverse affect over visual acuity.

• 4635

A study of the real life performance of OOKP optical cylinders

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Purpose To evaluate the optical and visual functional characteristics of the Osteo-Odonto-Keratoprosthesis (OOKP)

Methods Nine patients with implanted OOKP devices were examined. Glare effect (Low, Medium and High intensity) was measured with a brightness acuity test (BAT) and contrast sensitivity was assessed using Metropsis Visual Stimulus Generation software (Cambridge Research System) at 0.3; 0.7; 2.20; 3.50; 10.4 and 14.5 cpd. Kinetic Goldmann perimetry and wavefront aberrometry (Nidek OPD-scan) were performed in each patient. All patients completed a Quality-of-Life questionnaire (NEI VFQ-25)

Results A reduction in mean visual acuity (logMAR) with increasing glare settings was observed from 0.12 without BAT to 0.27 with BAT at High. Mean visual acuities (logMAR) measured with BAT at Medium (Mann Whitney U-test $p<0.05$) and High (U-Test $p<0.01$) intensity settings were found to be significantly reduced statistically when compared to VA without BAT.Contrast Sensitivity was significantly reduced when compared to age-matched control at medium and high spatial frequencies. Several vision-related VFQ-25 sub-scales correlated significantly with visual acuity at various BAT levels such as General Vision, Near Activities and Distance Activities (correlation coefficients: -0.71 to-0.86; $0.05>p>0.001$). Correlation with these subscales was also observed with contrast sensitivity at medium spatial frequencies (-0.67 to -0.83; $0.05>p>0.001$)

Conclusion The optics of the OOKP can provide patients with excellent visual acuity that correlates well with visual function. Visual acuity is significantly reduced by glare and patients experienced a lower contrast sensitivity compared to age-matched controls. Glare reduction and cylinder alignment could further improve function

• 4636

Psychological factors and complications in OOKP assessment and surgery

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Purpose To highlight how psychological factors can complicate OOKP assessment , surgical outcome and adaptation to living with OOKP and to demonstrate how these issues can be addressed.

Methods Single case studies will be used to illustrate the clinical presentation of psychological issues and how these may have impacted on medical progress and adjustment post surgery.

Results Cases will illustrate how a previous psychological trauma history, mood disorder and identity issues can impact on physical, psychological and social adjustment to OOKP. The case studies will also illustrate interventions which addressed these.

Conclusion For some patients ,the identification of psychological problems and their appropriate management is important for succesful outcome and adaptation in OOKP surgery.

• 4641

Evaluation of lower tear meniscus shape with OCT

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Purpose When measuring the tear meniscus radius and calculating tear volume, the anterior radius of the meniscus is assumed to be spherical. This study aimed to define the shape of the meniscus more precisely using high-resolution optical coherence tomography (OCT).

Methods Images of the lower tear meniscus of 30 normal subjects (8M, 22F; mean age 27.5±9.6yrs), recruited from the patient pool of Höhere Fachschule für Augenoptik, Cologne, Germany, were taken using the Zeiss Cirrus HD OCT. Applying ImageJ software, the tear meniscus height (TMH) was measured and the xy-coordinates of 12 marked points on the anterior tear meniscus curve were determined. With these coordinates a graph was plotted and the best fitting trend-line (defining TM curvature) was calculated. Furthermore, the distance between the edge of the lower eyelid and the vertex of the curve (TMH-V) was calculated and compared to the half TMH (TMH-H).

Results Mean TMH was 0.24 SD±0.06mm. The mean fitting trend-line appeared to be a quadratic equation (R-squared range from 0.908 to 0.996). TMH-V (0.12±0.04mm) and TMH-H (0.12±0.03mm) were significantly correlated ($r=0.62$; $p<0.001$). The 95% LoA showed that the TMH-V could be expected to be up to -0.07 mm below and 0.07 mm above the TMH-H.

Conclusion With high-resolution OCT the anterior surface of tear meniscus was found to have a parabolic shape, which will help to calculate tear volume more precisely. To know the position of the parabolas vertices is useful when explaining the position of light reflexes from the tear meniscus particularly in reflective meniscometry.

• 4642

In vivo laser scanning microscopy of cornea, conjunctiva and ocular adnexa with a handheld dermatological laser-scanning microscope: new perspectives

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Purpose In vivo confocal microscopy (IVCM) is routinely used in well-equipped reference centers for the diagnosis of complicated corneal and conjunctival diseases, mainly infectious and tumoral ones. At present, only two CM are available for ophthalmology. Both are attached on a classical ophthalmology stand optimized for corneal examination. Aim: to expose new perspectives in examination of cornea, conjunctiva and ocular using a handheld dermatological CM

Methods Using the handheld dermatological reflectance laser-scanning microscope (Vivascope 3000, MAVIG GmbH) equipped with a 830nm laser, we observed cornea, bulbar and tarsal conjunctiva, eyelid margin, lacrimal puncta and palbebral skin of healthy volunteers as well as none pigmented or pigmented lesions of these sites. Correlations with histopathology were established whenever surgery was necessary

Results Thanks to its compact configuration and flexible, handheld positioning, the Vivascope3000 made it possible to easily access ocular and periocular tissue that remained challenging to observe with ophthalmological CM. With a definition of 1pixel/µm and 1000x1000 µm images, the handheld CM allowed non-invasive optical biopsy of all normal and pathologic ocular surface as well as periocular tissues. Diagnosis of benign or malignant tumors (melanoma or epidermoid carcinoma) could be highly suspected. Confocal images were well correlated with conventional histopathology

Conclusion The compact handheld Vivascope 3000 offers new perspectives for diagnosis, optimization of treatments, and follow-up of ocular surface and ocular adnexa diseases

• 4643

Fluorescence multi-laser scanning microscopy of the cornea and ocular adnexa: a new era for functional confocal microscopy in ophthalmology

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Purpose In vivo confocal microscopy (IVCM) is a routine investigation for the ocular surface in reference centres. It provides high resolution pseudo histology. Nevertheless its unique laser source and imaging principle (reflectance) only provide morphological information. Multi-laser and fluorescence laser scanning microscope add a supplementary dimension by allowing the use of fluorescent markers liable to provide specific functional data

Methods Ex vivo animal and human corneas, healthy volunteers and patients were successively examined using the multilaser vivascope 1500 (MAVIG GmbH, Germany) equipped with 3 lasers (488, 658, 785nm) and the corresponding emission (Em) filter sets. For each excitation (Ex) wavelength (λ), 3 observation modes were available: reflexion (all λ), pure reflectance (λEx = λEm), fluorescence (3 specific band pass). Ex vivo, all corneal layers were analysed without preparation and after topical application of Fluoresceine (F) and Indocyanine green (ICG) and of numerous other molecules. Topical instillation and of intraveinous injection of F and ICG were analysed in healthy volunteers and in patients

Results Using reflexion and reflectance, the 3 Ex λ gave complementary structural informations with the highest resolution obtained at 488nm. Topical markers helped identify specific cell populations and intracellular structures. Intraveinous ICG was inefficient whereas fluo provide highly contrasted conjunctival images

Conclusion IVCM coupled with fluorescence opens a new era in the clinical imaging of the ocular surface and probably more largely in Ophthalmology. A new semeiology remains to be learned

• 4644

Spatial arrangement of collagen fibrils in normal and keratoconus human cornea studied by low-frequency dielectric spectroscopy

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Purpose Spatial structure of collagen lamellae of the human cornea is thought to be an important determinant of corneal rigidity. Analysis of the low-frequency (1–107 Hz) dielectric spectra of the normal and keratoconus human cornea in the temperature range of 140-300 K and for different hydration states were examined.

Methods For the measurements, the 100 – 200 µm specimens containing the middle layers of corneal stroma were used. The 9 specimens of healthy, control corneas from Eye Bank were obtained with second microkeratom section during Ultra Thin-DSAEK. The 12 specimens of keratoconus corneas were manually prepared from corneas removed during penetrating keratoplasty.

Results Experimental results were interpreted in terms of ionic diffusion and space charge polarization according to the Sawada's theory. The new presentation of the dielectric spectra, i.e.: (delta eps'/delta ln f)*f, was used. The presented method and the Sawada's expression were applied to the analysis of the changes in spatial molecular structure of collagen fibril network in human cornea.

Conclusion Fitting procedure of the theoretical function to the experimental data allowed us to determine two diffusive relaxation regions with two structural distance parameters ds, describing spatial arrangement of collagen fibrils in cornea.

• 4645 / T031
Tear film break-up time evaluation by real-time wavefront aberrometry in normal subjects

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Purpose To evaluate tear break-up time (BUT) with repeated higher order wavefront aberrations (HOA) measurements.

Methods Wavefront aberrations up to the sixth order for a 4-mm pupil were measured in 10 subjects using the IRX3 (Imagine Eyes, Orsay, France) Hartmann-Shack (H-S) aberrometer. The aberrometry was performed once every second for up to 20 seconds. HOA measurements were performed 3 times in a row. HOAvariations were compared with the BUT by the conventional fluorescein method (CFM).

Results In 9 patients out of 10 there was an excellent correlation between the HOA variation and the BUT recorded by the CFM. There was also an excellent reproducibility of the HOA measurements in all patients.

Conclusion H-S aberrometry can be used in our daily practice for an objective and reproducible assessment of the BUT.

• 4646 / T030
Tear film break-up time evaluation by real-time wavefront aberrometry in adult patients with meibomian gland

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Purpose To evaluate tear break-up time (BUT) with repeated higher order wavefront aberrations (HOA) measurements in adult patients with Meibomian Gland Dysfunction(MGD).

Methods Wavefront aberrations up to the sixth order for a 4-mm pupil were measured in 10 normal subjects (Group 1) and 10 patients with severe MGD (Group 2) with corneal involvement, using the IRX3 (Imagine Eyes, Orsay, France) Hartmann-Shack (H-S) aberrometer. The aberrometry was performed once every second for up to 20 seconds. HOA measurements were performed 3 times in a row. HOA variations were compared with the BUT by the conventional fluorescein method(CFM).

Results There was an excellent correlation between the HOA variation and the BUT recorded by the CFM in both groups. There was also an excellent reproducibility of the HOA measurements in all patients. BUT was significantly decreased ($P<0.005$) in all patients in Group 2 compared to the normal tests subjects(Group 1).

Conclusion Studying the HOA variation is a valuable method for evaluatingboth the quality visionand the BUT in patients with MGD and evaporative Dry Eye.The IRX3 H-S aberrometer can be used for an objective and reproducible assessment of the BUT in the follow-up of patients with severe MGD.

• 4647 / T032
Corneal respiratory function by FAD autofluorescence lifetime

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Purpose We intend to develop an efficient method to assess in-vivo the corneal respiratory function in order to diagnose corneal cells dysfunction prior to its pathologic expression.

Methods Metabolic alterations can be assessed by measuring the amount of the metabolic co-factors flavin adenine dinucleotide (FAD) and nicotinamide adenine dinucleotide (NADH). FAD has advantages over NADH, like being present only in the mitochondria. Furthermore, using fluorescence lifetime imaging microscopy (FLIM) we are able to discriminate between its free or protein-bound states.We resorted to a PicoQuant MicroTime 100 (PicoQuant GmbH, Berlin, Germany) coupled to an Olympus BX51 Microscope (Olympus Corporation, Tokyo, Japan). This setup uses a pulsed blue diode laser with a trigger frequency of 40 MHz with an excitation filter of 440±10 nm. Intensity decay curves were processed with SymPhoTime v5.3 Software (PicoQuant GmbH). The instrument response function was acquired to improve data analysis precision.

Results We successfully acquired ex-vivo autofluorescence images of male Wistar rat and Bovine corneas. A bi-exponential decay was observed in both cases with a fast decay around 1 ns and a longer one around 4 ns, which correspond to protein-bound and free FAD, respectively. These results are in accordance with other studies, although there is some controversy regarding FAD lifetimes.

Conclusion We showed that it is possible, with our apparatus, to acquire metabolic images of the cornea using FAD autofluorescence.We intend to modify the instrument optical setup in order to acquire reflectance and fluorescence lifetime images simultaneously for corneal layer identification.

• 4648 / T070
Assessment of angle and anterior chamber changes after keratoplasty

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Purpose To quantify angle and anterior chamber changes after corneal transplantation using Visante OCT®

Methods In this retrospective study, Visante OCT® examinations were performed in patients, awaiting keratoplasty, preoperatively(J-1) and one month postoperatively(M+1). The anterior chamber depth(ACD), the angle-opening distance at 500µm(AOD), the trabecular-iris space area at 500µm(TISA) and the scleral spur angle(SPA) in the temporal and nasal quadrants were measured. Patients were classified based on their surgery: the surgery was penetrating keratoplasty(PK group), it was descemet's stripping automated endothelial keratoplasty(DSAEK group).Preoperative and postoperative measurements were compared using signed rank test of Wilcoxon.

Results Twenty patients were evaluated: fifteen(75%) in the DSAEK group, five(25%) in the PK. Mean anterior chamber depth width increased from 3,31mm(SD 0,69) to 3,35mm(SD 0,341) after PK(p=1) , and from 3,32mm(SD 0,666) to 3,44mm(SD 0,591) after DSAEK(p=0,719).In the temporal quadrant, after DSAEK, mean anterior chamber angle width increased from 0,281mm(SD 0,126) to 0,334mm(SD 0,100)(p=0,03) in the TISA and after PK ,mean anterior chamber angle width decreased from 0,273mm(SD 0,054)to 0,248mm(SD 0,118) (p=0,812).In the nasal quadrant, after DSAEK, mean anterior chamber angle width increased from 0,253mm(SD 0,089) to 0,285mm(SD 0,085)(p=0,207) in the TISA and after PK, from 0,269mm(SD 0,114)to 0,321mm (SD 0,069) (p=0,437).

Conclusion The angle change significantly in the temporal quadrant after corneal transplantation. Larger study need to be perform to confirm the angle changes.

• 4651

Oximetry in glaucoma: correlation of metabolic changes with structural and functional

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Purpose To determine whether retinal vessel oxygen saturation in glaucoma patients is associated with structural optic disc and retinal nerve fiber layer (RNFL) changes and visual field defects.

Methods Retinal oxygen saturation was measured in glaucoma patients with a non-invasive retinal oximeter (Oxymap ehf, Reykjavik, Iceland). Visuals fields and HRTs were performed on the same day. Statistical analysis was performed using Student's t-test and Pearson correlation coefficient when the data were normally distributed: otherwise Spearman correlation was used.

Results The mean oxygen saturation in the arterioles was 97% ± 2%, in venules 65% ± 6% and the arteriovenous (AV) difference was 33% ± 6%.The oxygen saturation in the venules correlated with the visual field mean defects (r= -0.42; p=0.001; n=59) as well as with the structural HRT parameters rim area and RNFL (r= -0.39; p=0.008 and r= -0.26; p= 0.05 respectively; n=53). The AV difference decreased significantly as the visual field defect worsened (r= 0.38; p=0.003), as the rim area diminished (r= 0.29; p=0.03) and as the RNFL decreased (r= 0.27; p= 0.05). No correlation was found between the oxygen saturation in the retinal arterioles and either of these parameters.

Conclusion Severe glaucomatous damage is associated with increased oxygen saturation in retinal venules and decreased AV difference in oxygen saturation. These data suggest that in eyes with severe glaucomatous damage, retinal oxygen consumption is decreased due to tissue loss.

• 4652

Blockade of the chemokine receptor CXCR3 lowers intraocular pressure and prevents retinal degeneration in an animal model of glaucoma

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Purpose Blockade of the chemokine receptor CXCR3 lowers intraocular pressure and prevents retinal degeneration in an animal model of glaucoma.

Methods Twenty Long-Evans male rats underwent episcleral vein cauterization in order to induce stable elevation in intraocular pressure (IOP). CXCR3 antagonist or the vehicle only were subconjunctivaly injected in glaucomatous eyes (n=10 in each), which were assessed for IOP weekly during two months. Aqueous humor outflow and trabecular filtrating function were studied using fluorophotometry and microsphere trabecular trapping respectively. Retinal nerve fiber density was quantified by scanning laser ophthalmoscopy, and optokinetic testing was performed to assess visual function.

Results IOP was significantly decreased during 6 weeks in glaucomatous eyes treated with CXCR3 antagonist as compared to untreated eyes.(P<0.01 at each time point) CXCR3 antagonism increased aqueous humor outflow (P<0.01) by improving the trabecular filtrating function.(P<0.01) Retinal nerve fiber density was higher in treated glaucomatous eyes than in untreated eyes,(P<0.01) and correlated with a better visual function in eyes receiving the CXCR3 antagonist.(P<0.01)

Conclusion In vivo blockade of CXCR3 in a rat model of glaucoma improves the trabecular filtrating function and subsequent aqueous humor outflow, further protecting the retina against IOP-related degeneration.

• 4653

The effect of Benzalkonium chloride on the intraocular pressure lowering efficacy of a local ROCK-inhibitor (AMA0076)

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Purpose To elucidate the effect of Benzalkonium chloride (BAK) on the intraocular pressure (IOP) lowering efficacy of a local ROCK-inhibitor AMA0076 (Amakem NV) in the rabbit eye.

Methods Topical administration of AMA0076 (0.1%, 0.3% and 0.5%) was tested in a normotensive New Zealand White rabbit model (5 rabbits/group). The IOP lowering efficacy of the compound was determined with or without the addition of 0.01% BAK. The contralateral eye was used as a control and was treated with vehicle (H2O PEG) in all groups. IOP was measured at baseline and at 1, 2, 3, 4, 5, 6, 7 and 8h post administration. Data at individual time points were analyzed using mixed model analysis for repeated measures. $P < 0.05$ was considered to be statistically significant.

Results Single topical administration of AMA0076 significantly lowered IOP in a concentration dependent manner compared to the control eye (p<0.05). Placebo/vehicle administration did not induce significant changes in IOP. The maximal IOP lowering effect of AMA0076 0.1%, 0.3% and 0.5% containing 0.01% BAK was 38%, 45% and 53%, which was significantly stronger compared to their BAK-free equivalents: 21%, 28% and 37% (p=0.005, p=<0.001; p=0.008 respectively).

Conclusion The local ROCK inhibitor, AMA0076 was significantly more effective in lowering IOP in the presence of 0.01% BAK.

• 4654

Outcome improvement of glaucoma filtration surgery through the effect of local rock-inhibition on wound healing

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Purpose The aim of this study was to investigate the efficacy of a local ROCK-inhibitor; AMA0076 (Amakem NV) for improving surgical outcome, after glaucoma filtration surgery in a rabbit model.

Methods The in vivo effects of local ROCK-inhibition were investigated in a rabbit model of glaucoma filtration surgery (n=5 per histological analysis group). Topical treatment with AMA0076 (study eye) and vehicle (control eye) was administered every day 3x/day (9h/13h/17h) from day 1 after surgery. Treatment outcome was studied by clinical investigation (IOP; intraocular pressure, bleb area and bleb survival) as well as immunohistological analyses for inflammation (CD45), angiogenesis (CD31) and collagen deposition (Sirius Red) at day 3, 8 and 14 after surgery.

Results Bleb survival showed no difference between treated and non-treated eyes however, there a trend (p=0,09) can be distinguished. Topical treatment of AMA0076 reduced inflammation on day 3 (p=0.036) and day 8 (p=0.044) as well as angiogenesis on day 8 (p=0.04). There were no differences in collagen deposition.

Conclusion Targeting ROCK with a local ROCK inhibitor, AMA0076, is efficacious in reducing inflammation and angiogenesis on several time points in a rabbit model of glaucoma surgery. These results render ROCK an interesting target to increase the success rate of filtration surgery and point to potential therapeutic benefits of the local ROCK inhibitor, AMA0076.

• 4655

Inhibition of placental growth factor improves surgical outcome of glaucoma surgery

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Purpose We checked the hypothesis that placental growth factor (PlGF) plays a role in scar formation after glaucoma filtration surgery (GFS), and that it may be a target for improvement of the outcome of this surgery.

Methods The effect of the anti-murine PlGF-antibody (5D11D4) was investigated in a mouse model of GFS in C75Bl/6 mice. Immediately after surgery 5D11D4 (1µl; 5.2mg/ml) or 1C8, an irrelevant mouse IgG antibody (1µl; 4.8 mg/ml), was injected in the anterior chamber (n=10 eyes for both groups). An anti-murine VEGF-R2 antibody (DC101) was used as a positive control (1µl; 6.2 mg/ml; n=10). Mice were killed on post-operative day 8. Treatment outcome was studied by clinical investigation of bleb area and bleb survival every other day. All antibodies were kindly provided by ThromboGenics NV.

Results In the mouse model of GFS, treatment using the anti-PlGF antibody (5D11D4) significantly improved surgical outcome by increasing bleb survival (p=0.04) and bleb area (p=0.01) with 29% compared to negative control (1C8). A single administration of anti-VEGF-R2 (DC101) also significantly improved bleb area with 7% as compared to 1C8 (p=0.05), but had no effect on bleb survival (p=0.23). A trend towards an increased bleb area after 5D11D4 administration was observed compared to DC101 delivery (p=0.07).

Conclusion Targeting PlGF with an inhibitory monoclonal antibody is efficacious in improving GFS outcome, possibly even more effectively than inhibition of VEGF-R2. These results render PlGF an appealing target for ocular wound healing and point to the potential therapeutic benefits of PlGF-inhibition.

• 4656

Topical application of AMA0076, a locally acting rho kinase (ROCK) inhibitor, results in a robust IOP control in Dutch Belted Rabbits

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Purpose To determine the intra ocular pressure (IOP) lowering efficacy of the local ROCK inhibitor, AMA0076, in Dutch Belted rabbits.

Methods Dutch Belted rabbits (5 rabbits/group) received topically a single dose of AMA0076 in one eye. A concentration range of 0.031 - 0.625% AMA0076 was tested. The contralateral eye served as control and was treated with saline. IOP was measured at baseline and 30 min, 1, 2, 3, 4, 5, 6, 7, 8h post topical administration.

Results Single topical administration of AMA0076 significantly lowered IOP in all groups compared to the control eye ($p<0.05$). Mean baseline IOP during the experiments was between 20.6 and 21.5 mmHg. Thirty minutes after topical treatment, a concentration dependent reduction in IOP was demonstrated with a ΔIOP ranging from 3.9mmHg – 7mmHg compared to the control eye. Maximal IOP reduction of each concentration following single dose administration of AMA0076 was observed ±2 hours after instillation with a ΔIOP ranging from 4.6mmHg and 7.5mmHg. The IOP lowering effect with the highest concentrations of AMA0076 (0.625% and 0.125%) was sustained during the experiment.

Conclusion AMA0076 was effective in rapidly lowering IOP in a dose depended and sustained manner after a single topical dose in Dutch Belted rabbits. This new class of local ROCK inhibitors has potential therapeutic value for the IOP lowering treatment of glaucoma.

• 4657 / F050

Retinal MMP expression is upregulated in an excitotoxic mouse model of glaucoma

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Purpose Multiple studies in glaucoma patients and animal models, have reported differential expression and activity of matrix metalloproteinases (MMPs). These data have led to the hypothesis that MMPs are involved in glaucoma disease onset and/or progression. However, their in vivo functions remain poorly understood and contradictorily results prevent a clear definition of their role. Here, we describe the expression of MMP-2, -3, -9 and -14 in the retina of mice subjected to an acute excitotoxic glaucoma model.

Methods Excitotoxic RGC death was induced via intravitreal injection of 20 mM NMDA. Expression of MMP-2, -3, -9 and -14 was examined via immunohistochemistry, Western blot and quantitative RT-PCR.

Results MMP-2 and -3 are expressed by glia, presumably Müller glia, in the healthy retina and are strongly upregulated at 24h after NMDA injection. MMP-9 expression, which is not detectable in naive retinas, is observed in RGCs at 24h post NMDA injection, which confirms its suggested role in RGC apoptosis. In the naive retina, MMP-14 is expressed by bundles of RGC axons in the nerve fiber layer, from where its expression is extending through the optic nerve to the primary visual areas in the brain. Within the first 48h after NMDA injection, MMP-14 expression increases and is also seen in the inner nuclear layer and both plexiform layers.

Conclusion Our results reveal a strong upregulation of MMP-2, -3, -9 and -14 in the mouse retina after NMDA injection, suggesting that these proteinases might be involved in excitotoxic neurodegeneration and/or glial reactivity. Further analysis of their involvement, including studies in MMP knockout mice, is currently ongoing.

• 4661

Successful treatment of macular retinoblastoma with superselective ophthalmic artery infusion

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Purpose To report our experience with superselective ophthalmic artery infusion of Melphalan (SOAIM) for macular retinoblastoma, in order to obtain tumor control while preserving as much as possible useful vision.

Methods This report concerns 5 cases with 'naïve' unilateral retinoblastoma involving the macula, selected from a group of patients scheduled for SOAIM as the primary treatment. Follow-up ranged from a minimum of 6 months to a maximum of 30 months.

Results Each eye of each patient was treated with a cycle of three SOAIM procedures, made of 3-5 mg of Melphalan per eye per treatment. SOAIM procedure was well tolerated in all 5 patients. One of the eyes was also treated with cryotherapy while all eyes underwent transpupillary thermo-therapy and/or argon laser during or after the intra-arterial treatment cycle. All patients are alive and free of metastatic spread. All the eyes achieved ophthalmoscopic remission of the tumor foci, showing types I to III regression, and no enucleation was necessary.Ultrasounds and fluorangiography were performed.

Conclusion SOAIM is effective for the treatment of macular retinoblastoma, when performed in adequate settings by operators with skills in angiographic diagnosis and treatment of intracranial vascular diseases. Moreover, Melphalan selectively delivered in the ophthalmic artery may allow the salvation of eyes which should otherwise be enucleated, showing a very low rate of complications due to local and systemic toxicity.

• 4662

Indications for intraarterial chemotherapy in patients with advanced retinoblastoma

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Purpose Despite the use of new methods of treatment for retinoblastoma their efficacy remains debatable and depends on different factors. Our aim was to determine the indications and efficacy of intraarterial chemotherapy in patients with different growth pattern in advanced retinoblastoma.

Methods For the period of last year 20 children (26 eyes) were treated for advanced and resistant retinoblastoma . 12 had monocular and 8 binocular RB. Age from 12 months to 6 years. 16 out of 20 children have had systemic chemotherapy. 13 patients have had exophytic growth and 7 – endophytic. All patients were treated with intraarterial chemotherapy with melfolan 7.5 mg (1-3 injections).

Results We were able to preserve 21 eyes out of 26 eyes. The retrospective analysis has showed that the enucleated eyes had endophytic growth with massive seeding of tumour into the vitreous body. The best effect after chemotherapy has been observed in untreated patients with exophytic growth and juxtopapillary localization.

Conclusion Our experience shows that intraarterial chemotherapy in patients with endophytic growth of retinoblastoma has very low efficacy. The choice of method of treatment depends on tumour growth pattern, localization and duration of earlier done systemic chemotherapy.

• 4663

Natural history of an early diagnosed retinocytoma: case report and literature review

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Purpose To study the ophtahlmoscopic evolution of a retinocytoma diagnosed in a 8 months old boy.

Methods The patient was referred at the Referral Center for Retinoblastoma of the University of Siena, with the suspect of unilateral retinoblastoma. The boy was diagnosed as having retinocytoma based on ophthalmoscopic appearance. Monthly ophthalmoscopic and ecographic evaluation were recommended. Detailed fundus drawings and fundus photographs and descriptions of the retinocytoma were collected. The little boy underwent also MRI, genetic testing and fluorangiography.

Results Throughout the months, we observed a tumor regression from avascular mass with fish-flesh appearance and microscopic calcifications to a retinal transparent mass with calcifications, retinal cysts and surrounded by chorioretinal atrophy.

Conclusion Retinocytoma is a rare benign retinal tumor with characteristic clinical features. Usually diagnosed in parents of retinoblastoma children, "silent" retinocytoma diagnosis is more rare in babies. In our case, we observed a natural "regression" of a retinocytoma in a 8 months old boy kept under close RETCAM follow-up for the risk of malignant transformation.

• 4664

Bilateral primary iris pigment epithelial cysts

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Purpose To report a patient who presented with bilateral primary iris pigment epithelial cysts.

Methods Interventional case report.

Results A 30-year-old lady with the diagnosis of bilateral primary cysts of the iris pigment epithelium was referred. Her father had been diagnosed with a uveal melanoma 13 years earlier. Two smaller circumferential midzonal iris pigment epithelial cysts and a larger inferonasal cyst located in the temporal area were observed in her right eye, and a similar but much larger cyst was observed in her left eye temporally between 1 o'clock and 6 o'clock meridians. Otherwise, the anterior and posterior segment as well as the intraocular pressure (16 mmHg) were normal. The visual acuity was 20/20 without correction, right eye, and 20/20 with a +0.75 sphere, left eye, with a shadow in the field. For the decrease of vision in her left eye the cyst was treated with neodymium-doped yttrium aluminum garnet (Nd:YAG) laser cystotomy without any ocular tissue damage using the Abraham iridectomy lens and a 1.0 mJ single pulse. Cystotomy resulted in immediate collapse of the cyst with no change in intraocular pressure.

Conclusion Laser cystotomy yielded a favorable result. Generally, these cysts which most frequently occur in young females do not need any treatment, but transpupillary laser cystotomy is an alternative to a conservative regimen if iris the cyst is symptomatic.

• 4665

Combined topical 5-Fluoruracil and extensive surgery in the management of corneo-conjunctival squamous cell carcinoma.

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Purpose To evaluate safety and efficacy of combined neo-adjuvant topical chemotherapy with 1%5-Fluoruracil (1%5-FU), followed by extensive surgery and adjuvant (post-surgical) 1%5-FU topical chemotherapy in the management of corneo-congiuntival squamous cell carcinoma (SCC).

Methods Twenty-nine consecutive patients, with histological evidence of SCC, were included in this prospective study. Each patient was treated by combined neo-adjuvant topical chemotherapy (1%5FU, four time daily for four week, 1 cycle), followed by extensive surgery (5 mm of free conjunctival surgical margins) with contemporary amniotic membrane reconstruction. Adjuvant topical chemotherapy was started 3 months after surgery (1%5-FU, four time daily for four week, 1 cycle). Follow-up was performed every 3 months for the first year and every 6 months thereafter, including clinical confocal microscopy. Follow-up was longer than 36 months.

Results Mean follow up was 56±11(range, 36-78 years). Good functional, anatomic and aesthetic results were obtained by surgery. Two patients (5%) needed short-term surgical amniotic membrane repositioning due to early sutures dehiscence. 1%5FU, used both as an adjuvant or neo-adjuvant treatment caused low-to-mild temporary local irritation. No-one patient discontinued therapy because of 5-FU side effects. No other long- or short-term side effects were documented. No local recurrences were documented during follow up.

Conclusion Combined neo-adjuvant topical chemotherapy with 1%5FU, extensive surgery and adjuvant 1%5FU topical chemotherapy appear a safe and effective combined treatment in the management of conjunctival SCC.

• 4666

MicroRNA profiling in ocular adnexal extranodal marginal zone lymphoma and diffuse large B-cell lymphoma

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Purpose To investigate changes in microRNA (miR) expression in ocular adnexal extranodal marginal zone lymphoma (EMZL) and diffuse large B-cell lymphoma (DLBCL), and to perform a pathway analysis of differentially expressed miRs.

Methods Global miR expression profiling was performed using miRCURYTM LNA miR-arrays, v. 11.0, (Exiqon) on formalin-fixed paraffin-embedded tissue from 18 ocular adnexal EMZLs and 25 DLBCLs. The result of microarray was confirmed using quantitative real time (RT)-PCR. Predicted and validated targets of the significantly differentially expressed miRs were obtained from MiR-walk. Transcription factor (TF)-miR interactions were obtained from the TransmiR database.

Results The microarray results revealed two up-regulated and 41 down-regulated miRs in the DLBCLs compared to the EMZLs. Further, the differentially expressed miRs separated EMZLs and DLBCLs into two distinct entities using a supervised clustering analysis. These findings were confirmed by quantitative RT-PCR.Five of the down-regulated miRs (let-7g, miR-26a, miR-29a, miR-29c and miR-221) were identified to be regulated negatively by MYC. A small set of miRs (let-7g, miR-199a-5, miR-26a, miR-27a* and miR-342-3p) that regulate NFKB1 were all down-regulated in the DLBCLs compared to the EMZL samples. Further, the NFKB1 regulated miRs (miR-29a/b/c and miR-125b) were down-regulated significantly in the DLBCLs compared with the EMZLs (log2 fold-changes: miR-29a/b/c < -1.9 and -1.1 for miR-125b).

Conclusion We demonstrated that fundamental differences in miR expression exist between ocular adnexal EMZLs and DLBCLs, mainly due to differences in MYC and NF-kB regulatory pathways.

• 4667

Acute lymphoblastic leukemia in the eye region

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Purpose Manifestations of acute lymphoblastic leukemia (ALL) in the eye area are rare and mainly occur in children. The purpose of this study was to investigate clinical, histopathological and genetic characteristics of Danish cases with ocular manifestations of ALL.

Methods Patients with orbital and adnexal leukemia were identified by searching the Danish Registry of Pathology between 1980 and 2009. Clinical files from the patients were collected. Specimens were re-evaluated using a panel of monoclonal antibodies.

Results We report two cases with extra-ocular manifestations of ALL as first presenting symptom, and one case with late manifestations of ALL in the eye. Case 1 was a 5-year-old boy with a tumour mass in the left orbit extending along the orbital roof. Case 2 was a 9-year-old girl with a tumour in the upper left eyelid that laterally encircled the lacrimal gland. Case 3 was a 32-year-old man relapsing with leukemic infiltration of the iris. Histologic and immunophenotypic examination revealed that all cases were pre-B-cell ALL. Cytogenetic analysis of case 1 revealed a pseudodiploid karyotype with a t(2;3) translocation and case 2 showed a hyperdiploid karyotype with a t(12;21) translocation and trisomy 21. Cases 1 and 2 were successfully treated according to the NOPHO ALL 1992 and 2000 protocols and were in complete remission nine and five years after respectively. Case 3 did respond to therapy, and was alive with disease 29 years after primary diagnosis.

Conclusion Ocular and extra-ocular manifestations of leukemia are rare with only three cases observed during 30 years in Denmark. All cases were pre-B-cell ALL. Our patients responded well to therapy.

• 4668 / S007

Pink pseudohypopyon as a presenting feature of large B-cell lymphoma

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Purpose To describe the clinicopathologic features of a patient who developed an anterior chamber (AC) infiltrate mimickina pink pseudohypopyon as a presenting feature of large B-cell lymphoma.

Methods The clinical and pathologic findings in a patient with AC infiltrates secondary to systemic B-cell lymphoma are reviewed. Main outcome measurements were clinical observation and cytologic/flow cytometric examination of the infiltrate after AC aspiration.

Results A 51-year-old woman was evaluated for decreased vision in her right eye.On examination, her visual acuity was 20/30 in the right eye (RE) and counting fingers in the left eye. Abnormalities were confined to the RE. Slit lamp examination revealed +1 AC cells with a pink pseudohypopyion occupying 40% of the AC. The iris was corrugated and had small new vessels in the stroma. An anterior chamber aspirate was performed, and 0.8 ml of fluid was obtained. The sample was formed by 32% of lymphocytes and 54% of neutrophils. B-lymphocytes were predominant over T-lymphocytes (91% and 8%, respectively). Cytologic examination showed scattered atypical mononuclear cells. Immunohistochemical stains were positive for CD19 in the atypical cells. Flow cytometric immunophenotyping revealed a clonal, kappa restricted population of B-lymphocytes comprising 97% of the viable cells in the sample. These results were consistent with a large B-cell extranodal lymphoma.

Conclusion Anterior chamber/iris infiltration from systemic lymphoma is exceedingly rare, present in less than 10% of patients. Herein, we describe a patient with systemic lymphoma in whom the first manifestation was a pink pseudohypopyon.

• 4669

Diagnosis of choroidal lymphoma, difficulties and possibilities

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Purpose To describe a case of choroidal lymphoma

Methods A 66 y old man presented with left vitritis; 3y before presentation a testicular large B-cel lymphoma was detected and treated by 8x R-CHOP and 4x intrathecal chemo. General and hematologic examination failed to indicate a recurrence; because of the negative vitreous biopsy, the hematologists decided to give no systemic treatment. The left eye lost slowly vision and had the aspect of diffuse uveal melanocytic proliferation (BDUMP). After 6 methotrexaat vitreal injections, the choroid remain flat with the image of BDUMP, then very fast, a tumour was growing in the choroid and an enucleation was unavoidable

Results The first vitreous biopsy showed multiple cells with a majority of macrophages (CD68+, 75%), small mature T-Lymphocytes (CD3+, 20%) and very few larger B-lymfocytes (CD20+, 5%). A second vitreous biopsy after 2 years showed a very cellular sample with a majority of macrophages, and small T-lymphocytes, there were no B-lymphocytes. 3 months later a spectacular tumour growth in all parts of the uvea necessitated an enucleation. This confirmed the diagnosis of uveal large B-cell lymphoma, with a Ki-67 positivity of nearly 100%

Conclusion Lymphoma in the eye is a difficult diagnostic problem

• 466a

Schwannoma of the ciliar body (clinical case)

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Purpose Schwannoma is a very rare benign intraocular tumor, arising from the uveal tract. Only several cases have been described so far in literature. We describe a case of ciliar body schwannoma.

Methods A 13-year-old girl presented with rapid decreasing visual acuity and intraocular pressure increase for 3 months. The patient was examined with standard ophthalmological procedures. Ultrasonography with Doppler techniques and computed tomography revealed a huge tumor mass, totally filling the eye cavity. IOP was measured as 26 mmHg. The fine needle aspiration biopsy revealed no signs of tumor (retinoblastoma or uveal melanoma were expected). To prevent the tumor spread and further IOP increase, we performed the enucleation of the eyeball.

Results Histologically the tumor was determined as Verocai schwannoma (cellular solid component or Antoni A type). Immunohistochemical study revealed a positive reaction for vimentin, protein S-100 and neuronspecific enolase.

Conclusion Unfortunately, it is not easy to make a differential diagnosis between the nonpigmented melanoma and schwannoma without performing an enucleation in advanced cases. Nevertheless, in our case enucleation was the appropriate method to determine this rare tumor and to administer further treatment.

• 4671
New straylight issues in treatment of the eye

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Purpose Straylight exerts its deleterious effect on visual function by reducing the sensitivity of the retina for whatever visual task the retina must perform: face recognition, movement detection, color discrimination etc. It can be expected that patients suffering from a retinal condition will be handicapped by straylight twice as much. To assess retinal condition in a non-confounded way, flicker sensitivity has been proposed. Such a test was developed on the C-Quant. Moreover, the test serves to assess whether a paptient has sufficient flicker sensitivity for the normal straylight test itself.

Methods Visual field lay-out was identical, as well as the subject's 2AFC task, but the peripheral annulus was silent, as well as one of the two half fields in the center. The other half flield flickered at 8 Hz, with modulation depth according an adaptive staircase procedure. Outcome measure is logTCS (temporal contrast sensitivity). An uncertainty parameter (Unc) was included. Population test was performed in science fair settings on 400 subjects. Moreover in the laboratory 2 subjects were extensively tested to check whether optical defects, mimicked with trial lenses and scatter filters, affected the TCS outcome.

Results Repeated measures standard deviation was 0.11 log units for the reference group using as reliability criterion unc<0.15. Normal values for logTCS were around 2 (threshold 1%) with some dependence on age (range 6-85 years). Test outcome did not change upon a ten-fold (optical) deterioration in visual acuity or straylight.

Conclusion The test has adequate sensitivity to check a subject's capability to perform straylight assessment. The unc reliability criterion secures sufficient precision, also for assessment of retinal sensitivity loss.

Commercial interest

• 4672
A statistical eye model that incorporates straylight

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Purpose To illustrate how a recently developed statistical eye model can be expanded to include light scattering.

Methods This work uses previously measured biometric data from a large group of normal eyes. After confirmation of the Gaussian shape of their distributions, these parameters were then used to calculate their mean and covariance matrices. From these matrices a multivariate Gaussian distribution was calculated, which was then used to generate an amount of random, but plausible, biometric data. After a refractive filtering procedure, this data had a realistic refraction distribution and could be combined with the recent literature on the relations between straylight and ocular biometry, as well as on straylight and types of cataract

Results The straylight distributions of the simulations closely resemble those measured in the population.

Conclusion Using these methods a fair straylight simulation can be made for the general population.

• 4673
Straylight as indication for cataract surgery

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We know that there are many sources of physiologic scatters such modified cornea (after refractive surgery, haze, dystrophies, ocular surface disease) , vitreous alterations and lens changes with the aging process inducing progressive cataract and impairing light diffusion. Nowadays, thanks to the access to scatter measurement, we might be able to assess tear film quality dynamics (with an increase in ocular surface desiccation commonly observed in old patients), but moreover we could detect early cataract at the stage of no induced visual acuity decrease but quality of vision degradation. We will present the preliminary results of a multicenter French study based on the use of the Double Pass Image Analyser (OQAS) for the potential diagnosis of cataract, on a standardized questionnaire of life and taking also account the integrity of ocular surface in addition to visual performances. The key parameter provided by this platform is the OSI (Ocular Surface that increases when scatters are in elevation (superior to 4). Our preliminary pilot results show a significant correlation between quality of life and OSI changes, suggesting that the objective measurement of light scatter might be of interest for detection of early cataract and that the consideration of quality of life (based on a basic questionnaire) should be considered in the modern new definition of cataract.

• 4674
Straylight values in pseudophakes - standard IOL versus bag-in-the-lens IOL

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Purpose To evaluate straylight and contrast sensitivity (CS) in eyes with various cataract morphologies, to determine which type of cataract presents a higher impairment of visual function with respect to proposed norms for driver safety and to compare retinal straylight and CS before and after implantation of a Morcher 89A IOL.

Methods BCVA, CS and straylight were measured in 97 cataractous eyes using respectively a Snellen chart, a Pelli-Robson chart and the C-Quant. Cataracts were graded using the LOCS III scale and divided into four groups: nuclear, cortical, nuclear-cortical and posterior subcapsular cataract. A separate group of 71 eyes had their straylight measured before and after cataract surgery.

Results CS was reduced and straylight increased in all cataract patients, most notably in posterior subcapsular and nuclear-cortical cataract. CS and BCVA were correlated ($r = 0.44$), whereas straylight and BCVA were not. Applying cut-off values as proposed by European drivers studies of 1.25 log CS and 1.4 log straylight as safe margins for driving, 31% would be considered unfit to drive on the basis of CS and 78% on the basis of straylight although their visual acuity was still above the current European visual acuity requirement for driving. Retinal straylight reduced significantly from 1.56 ± 0.26 to 1.25 ± 0.22 log units ($P < 0.001$) after IOL implantation and the group eligible to drive increased from 26% to 76%.

Conclusion Straylight and, to a lesser extent, CS are complementary to BCVA and should be taken into account when considering driving eligibility. After IOL implantation straylight reduces significantly, resulting in a significant increase in driving eligibility

Commercial interest

• 4675

Clinical relevance of straylight in patients with retinitis pigmentosa

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Purpose The importance of straylight derives from the fact that it reduces retinal sensitivity. This may be particularly relevant in conditions with retinal dysfunction, such as Retinitis Pigmentosa (RP). Moreover in RP often early in life PSC cataract develops. The question of this study is whether straylight substantially contributes to visual disability in RP patients, potentially aggravated due to the combination of retinal degradation and increased straylight from cataract formation. In addition, straylight was used to predict possible benefit of (early) cataract surgery.

Methods Twenty-five RP patients scheduled for cataract extraction (CE) participated. Before and after CE, best corrected visual acuity (BCVA) in logMAR, contrast sensitivity (CS) in log(CS), temporal contrast sensitivity (TCS) in log(TCS), and straylight (log of the straylight parameter s, log[s]) were tested. TCS, or flicker sensitivity, was tested with a new test, using the C-Quant hardware. TCS measurement was performed to assess foveal function isolated from the eye's optical quality.

Results Average pre CE log(s) value was 1.72, corresponding to a factor 6 straylight increase as compared to a healthy, young eye. Functionally significant improvement defined as >0.2 log, was only found for log(s). Only log(s) improvement was related to pre CE values. LogMAR and log(TCS) were correlated (pre CE $r(19) = .57$, $p < .01$; post CE $\rho(19) = .47$, $p < .05$). Pre and post CE log(TCS) values were similar ($p = .14$).

Conclusion Straylight effects of cataract may substantially aggravate visual disability in RP patients, whereas BCVA may (not yet) be affected. Loss of BCVA may reflect foveal function rather than cataract. For proper CE referral straylight must be assessed.

• 4711
Indications and contraindications

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The modern vitrectomy procedures have replaced the conventional buckle operation in the treatment of rhegmatogenous retinal detachment (RRD) in the majority of cases. The present indications of buckle surgery depend on surgeon's skills, patient to doctor communication and the availability of specialised personnel. On the other hand the contraindications such as proliferative vitreoretinopathy, thin bluish sclera, are more clear and delineate the grey zone of the preoperative dilemma 'vitrectomy or buckle.' The presentation will try to answer why buckle surgery may be beneficial in special cases and when a modern surgeon must avoid this procedure for the treatment of a patient with RRD

• 4712
General planning and thoughts for the operation

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For any surgical procedure you must get prepared prior to theatre. Technically you have to use all necessary instruments and or consumables to achieve a good result and practically you must have all the support from the stuff. Thus it is necessary to organise a plan prior to operation. A "battle plan" that allows you to get prepared for any scenarios. In order to follow your plan you will need a very good examination and documentation of all the findings. Any prioritised information prior to the surgery could improve the efficiency. In example the number and the type of breaks, the location, the possible type of sponge you may use as well as an alternative option. The decision in advance to perform or to skip significant parts of the procedure such as drain or not drain may provide as well more safety and /or efficiency.

• 4713
Local v 360 degree plomb

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There are some strict lows concerning the placement of the buckle on the scleral wall mainly in accordance to the retinal pathology which created the RD. The question is whether buckling should be limited to the area of the break or extended over the retinal periphery.

• 4714
To drain or not and how to drain

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There is a basic question. Is it necessary to drain??Because if it is not necessary then is better to avoid drainagebecause complications are always possible to happen.

• 4715

Cryo treatment and problems

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Cryo from one point is necessary to create adhesions around the break.But from the other point of view it is possible to facilitate the development of PVR.We will discuss all these details for the cryo.

• 4716

Complications following conventional surgery for retinal detachment

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Purpose To describe the possible complications following conventional surgery for retinal detachment Scleral buckling procedure has a primary success rate of 85–90%. Complications, although rare, may occur. Some of them may be severe. In some instances, patients lose sight in the affected eye or lose the entire eye.

Methods Conventional retinal detachment surgery under general anaesthesia.

Results Possible, but infrequent, complications from scleral buckle surgery include failure of the operation, loss of some or all vision, loss of an eye (rare), double vision, retinal hemorrhage, cataract formation, glaucoma, further retinal detachment, proliferative vitreoretinopathy, vitreous hemorrhage, drooping of the upper lid, and infection. Drainage of the subretinal fluid during surgery, is associated with a higher risk of complications such as bleeding, perforation of the retina, incarceration of the retina at the drainage site, infection etc. Even though the incidence of such complications is low, the risks should be explained to patients. As the scleral buckle is left in place permanently and behaves as a foreign body to the eye there is a risk that there may infection and extrusion many years after the surgery. There is also the small risk of the buckle eroding into the eye, necessitating its removal. A change of patient's refraction is observed usually (increased shortsightedness) after scleral buckling surgery. In some instances, although the retina reattaches, visual acuity is not restored. The risk of surgery also rises with the use of general anesthesia.

Conclusion Scleral buckling, however, is considered a safe, successful procedure. Restored vision depends largely on the location and extent of the detachment, and the length of time before the detachment was repaired.

• 4721

Determination of the optimal colour space for distinguishing small retinal haemorrhages from dust artefacts

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Purpose To determine the optimal colour space from eight types of colour spaces for the purpose of distinguishing small retinal haemorrhages from dust artefacts in cases of early diabetic retinopathy.

Methods We constructed an experimental device, which comprised an illumination optical system and a photographic optical system separated by a mirror having a hole. The device included a canon EOS 50D camera, an EF 50 mm f/1.8-2 camera lens, a Speedlite 270EX flash, an object lens, four double-convex lenses, three aperture stops and six artificial eyes. The eye ground was a hemisphere made of polythene terephthalate painted with six matt colour sprays: red, white brown, ochre, yellow, ivory and orange. Five fragments of house dust on the object lens and the two lenses were photographed under each artificial eye. The RGB colour space, measured by Paint Shop Pro from pictures, was changed into seven kinds of colour spaces: XYZ, CMY, HSL, HSV, HSI, L*a*b* and L*u*v*.

Results The evaluation values of the following three colour spaces were favourable: the L*u*v* colour space (L*, 5.7±1.1; u*, 8.5±1.8 and v*, 6.7±1.1), the HSV colour space (hue, 2.0±0.5; saturation, 9.5±3.7 and value, 6.7±0.7) and the HSL colour space (hue, 2.0±0.5; saturation, 7.8±2.5 and lightness, 6.8±0.8). The other colour spaces did not show a good result.

Conclusion The L*u*v* colour space is highly sensitive; therefore, it is most effective in distinguishing small haemorrhages from dust artefacts. The HSV and HSL colour spaces were highly sensitive in terms of saturation, lightness and value. Using Scilab and SIVP software, we are currently researching methodology that applies the use of colour spaces such as L*u*v* and HSV for automatic distinction.

• 4722

Matched pairs analysis of retinal navigated laser versus conventional laser

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Purpose To compare clinical outcome and retreatment rate of a novel computer navigated laser versus conventional slit-lamp-microscope laser treatment of diabetic macular edema

Methods Focal laser for diabetic macular edema (DME) in 46 consecutive patients was digitally planned on fundus images and performed utilizing retinal navigation (Navilas® Laser System, OD-OS GmbH, Teltow / Berlin, Germany). We investigated the number of retreat-ments and monitored visual acuity (VA) over 6 months and compared to 119 patients treated with a conventional laser via a slit-lamp-microscope.To match control group and Navilas pa-tients propensity score matching was performed with STATA based on the nearest neighbour method.

Results The propensity score algorithm for age, gender, baseline VA and number of laser spots yielded 28 patients for the matched control group. All baseline characteristics were comparable, VA was 0.48 +/-0.37 Log MAR for Navilas and 0.43 +/-0.36 Log MAR for conventional laser. Visual outcome at 3 and 6 months follow-up was better for the Navilas group, but did not reach statistical significance. The Laser retreatment rate using Kaplan-Meier analysis showed separation of the survival curves after 2 months. For the first 6 months the cumulative retreatment rate was 18% in the Navilas and 31% in the conventional laser group (p=0.02)

Conclusion Lower retreatment rates were observed with navigated laser treatment compared to conventional laser within 6 months after treatment, indicating a more sustained effect and faster stabilization using navigated laser, hence, reducing the treatment burden for the patient.

Commercial interest

• 4723

A shift in the balance of vascular endothelial growth factor and connective tissue growth factor by bevacizumab causes the angiofibrotic switch in proliferative diabetic retinopathy

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Purpose In proliferative diabetic retinopathy (PDR), vascular endothelial growth factor (VEGF) and connective tissue growth factor (CTGF) may cause blindness by neovascularisation followed by fibrosis of the retina. It has previously been shown that a shift in the balance between levels of CTGF and VEGF in the eye is associated with this angiofibrotic switch. This study investigated whether anti-VEGF agents induce accelerated fibrosis in patients with PDR, as predicted by this model.

Methods CTGF and VEGF levels were measured by ELISA in 52 vitreous samples of PDR patients, of which 24 patients had received intravitreal bevacizumab 1 week to 3 months before vitrectomy, and were correlated with the degree of vitreoretinal fibrosis as determined clinically and intra-operatively.

Results CTGF correlated positively, and VEGF correlated negatively with the degree of fibrosis. The CTGF/VEGF ratio was the strongest predictor of fibrosis. Clinically, increased fibrosis was observed after intravitreal bevacizumab.

Conclusion These results confirm that the CTGF/VEGF ratio is a strong predictor of vitreoretinal fibrosis in PDR, and show that intravitreal anti-VEGF treatment causes increased fibrosis in PDR patients. These findings provide strong support for the model that the balance of CTGF and VEGF determines the angiofibrotic switch, and identify CTGF as a possible therapeutic target in the clinical management of PDR.

• 4724

Severity of colour vision loss in diabetes

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Purpose Vascular and structural changes in the retina are used to grade progression in diabetic retinopathy (DR) and this is often taken as an indicator of the severity of vision loss. Changes in visual function may, however, precede detectable structural damage. Red-green (RG) and yellow-blue (YB) thresholds were measured in patients with DR and related to their clinical grading classification.

Methods 66 patients diagnosed with diabetes were examined. DR was graded according to ETDRS severity scale as no retinopathy, mild, moderate, severe DR and presence/absence of macular oedema. Colour thresholds were measured using the CAD test (Expert Rev.Ophthalmol. 6:409-420, 2011) together with other patient-specific information: VA, duration of diabetes, HbA1c and central subfield (CSF) thickness, and response of macular oedema to Ozurdex intravitreal implant injection.

Results All diabetic patients showed loss of chromatic sensitivity (with mean RG and YB thresholds exceeding six times normal values). The clinical grading of disease progression showed negligible correlation with either RG (r2=-0.0004) or YB thresholds (r2=0.052). Patients with no DR often exhibited normal visual acuity (~ 1 min arc), but showed significant loss of colour vision. Ozurdex treatment was associated with significant initial improvement in colour thresholds.

Conclusion RG and YB colour thresholds provide a sensitive measure of functional change in diabetics that does not relate well to observed vascular and structural changes. These preliminary findings also suggest that measurement of colour thresholds can be used to monitor the efficacy of treatment in diabetic macular oedema.

• 4725 / S108

A novel co-culture model of the blood-retinal barrier based on primary retinal endothelial cells, pericytes and astrocytes

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Purpose Loss of blood-retinal barrier (BRB) is an important cause of diabetic macular edema (DME), but cellular mechanisms underlying BRB dysfunction are poorly understood. Therefore, we developed and characterized a novel in vitro BRB model.

Methods The model is based on primary bovine retinal endothelial cells(BRECs).These cells were shown to maintain specific in vivo BRB properties by expressing high levels of endothelial junction proteins and specific BRB transporters. To investigate the influence of pericytes and astrocytes on BRB maintenance in vitro, we compared five different co-culture BRB models, based on BRECs, bovine retinal pericytes (BRPCs) and rat glial cells.

Results Co-cultures of BRECs with BRPCs and glial cells showed the highest trans-endothelial resistance (TEER) as well as decreased permeability of tracers, even after vascular endothelial growth factor (VEGF) stimulation, suggesting a major role for these cell types in maintaining barrier properties. To mimic the in vivo situation of DME, we stimulated BRECs with VEGF, which downregulated MDR1 and GLUT1 mRNA levels, transiently reduced expression levels of endothelial junctional proteins and altered their organization, increased the number of intercellular gaps in BRECs monolayers and influence the permeability of the model to differently-sized molecular tracers. Moreover, as has been shown in vivo, expression of plasmalemma vesicle-associated protein (PLVAP) was increased in endothelial cells in the presence of VEGF.

Conclusion This in vitro model is the first co-culture model of the BRB that mimicks in vivo VEGF-dependent changes occurring in DME.

• 4726 / S109

Measurement of subfoveal choroidal thickness before and after cataract surgery using enhanced depth imaging optical coherence tomography

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Purpose To compare subfoveal choroidal thickness (SFCT) before and after cataract surgery using enhanced depth imaging optical coherence tomography (EDI OCT)

Methods Cross-sectional observational prospective study. Spectral-domain EDI OCT was performed with a Heidelberg Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) using a standardized protocol. SFCT of 67 patients was measured manually from the posterior edge of the retinal pigment epithelium to the choroid/sclera junction before surgery, 1 day, 7 days, 1 month, 3 month after. Choroidal thicknesses were independantly assessed by two masked graders. Statistical analysis was performed to evaluate variations of choroidal thickness before and after cataract surgery.

Results Eighty four eyes of 67 patients who had cataract surgery were included. Mean SFCT ± SD was 215,9 ± 69,4 µm before surgery, 213,3 ± 67,3 µm at Day 1, 221,9 ± 67,8 µm at Day 7, 226,5 ± 68,9 µm at 1 month and 230 ± 62,2 µm at 3 months. Mean SFCT increased significantly between before and 3 months after surgery ($p<0,04$). For diabetic patients mean SFCT increased in the same proportion as in general population but later (Day 7 versus Day 30). No significative difference was observed between group with Diabetic Retinopathy (DR) and group without. For the only patient who developed an Irvine Gass Syndrom, SFCT increased.

Conclusion Mean SFCT seems to increase after phacoemulsification. EDI OCT can be used to evaluate choroidal changes after cataract surgery in diabetic patients, and to detect patients who would develop an Irvine Gass syndrome.

• 4727 / S110

Subthreshold micropulse photocoagulation with true yellow 577nm diode laser for macular oedema

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Purpose Subthreshold, or tissue sparing, Diode Micropulse Photocoagualtion (SDM) is a treatment used to produce a therapeutic effect without inducing detectable intraretinal damage. Actually treatment options are available for diabetic macular edema (DME), proliferative diabetic retinopathy (PDR), central serous chorioretinopathy (CSR), macular edema secondary to branch retinal vein occlusion (BRVO), and even glaucoma.

Methods We used micropulse technology with 577nm yellow diode laser to produce a therapeutic effect without inducing intraretinal damage detectable on clinical examination during or after the treatment. All patients were affected by clinically significative macular edema (CSME) due to diabetic retinopathy, venous branch retinal occlusion and central serous retinopathy.

Results Controls prefomed at 1, 3 and 6 months showed no detectable retinal scars in any case. Foveal thickness decreased in all patients, visual acuity remained stable (<10 ETDRS letters) or improved (≥10 ETDRS letters).

Conclusion The results of our study indicate that, in the treatment of CSME due to PDR, BRVO and CSR,SDM photocoagulation is at least as effective as conventional photocoagulation without any clinically discernible evidence of laser-induced iatrogenic damage.

• 4728 / S111

Peripheral capillary network enlargement in diabetic maculopathy

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Purpose Diabetic macular edema has been associated with increased intravitreal levels of VEGF. Therefore, ischemia is probably part of the physiopathology. The purpose of this study is to evaluate the rarefaction of peripheral capillaries.

Methods A retrospective analysis of large field angiographic images with a scanning laser ophthalmoscope (OPTOS, Edinburgh, Scotland) was performed between Novembre 2011 and March 2012was performed. After excluding patients with previous panretinal laser photocoagulation and those with peripheral non-analyzable images, the peripheral area on early phase images in 112 patients were evaluated. 38 had a diabetic maculopathy and 78 served as non diabetic controls. The enlargement of the peripheral capillary network was graded from 1 to 3 (1: normal, 2: moderate, 3: severe).

Results A total of 43 patients were excluded because of panretinal photocoagulation in the diabetic group, possible VEGF involvement in the control group and poor image quality in either group.When comparing the remaining patients of the two groups, no significant difference in peripheral capillary network changes was observed.

Conclusion The peripheral capillary rarefaction is difficult to analyze on conventional angiography (peripheral images are usually obtained in the late phase). This angiographic finding is probably not encountered more often in diabetic maculopathy than other retinal diseases. It remains to be demonstrated in which cases peripheral capillary rarefaction should be considered as significant and whether targeted laser treatment as a part of diabetic macular edema therapy should be discussed.

• 4731

Where are the limits of corneal transplantation - why is there a need for biomaterials?

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Düsseldorf

Purpose This presentation will give insight into clinical limitations of corneal allografting and ocular surface reconstruction. this provides the rationale for the development of novel biomaterials for ophthalmosurgery.

Methods Novel developments of tissue engineering covering the three major layers of the cornea (epithelium, stroma, endothelium) will be presented.

Results Different success rates (in animals and human trials) and limitations will be presented and will provide a platform for discussion.

Conclusion Biomaterials will be a part of ophthalmosurgery in the decades ahead.

• 4732

Is a synthetic lamina the ultimate goal for osteo-odonto-keratoprosthesis (OOKP) surgery? Options for the edentulous patient who require OOKP surgery

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Purpose To list the options for an edentulous patient requiring OOKP surgery for rehabilitating corneal blindness.

Methods Literature review, personal experience, and theoretical considerations.

Results Options include an OOKP allograft from a living (related or unrelated) donor which necessitate systemic immunosuppression, a tibial bone allograft (depends on good bone density), and a Pintucci (Dacron) keratoprosthesis. None of these has the longevity of an OOKP proper. Other options, as yet not properly studied, include cadaveric OOKP allografting, and synthetic OOKP analogues. The latter has the advantage of the possibility of mass manufacture, no risk of transmission of blood-borne infections, and no size constraints limiting optical cylinder design.

Conclusion Options do exist for the edentulous patient requring OOKP surgery for rehabilitation of corneal blindness. In the long term, the synthetic OOKP analogue holds the best promise.

• 4733

Plastic compressed collagen as a biomimetic substrate for human limbal epithelial culture

DANIELS JT

ABSTRACT NOT PROVIDED

• 4734

Synthetic eye prosthesis – phase I results of a succesfully developed biomaterial

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Purpose Development of an biomimetic artificial cornea to provide a long term stable keratoprostesis for ultima ratio patients

Methods A hydrophobic biomaterial was selectively modified by physical and chemical nanotechnological methods. The modified biomaterial was tested in cell culture experiments (primary epithelial cells, porc), implanted into rabbits eyes and finally into eyes of ultima ratio patients.

Results After very successful in vitro evaluation, keratoprostheses were implanted to rabbit eyes (New Zealand white rabbit) and showed excellent in vivo performance in the animal experiment. After a follow-up of 2.5 years, the implanted keratoprosthesis into human eyes showed no significant sign of complication such as infection or protrusion. There was a substantial increase in vision.

Conclusion We could develop a new keratoprosthesis for ultimo ratio patients which is well tolerated in human eyes.

• 4735

Biomimetic materials for regenerating the cornea

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ABSTRACT NOT PROVIDED

• 4741
Choroidal blood flow in central serous chorioretinopathy (CSC)

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Purpose Central serous chorioretinopathy (CSC) has been linked to alterations in perfusion and metabolism. In the present study we investigated arterial and venous oxygen saturation in patients with active CSC and compared it to the data in healthy subjects.

Methods A total of 13 subjects with active CSC and 13 healthy age- and sex-matched control subjects were included in this study. Retinal arterial and venous oxygen saturation was measured in an annular area centered at the optic disk using the Imedos Oxygen Module for the Retinal Vessel Analyzer (RVA).

Results No significant difference was observed between the patients with CCS and healthy control subjects. This was the case for retinal arterial oxygen saturation (95.0 ± 4.5 % in patients with CCS, 96.2 ± 4.2 %; p = 0.463) and for retinal venous oxygen saturation (66.6 ± 5.5 % in patients with CCS, 63.7 ± 6.1 %; p = 0.392).

Conclusion Previous studies have shown that CSC is associated with abnormalities in choroidal blood flow regulation. Our data indicate, however, that retinal oxygenation is normal in CSC patients during the active phase.

• 4742
Volumetric flow rate of ophthalmic artery in healthy individuals using a new magnetic resonance imaging technique

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Purpose To measure the volume flow rate of the ophthalmic artery (OA). A phase contrast magnetic resonance imaging (PCMRI) protocol was developed to assess volume flow rate of OA in healthy young (HY) and elderly (HE).

Methods The study was performed with a 3-Tesla scanner on HY (n=51,28females,age=64-80ys) and HE (n=51,28females,age=21-30ys). The OA were localized by a 3D time of flight (3DTOF) sequence. To measure the volume flow rate, a 2D PCMRI sequence was optimized to reach a spatial resolution of 0.35mm/pixel. Based on 3DTOF data, the flow measurement was perpendicular to OA. Mean volume flow rate (Qmean), resistive index (RI), arterial volume change (ΔV) and symmetry index (SI) were computed from the volume flow rate curve. Accuracy of MRI measures was studied using a vessel-phantom (Ø=1.4mm). Six constant flow rates (5.54-34.41mL/min) were used as reference.

Results Phantom investigation showed good agreement between the reference and MRI measurements with a percentage error <7%. The mean and SD of RI (HE:0.68±0.08; HY:0.63±0.09), ΔV (HE:26.35±14.03uL; HY:18.51±7.23uL) and SI (HE:0.58±0.03; HY:0.63±0.03) of OAs volume flow rate curve were significantly higher in the elderly group compared to the young group (RI,$p<0.05$; ΔV,$p<0.001$; SI:$p<0.001$). No statistical difference was found in Qmean between HE(10.91±5.44mL/min) and HY (10.27±4.46mL/min) individuals ($p>0.05$).

Conclusion Volume flow rate measurement of OA vessels using PCMRI is possible. Contrary to color Doppler imaging, PCMRI technique does not alter IOP during the measurements. This method may provide a precise description of the dynamics of the volume flow rate of OA during the cardiac cycle.

• 4743
Retinal vascular caliber is associated with renal function in normotensive and never-treated hypertensive subjects

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Purpose The aim of this study was to assess the relation between retinal vascular caliber and renal function in normotensive (systolic/diastolic blood pressure <140/90 mmHg) and never-treated uncomplicated hypertensive subjects.

Methods Eighty subjects (51 normotensive and 29 hypertensive , mean age 47 yrs and 51% female) with serum creatinine < 1.2 mg/dL and without diabetes were recruited. Retinal vascular calibers were measured from fundus photographs and expressed as central retinal artery and venular equivalent (CRAE and CRVE, respectively). Renal function was assessed by measurement of glomerular filtration rate (GFR, urinary clearance of 99mTc-DTPA) and urinary albumin/creatinine ratio (UACR).

Results Mean GFR was 117 ml/min/1.73m². The adjusted mean CRAE was smaller in the hypertensive group as compared to the normotensive group (mean±standard error: 135±24µm vs. 142±18µm; P=0.03); whereas adjusted mean CRVE was similar. In all participants, CRAE and CRVE were positively correlated to GFR (r^2=0.09, P=0.005 and r^2=0.09, P=0.006, respectively). In addition, CRAE was negatively correlated to UACR (r^2=0.12, P=0.02) and no significant relationship between CRVE and UACR was found (r^2=0.01, P=0.31). The observed relations between retinal vascular calibers (CRAE and CRVE) and renal function parameters (GFR and UACR) remained significant after adjusting for age, gender, mean blood pressure, smoking, glycemia, body mass index and lipid profile.

Conclusion In normotensive and never-treated hypertensive subjects with normal renal function, the decrease in retinal arteriolar and venular calibers was associated with reduced kidney function, suggesting common determinants of these preclinical target organ damages.

• 4744 / F120
Role of nitric oxide in optic nerve head blood flow regulation during experimental increase of intraocular pressure in healthy humans

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Purpose Several studies have indicated that the choroid shows some regulatory potential during changes in ocular perfusion pressure (OPP). For the optic nerve head (ONH) only few data are available. The present study set out to investigate the behavior of ONH blood flow (ONHBF) during an experimental decrease in OPP and to explore whether inhibition of Nitric Oxide Synthase (NOS) alters this response.

Methods Twelve healthy subjects participated in this randomized, double-masked, placebo-controlled three-way crossover study. For each subject, three study days were scheduled, on which they either received intravenous infusions of NG-monomethyl-L-arginine (L-NMMA), phenylephrine, or placebo. OPP was increased stepwise by the suction cup method. ONHBF was assessed continuously with laser Doppler flowmetry and OPP was calculated as 2/3*mean arterial pressure-intraocular pressure.

Results Administration of L-NMMA and phenylephrine significantly increased resting OPP compared to placebo ($p<0.001$ and $p=0.016$, respectively). As expected, L-NMMA decreased resting ONHBF compared to phenylephrine ($p=0.04$). The relative decrease in OPP during suction cup application was comparable with all drugs administered (between -69% and -72%, $p=0.19$). In all three groups, the decrease in ONHBF was less pronounced than the decrease in OPP, but not significantly different between groups.

Conclusion The present data indicate that NO plays an important role in the regulation of basal ONHBF, but not in ONHBF autoregulation.

• 4745

Quantitative and qualitative label free imaging using mass spectrometry in the context of an ophthalmic application

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Purpose We present a new Label free quantitative imaging of small molecules in order to investigate their roles in ophthalmic disorders (toxicity, inflammation)

Methods Quantitative Mass Spectrometry imaging has been developed and applied to ophthalmology to assess the distribution and quantification of Benzalkonium chloride (BAK) compound in specific areas of the eye after instillation. This method has been compared to gold standard technique as liquid chromatography - Mass spectrometry to validate the data.

Results The distribution of two BAK compounds (BAK C12 and BAK C14) were investigated in small specific histological regions of the eye (such as iridocorneal angle or sclera, choroid, retina regions) in order to estimate efficiency of action or adverse effects of the treatment. High spatial resolution images were performed at cells level (30 µm). Molecular distribution was also correlated to tissue histology using H&E staining. Then, our methodology of quantification by MSI was applied.

Conclusion MSI offers new insight in ocular therapeutic/pharmaceutical research, especially for high-precision distribution and quantification studies

• 4746 / F121

Eye motion increases temporal visual field extent

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Purpose To study the impact of eye motion on visual field extent.

Methods Visual fields were tested in 15 healthy volunteers with the Goldmann perimeter using a V4 test-object, from seen to unseen, first in primary position of gaze, then allowing eye motion. Temporal points falling out of the cupola were tested again after a controlled nasal head rotation using a headband prototype fitted with a line-laser level having two orthogonal vial levels. Visual field surface areas (cm2) were calculated as projections on a 30 cm virtual Goldmann cupola whose extent would have been large enough to include all points. Reproducibility error of the method assessed by calculation of the relative difference between surface areas of 12 visual field tests and 12 visual field retests was estimated at 14%. Hertel exophthalmometry was recorded to study the influence of globe position on visual field extent.

Results Binocular visual field surface area increased by 37% with eye motion (p-value = 1.20.10-9). This increase was highest (46%; p-value = 1.2.10-24) in the temporal quadrant. Median maximal visual field temporal excentration with eye motion was 128.3° (minimum: 109.5°; maximum: 137.7°) and more than 135° in 4 eyes of three subjects. Hertel exophthalmometry was positively linked to visual field temporal surface area with eye motion (p-value = 0.013).

Conclusion Eye motion greatly expands the temporal visual field. This peculiarity is likely an adaptation to terrestrial life with upright bipedal locomotion, and may save head movements through horizontal eyeball scanning.

• 4751

How to get your work published ?

PLEYER U
Charité - Universitätsmedizin Berlin, Berlin

Junior researchers often face the challenge of get their interesting work published. The goal of this course will be to provide some keys to write a high quality paper that will help to transform innovative ideas into a research article. The panelists will discuss major aspects of the editorial process including basic decisions: where to submit the work, how to organize and prepare a manuscript, how to deal the review process in particular the revision process for eventual resubmission. The panelists will raise the discussion on issues like:How to choose a journal ?How to organize your paper ?What are the characteristics of a good manuscript ?Delayed response: When is it appropriate to ask for the status of your manuscript ?How to interpret the letter from the editor ?How to write a good reply to the reviewers ?What to do when your paper is rejected ?When can it be appropiate to request a reevaluation of a rejected paper ?In addition, the personal view from an authors and editors perspective will be given in a vivid discussion with the participants.

• 4752

How to get your work published ?

DUA H
Nothingham

ABSTRACT NOT PROVIDED

• 4753

How to get your work published ?

KIVELÄ T
Helsinki

ABSTRACT NOT PROVIDED

• 4754

How to get your work published?

STEFANSSON E
Reykjavik

Purpose The intrinsic quality of a scientific article depends first and foremost on its scientific content. However, the way in which the scientific material is presented and the paper is written may determine whether the scientific content will ever receive the attention it deserves. There may not be any perfect recipe for a perfect paper, but it is possible to point out some general characteristics of good papers, and we will try to do so.The title sometimes decides whether a potential reader will give your article a proper look. A good title is descriptive, and it may also give a statement if the journal style allows. The abstract is the most important part of your article. It is what most people will read, and they will proceed to read the article proper only if they find the abstract to be interesting. If you excuse the parable, a good abstract is like a miniskirt – short enough to be exciting and long enough to cover the essentials.

Methods Describe the material or patients and the methods in brief. It is advisable to specify the study design.

Results Present the most important results in a brief manner. Please give quantitative data with confidence limits whenever applicable. The reader wants to know what your results were, not just whether they were "statistically significant" or not.

Conclusion Put your data into context with the clinical practice, literature or both. How do your results add to the scientific knowledge or preferred practice? What have we learned? A common mistake is to include general conclusions which are not specifically supported by the data presented. Please check that the conclusions are in line with the stated aim of the study.

Commercial interest

• 4771
Surgery of the inflammatory cornea or sclera

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Paris

ABSTRACT NOT PROVIDED

• 4772
Cataract surgery in uveitis

MONNET D, BREZIN A
Paris

ABSTRACT NOT PROVIDED

• 4773
Glaucoma surgery in uveitis

LACHKAR Y
Paris

Glaucoma surgery and uveitis (course) Management of uveitis glaucoma requires careful diagnosis and managment of both uveitis and glaucoma. Before deciding surgery it is essential to identify the mechanisms of IOP elevation and to differentiate secondary open angle glaucoma, secondary angle closure glaucoma with or without pupillary block. In case of secondary glaucoma with pupil block in phakic patients lens extraction might be considered if the uveitis is well controlled. Uveitis can negatively affect the outcome of glaucoma surgery. Filtration surgery with the use of adjunctive mitomycin C is the standard of care because of the risk of fibosis of the filtration bleb. Non penetrating surgery is an attractive option if the angle is open avoiding anterior chamber entry and hypotony. Aqueous shunt implantations is another option and could be proposed as a primary surgical procedure. Cyclophotocoagulation is best avoided in uveitics because the ciliary body is compromised by cyclitis. This procedure should be used cautiously because patients with uveitis already have atrophic ciliary epithelium, and the risk of permanent hypotony is increased with a cyclodestructive procedure

• 4774
Vitreo-retinal surgery in uveitis

BEHAR-COHEN F
Paris

ABSTRACT NOT PROVIDED

Posters

• T001

Relationships between estradiol, progesterone, and plasminogen activator inhibitor longitudinally during normal human pregnancy

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Purpose To investigate the hypothesis that the plasminogen activator proteolysis cascade in the eye is controlled locally instead of systemically. During pregnancy, systemic blood levels of estradiol (E2), progesterone (P4) and plasminogen activator inhibitors (PAI) are expected to rise with gestational age; is there a consequent rise in PAI normally present in tears?

Methods PAI-2 levels were measured, using Imubind ELISA, longitudinally from three to four tear samples collected from each of 13 women between 8 and 36 weeks of pregnancy. During the same visits, blood samples were analyzed for PAI-2, E2 and P4. The analysis included successful results from 36 tear samples (PAI-2) and 45 blood samples (PAI-2, E2 and P4).

Results Increases in blood levels of PAI-2, E2 and P4 occurred over the measured gestational period, significantly correlated with time and with each other (all $R2>0.75$). Tear levels of PAI-2 did not increase and were not correlated with gestation or blood PAI-2 (both $R2<0.06$).

Conclusion Our finding is that tear PAI-2 levels are dissociated from the progression of pregnancy and the concommitant elevated systemic blood E2 and P4 hormone and PAI-2 levels, indicating the possibility of local control of proteolysis in the eye, perhaps due to a blood-brain barrier to the elevated systemic blood composition levels.

• T002

Pirfenidone inhibits the induction of COX-2 stimulated by IL-1β at a step of NF-κB DNA binding in orbital fibroblast

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Purpose The aim of this study was to determine the effect of pirfenidone on interleukin-1β(IL-1β)-induced cyclooxygenase 2(COX-2) increase in orbital fibroblasts from patients with thyroid-associated ophthalmopathy(TAO).

Methods Orbital fat tissues were obtained during decompression surgery of patients with TAO and orbital fibroblasts were primarily cultured. After treatment of cells with IL-1β in the presence and absence of pirfenidone, COX-2 induction and its signal including NF-κB were analyzed. The effect of pirfenidone on the IL-1β-induced prostaglandin E2(PGE2) production in orbital fibroblast was also evaluated.

Results Pirfenidone attenuated the IL-1β-induced COX-2 mRNA and protein increase. In electrophoric mobility shift assay, pirfenidone showed the inhibitory effect on NF-κB DNA binding. However, pirfenidone showed no effect on the degradation and phosphorylation of IκB, and could not prevent nuclear translocation of p50/p65. Finally, the production of PGE2 was nicely inhibited by pirfenidone.

Conclusion The results of this study indicate that pirfenidone effectively attenuates IL-1β-induced COX-2 gene expression at a step of NF-κB DNA binding, which suggests that pirfenidone could be considered as a candidate for treatment of thyroid-associated ophthalmopathy.

• T003 / 2785

Detection of a novel premature stop codon in the OPA1 gene in autosomal dominant optic atrophy

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Purpose Autosomal dominant optic atrophy (ADOA) is a genetically heterogeneous disease, with OPA1, OPA4, and OPA5 representing the main ADOA loci. The aim of the study was to identify genetic etiology of inherited optic neuropathy in a Polish family.

Methods We report on a 2-generation Polish family with ADOA in which nine family members are affected. MRI and detailed ophthalmological examination with visual field and electrophysiological testing were performed. DNA was obtained from blood samples and linkage to known ADOA loci as well as sequencing of 29 OPA1 exons were conducted. Amplified fragments were analyzed on an automatic DNA sequencer.

Results MRI and ophthalmological examination confirmed the diagnosis of bilateral optic neuropathy. Pattern visual evoked potentials (PVEP) presented delayed P100 wave latency, reduced N75/P100 amplitude and abnormal morphology of waves. Pedigree analysis demonstrated a dominant mode of inheritance. Linkage studies allowed the exclusion of OPA4 and OPA5 loci but revealed linkage to the major OPA1 locus in the investigated family. Sequencing of the OPA1 gene identified a novel C-to-T transiton in exon 2 prediciting a premature stop codon (Q31X). The mutation co-segratated with the phenotype in this family. No other alteration was found in the OPA1 gene.

Conclusion Occurrence of the premature termination codon at the beginning of the transcript strongly suggest that ADOA in the investigated family is a consequence of OPA1 haploinsufficiency. The novel variant broadens the spectrum of the reported OPA1 mutations causing ADOA.

• T004 / 2786

Analysis of lincRNA at 13q32 keratoconus locus

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Purpose Keratoconus (KC) is a disease of the eye characterized by thinning and protrusion of the cornea. The causes of KC remain unknown. Our mutation screening of genes from 13q32 KC locus have revealed substitution in STK24 showing 100% segregation with KC phenotype in the Ecuadorian family. To continue the KC causes search, some non-coding RNA from 13q32 locus were selected for further molecular analysis. Here, we present sequencing results of lincRNA localized ~1kb from 5' end of STK24.

Methods The lincRNA was screen by sequencing technique using DNA samples from 23 members of KC-014 family and selected affected and unaffected individuals from Ecuador.

Results Sequencing analysis of lincRNA localized ~1kb from 5' end of STK24 have revealed g.99230266C>T substitution showing segregation with KC phenotype in the Ecuadorian KC-014 family.

Conclusion Mutation analysis of lincRNA mapped at the 13q32 locus have revealed sequence alteration segregating with the KC phenotype in Ecuadorian family. Since it is known, that lincRNAs are co-expressed with neighboring coding genes and may function as a regulator of epigenetic marks and gene expression, we suggest that this lincRNA localized in close proximity to STK24 gene might play a role in development and/or progression of familial KC in patients from Ecuador. To our knowledge, this is the first report presenting lincRNA analysis in KC.Support: Polish Ministry of Science and Higher Education, Grant NN402591740

• T005
The Brittle Cornea Syndrome: Study of a family with five affected siblings

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Purpose To define the natural history,genotype-phenotype correlation and differential diagnosis of the Brittle Cornea Syndrome (BCS),or Ehlers Danlos Syndrome (EDS) type VIB,caused by mutations in ZNF469 and PRDM5

Methods We evaluated one family in which 5 out of 8 siblings suffered from BCS. We performed complete eye and systemic evaluations of the siblings and their parents. We sequenced the candidate gene,ZNF469

Results On ocular evaluation we found keratoglobus and thinned corneas that tended to perforate spontaneously,as well as refractive errors caused by high myopia and irregular astigmatism. Progressive thinning of the corneas with keratoglobus led to visual deterioration due to spontaneous perforations and scarring. K readings were above 60 D and corneal thickness below 300um in 4 eyes that had not developed perforation. Systemic manifestations included joint hypermobility,increased elasticity of the skin but no cigarette paper scars, kyphoscoliosis,and progressive conductive hearing loss. Cardiovascular disease was not observed.The systemic findings overlap the kyphoscoliotic type of EDS VIA,the ocular manifestations of which consist of flattened corneal curvatures,fluid vitreous,radial perivascular lattice. Patients with BCS are often diagnosed as having the Marfan syndrome,even though spontaneous perforation of the cornea is not a feature of the latter condition. A 14bp insertion was found in exon 2 of ZNF469

Conclusion EDS VIB is a connective tissue disease referred to as BCS; it is characterized by keratoglobus,thinned corneas and Marfanoid body habitus. Two causative genes for BCS have been identified to date,ZNF469 and PRDM5. A 14bp insertion was found in exon 2 of ZNF469. It is possible to provide genetic counseling in the extended family

• T006
Unusual phenotype in a family with the R124C mutation in the TGFBI gene

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Purpose To report on a Polish family with unusual corneal changes associated with the arginine-124

Methods We report on a 2-generation Polish family in which corneal phenotype was assessed by slit lamp and confocal microscopy in vivo. Genomic DNA was obtained from blood samples and all exons known to contain mutation hot spots within the TGFBI gene, were PCR amplified and sequenced on both strand

Results Affected family members complained of ocular discomfort, pain and visual impairment. The symptoms in the proband began in the third decade of life, while in the daughter in the second decade and have progressed slowly. Ophthalmologic examination revealed the presence of linear and branching structures within the anterior stroma, typically observed in lattice corneal dystrophy. Interestingly, these changes were accompanied by the presence of highly reflective deposits characteristic for granular corneal dystrophy. Genetic testing identified a heterozygous missense (CGC to TGC) mutation, which changed arginine in codon 124 to cysteine in the TGFBI gene in both affected family members

Conclusion Mutation of arginine 124 to cysteine (R124C) of the TGFBI gene represents one of the most frequent mutations detected in patients with lattice corneal dystrophy. However, to the best of our knowledge, this is the first report on a family carrying the R124C mutation and presenting features of both granular and lattice lesions. The state of compound heterozygosity does not account for the observed mixed phenotype, as no other mutation within the TGFBI gene was found. If corneal buttons are available, histopathological examinations will be carried out to identify the nature of the deposits and better understand the mechanism of the disease

• T007
NHS gene mutations in non syndromic cataract

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Purpose Many genes can be involved in congenital cataracts according to different inheritance pattern. NHS (Nance-Horan Syndrome) gene is involved in a rare X-linked syndromic cataract associating dental anomalies and facial dysmorphia. NHS gene mutations are essentially protein truncating mutations. Studies of gene localization show that non-syndromic form of congenital cataract have a gene located in the same region as the NHS gene. The purpose of this study was to determine if others mutations of the NHS gene might cause non syndromic cataracts and to analyse the expression of NHS in lenses.

Methods Genomic DNA was isolated from white blood cells from 30 patients diagnosed with non syndromic congenital cataracts. When a surgery was performed, lenses were collected (n=10). The 11 exons of NHS gene were amplified from genomic DNA by PCR, and the amplicon were directly sequenced. NHS gene copy number anomalies were search by real time PCR. mRNA was extracted from the front capsule of lenses. After reverse transcription mRNA expression was analyzed by real time PCR.

Results We identified 6 punctual mutations of NHS gene in different patients : 2 missenses mutations, 3 frameshift mutations and one intronic mutation. The analyze of NHS copy number revealed in one patient a duplication of exons 4 to 8. We manage to extract and amplified NHS mRNA in the front capsule. One patient with a missense mutation has a relative low expression.

Conclusion We found 23% mutations of NHS gene in our cohort study. For some patients we can't yet absolutely eliminate a Nance Horan Syndrom because of their young age. This high rate of mutations mean either the diagnostic of NHS is under evaluate or NHS gene is frequently involved in non syndromic cataracts.

• T008 / 2787
RDH12 mutation and early-onset retinal degeneration

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Purpose To show the clinical evolution of a child with RDH12 mutation (gene typically associated with Leber Congenital Amaurosis,LCA) and early-onset retinal degeneration

Methods A 8-year-old male who came to our department with a complaint of progressive decline in vision in his both eyes. Full clinical ophthalmological examination, including Best Corrected Visual Acuity (BCVA), anterior and posterior segment examination, Optical Coherence Tomography (OCT), color vision test, visual field, electrorretinogram and genetic study, was performed.

Results At first visit, BCVA was 10/100 in both eyes. Anterior segment examination was unremarkable. Fundus eye examination revealed a bilateral and symmetric pattern of macular hyperpigmentation (of three disk diameters in size)with reticular configuration and patches of hypopigmentation between hyperpigmentated areas. No peripheral atrophy with bone spicule nor optic nerve atrophy were observed. OCT showed an intense macular atrophy with severe disruption of complex pigment retinal epithelium-photoreceptors. Farnsworth Munsell 28-hue test revealed preserved color vision. Visual field showed a central scotoma. Electrorretinogram recordings demonstrated a still preserved rod and cone function. Genetic study revealed a compound heterocigotic mutation for RDH12 in exon 6 (p.Ala269fs and p.Arg234His).Two years later VA decreased to <10/100 and we observed progression of the macular damage.

Conclusion RDH12 mutation can be associated, although extremely infrequently, with an early-onset form of severe retinal dystrophy affecting both rod and cone function (preserved at first stages) and having a phenotype distinct from that resulting from mutations in other known LCA genes.

• T009

Progression of geographic atrophy and polymorphisms of genes CFH, BF, C3, FHR 1-3, FRH3 and ARMS2/HTRA in Age-Related Macular Degeneration

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Purpose To determine if genotype is associated with rate of growth of geographic atrophy (GA) in eyes with age-related macular degeneration (AMD). We assessed the relationship of GA progression, with previously identified genetic variants associated with AMD.

Methods A prospective analysis of participants in a controlled clinical trial from 9 Spanish Hospitals. Fundus autofluorescence photographs were taken at 0, 12 and 24 months from 214 eyes of 107 patients with GA form and evaluated depending on changes in cumulative area of GA. DNA samples were collected to analyse polymorphisms (SNP) of genes CFH, BF, C3, FHR 1-3, FRH3 and ARMS2/HTRA. Simultaneous detection of SNPs was based on Multiplex PCR technology and minisequencing.

Results Our data show that the 27,1% of patient presented a slow, 38,6% moderate and 34,3% a fast growth in the progression of GA. Individual analysis of each SNP showed that the R102G SNP of C3 gene was significantly associated ($P<0.05$) with a further increase in the rate of progression of the area of atrophy.

Conclusion Our results suggest that the genetic alleles related to the progression of atrophic AMD lesions are different than those to predict establishment of AMD. Supported by Grants FIS PI08/1705, FIS PI11/00898 and RETICS RD 07/0062. Ministerio de Ciencia e Innovación.

• T010 / 2467

Diabetic retinopathy in Greek Caucasian type 2 diabetic patients, relationship with polymorphism in the plasminogen activator inhibitor 1 and 2 genes

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Purpose Diabetic retinopathy is a sight thratening chronic complication of diabetes and the leading cause of acquired blindness in adults.Population and family studies showed that pathogenesis of diabetic retinopathy depends upon the interaction of several environmental and genetic factors.Plasminogen activator inhibitor 1 and 2 is the major inhibitor of fibrinolysis and gene polymorphism has been related to hypofibrinolysis.

Methods A case control study was carried out.Assesment of diabetic retinopathy was performed by ophthalmoscopy and fluoroangiography when indicated.The comparison of the groups of patients was performed according to the presence or absence of diabetic retinopathy.In each patient the genotype of pai-1 and pai-2 was determined using PCR and RFLP techniques.

Results 246 controls & 352 cases observed
SERPINB2Statistical significance of the observed linkage disequilibrium:

rs2070682	rs1050813	rs2227690	rs2227692	
rs2227667	1.55e-15	3.55e-15	1.11e-16	2.22e-16
rs2070682	-	2.22e-16	1.78e-15	0
rs1050813	-	-	2.04e-12	2.17e-7
rs2227690	-	-	-	3.02e-8

Global result:
Fisher's p value is 0.573984
Pearson's p value is 0.573939
SERPINE1
Statistical significance of the observed linkage disequilibrium:

rs2070682	rs1050813	rs2227690	rs2227692	
rs2227667	1.55e-15	3.55e-15	1.11e-16	2.22e-16
rs2070682	-	2.22e-16	1.78e-15	0
rs1050813	-	-	2.04e-12	2.17e-7
rs2227690	-	-	-	3.02e-8

Global result:
Fisher's p value is 0.573984
Pearson's p value is 0.573939

Conclusion Based on the primary analysis derived some important relationship between gene polymorphism and diabetic retinopathy that even last the bonferroni correction.

• T011

Non-syndromic retinitis pigmentosa: Phenotype-genotype correlation in twelve Tunisian families

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Purpose To evaluate the clinical phenotype of twelve families with non syndromic retinitis pigmentosa (RP), to characterize genes and mutations causing these conditions and to elaborate phenotype/genotype correlations.

Methods Ophthalmic examination and various visual tests were performed. DNA was analyzed using single nucleotide polymorphism, microsatellite genotyping and direct sequencing to determine the genes and mutations involved.

Results We identified 8 genes: RPE65, RDH12, USHER 2A, PDE6a, PDE6b, CRB1, NR2E3 and RGR. Many of the phenotypes were more prevalent with particular genes. Analysis of phenotype-genotype correlation indicated that some genes were associated with specific phenotypes. In RPE65 mutations we found early onset dystrophy, nystagmus, keratoconus, white dot deposits in earlier stages and clumped pigment in later stages. The RDH12-associated phenotype showed severe and early-onset dystrophy, diffuse spicule pigmentation, macular edema and tomographic re-organization of retinal lamination with thickened macula. CRB1 mutation was characterized by preserved para-arteriolar retinal pigment epithelium and yellow round deposits in the posterior pole and there was no hemeralopia.

Conclusion RP is clinically and genetically heterogeneous.The two ultimate goals of research are to provide efficient clinical diagnostic of affected gene by phenotype-genotype correlation and to design novel treatment regimes. Our aim is to create a specific chip for our population, and then future research will focus on the identification of the remaining causal genes, the elucidation of the molecular mechanisms of disease in the retina and the development of gene therapy approaches.

• T012

Vascular endothelial growth factor A genetic polymorphisms and AMD in Tunisians

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Purpose To determine whether vascular endothelial growth factor (VEGF) gene polymorphism plays a role in either susceptibility risk for exudative AMD, serum VEGF levels variations and treatment with intravitreal bevacizumab in Tunisians

Methods In this case–control study, we included 96 patients with exudative AMD and 207 age-matched controls treated with intravitreal bevacizumab. Single nucleotide polymorphism (SNP) genotyping was performed using restriction fragment length polymorphism (RFLP) analysis of polymerase chain reaction (PCR) products. The serum VEGF was assayed by ELISA (R&D).

Results The frequency of the VEGF -2578 A allele was significantly higher in AMD patients than in controls (p=0.005; OR: 2.12[1.23-3.66]) and was statistically associated to higher serum levels of VEGF (93.30 pg/ml versus 39.75 pg/ml for C allele) (p: 0.021). When examining the effect of this polymorphism on post-treatment visual acuities (VA), we observed that A variant allele was also statistically more prevalent among patients with better outcome for distance and reading visual acuity after three bevacizumab injections compared to those with loss of 3 or more lines in visual acuity (OR = 2.5, 95% CI [1.13-5.73], p = 0.02). Furthermore, the mean of VEGF plasma level is significantly higher (170.97 pg/ml) in patients with enhanced VA compared to those with worse outcome for distance and reading visual acuity (45.52pg/ml) (p=0.003).

Conclusion In addition to the higher risk for exudative AMD in Tunisian patients with the -2578 A VEGF, our results show that this allelic variant also correlates with better visual acuity outcome after treatment with bevacizumab probably through a functional or quantitative variation of plasma levels of this molecule.

• T013 / 2466

Polymorphism of endothelial nitric oxide synthase T786C in patients with normal tension glaucoma and primary open angle glaucoma

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Purpose Comparison of allelic variant frequency of eNOS gene T786C in patients with normal tension glaucoma and primary open angle glaucoma.

Methods The studied group constituted 97 patients with NTG and 49 patients with POAG. DNA was isolated from peripheral blood and T786C polymorphism was studied by RT-PCR method.

Results In NTG patients TT genotype was present in 36% patients, TC in 52.6% and CC in 11.3%. In POAG patients genotype TT was detected in 42.9% persons, TC in 48.9% and CC in 8.2%. The difference in allelic frequency was not statistically significant (p=0.75). In women with NTG the allelic frequency was similar to men (respectively, in women: TT-35.9%, TC-48.4%, CC-15.6% and men TT-36.4%, TC-60.6%, CC-3%; p=0.92). In group of women with POAG the allelic frequency was also similar to men (in women: TT-41.2%, TC-50%, CC-8.8% and men: TT-46.7%, TC-46.7% a CC-6.7%; p=0.09). Comparing the difference in genotype frequencies between both glaucoma types no significant difference was detected in women (p=0.9) and men (p=0.7). The CC genotype was most frequently present in NTG women (15.6%), comparing to NTG men (3%) and POAG women (8.8%).

Conclusion The frequency of particular genotypes of T786C polymorphism of eNOS gene did not significantly differ in patients with NTG and POAG, yet the mutated allelic form is most frequent in NTG women.

• T014

Nailfold capillaroscopic examination and T786C endothelial nitric oxide synthase polymorphism in normal tension glaucoma patients

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Purpose The purpose of this study was assessment of nailfold capillary changes and their possible relation to polymorphism of a gene encoding endothelial nitric oxide synthase (eNOS) in normal tension glaucoma (NTG) patients

Methods The study included 35 normal-tension glaucoma (NTG) patients (23 female and 12 male). Capillaroscopic examination of the nailfold capillaries of II to V fingers of both hands was performed (before and after the cold provocation test) by means of a videocapillaroscope. T786C eNOS gene polymorphism was determined by RT- PCR methods.

Results 31 (88.6%) patients suffered from cold extremities. In 24 (68.5%) patients nailfold capillaroscopy was within normal limits, in 11 (31.5%) patients the results were abnormal, 4 (11.4%) of them mimicked changes observed in sclerodermia. The cold provocation test was positive in 43.5% of NTG patients. The patients with NTG presented the following nailfold capillaries: megacapilaries or dilatated capillaries (44.4%), ramified/bushy (18.9%), coiled (17.1%). Assessing the T786C polymorphism of eNOS gene in NTG patients, TT genotype was present in 36% patients, TC in 52.6% and CC in 11.3%. There were no correlation between SNP variants and capillaroscopy results nor cold provocation test (p=0.9 and 0.5, respectively).

Conclusion The T786C polymorphism of eNOS gene does not influence the capillaroscopy results. The high incidence of sclerodermia - like changes in capillaroscopy in NTG needs further studies.

• T015 / 2465

Activity and epidemiology of a recently-opened ophthalmic emergency center in an University Hospital

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Purpose To investigate characteristics of ophthalmic emergencies in a new unit of emergency care in an University hospital in order to improve the management of patients.

Methods Prospective monocentric cross-sectional study of ophtalmic emergencies over a 2-month period. All patients presenting themselves have been included. Patients characteristics, waiting-time, pathology, and the reality of the emergency were analysed.

Results 1506 patients were examined (average 24 per day). Mean age was 47 years and 60% were male. The median of waiting time was 30 minutes and 24% of patients were registered during the on-call time. The main reasons for consultation were pain (37%), red eye (32%), vision loss (24%). The main diagnoses were ocular trauma (29%), ocular inflammation and infection (24%), normal examination and refractive error (13%). We have estimated that 38% of our patients did not need an ophthalmic specialized emergency examination or treatment.Numerus and various daily ophtalmic emergencies require relevant diagnosis and treatment. Better information of the population and prevention of trauma and infection could help to decrease the number and the severity of ophtalmic emergencies. An improvement of the general and emergency practitioners knowledges in regards to ophthalmic pathologies could allow them to diagnose and treat begnin cases.

Conclusion There is a real need for a permanent ophthalmic emergency department. However patient education and an improvement of care network could allow us to focus on cases that require specialized cares.

• T016

Prevalence and risk factors for refractive errors among the university students of Iran

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Purpose To determine the prevalence and risk factors of refractive errors in Iranian university students.

Methods In a randomized study, of 424 selected students from the six schools of Mashhad University of Medical Sciences (MUMS), 406 of them participated in the study (response rate: 95.7%). Refractive errors were corrected using auto refraction checked by retinoscopy and subjective refraction. Myopia defined as spherical equivalent (SE) refraction -0.50 dioptre (D) or worse, hyperopia as SE of +0.50D or more, and astigmatism as cylinder –1.0D or worse.

Results The prevalence of myopia, hyperopia and astigmatism were 38.4%, 13.8% and 12.8% among the university students respectively. The prevalence of spherical refractive errors were different in males and females (P=0.038).

Conclusion The results of this study indicated that nearly two-third of the university students have refractive errors. Myopia appears to be more common among highly educated persons and unversity students are at high risk for it.

• T017

Prevalence of visual impairment among the elderly: can it be corrected?

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Purpose To determine the prevalence of visual impairment,low vision and blindness among the elderly of Sari in north of Iran.

Methods Through cluster random sampling, 60 clusters were selected, out of which 20 people were systematically selected for this study. Participants received eye examinations including vision, actual visual acuity (AVA), optimal visual acuity (OVA) and refraction. Non-cycloplegic refraction was performed with an auto refractometer and the results were checked with retinoscopy and subjective refraction. Visual impairment , low vision and blind were defined as vision worse than 20/60, 20/60 to 20/400 and worse than 20/400 in the better eye respectively.

Results In this study, 937 people with mean age of 64.7±7.5 years old (from 55 to 87 years) were investigated. The prevalence of visual impairment, blindness, and low vision, based on actual visual acuity (AVA), were 11.0% (9.0-13.0 CI 95%), 3.7% (2.5-5.0 CI 95%), and 7.4% (5.7-9.0 CI 95%), respectively. These findings were 3.7% (2.3-5.1 CI 95%), 1% (0.2-1.7 CI95%), and 2.7% (1.5-3.9 CI 95%), based on OVA respectively. No significant difference was found between genders, but visual impairment was significantly higher in people over 75 years as compared with 55-59 years old. The most common reasons for visual impairment based on AVA were refractive errors (68.6%) and cataract (16.7%). After correcting refractive errors, the most common causes of visual impairment were cataract (61.3%) and diabetic retinopathy (25.8%).

Conclusion Refractive errors and cataract are the main causes of visual impairment in Iranian elderly. Correcting refractive errors and cataract reduces 85% of visual impairment based on AVA.

• T018

Ocular symptoms are not predictive of ocular inflammation in inflammatory bowel disease. A large cross-sectional survey

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Purpose The aims of this study were to assess the predictive value of ocular symptoms for predicting ocular inflammation and the impact of medications on ophthalmologic manifestations in a large prospective cohort of IBD patients.

Methods All consecutive IBD patients seen in the Department of Gastroenterology between April 2009 and July 2011 were interviewed for this cross-sectional study using a pre-established questionnaire. If the patient had at least one ocular symptom, he systematically underwent an ophthalmologic examination.

Results Three hundred and six patients were enrolled in this cross-sectional study: 169 were women (55.2%), 228 had Crohn's disease (74.5%), 77 ulcerative colitis (25.2%) and 1 microscopic colitis (0.3%). Ninety-eight patients (32%) reported at least one ocular symptom: ocular irritation (56.8%), red eye (40.5%), blurred vision (37.8%), ocular pain (31.1%), progressive visual loss (34.4%), myodesopsia (23.3%), eyelid secretion (12.2%), dry eye (9.5%), watering (6.8%), diplopia (5.4%), metamorphopsia (4%), and sudden visual loss (4%). Following ophthalmologic examination (n=79), 41.9% patients had evidence of dry eye (n=31), 14.9% blepharitis (n=11) and 1.4% scleritis (n=1). No uveitis was reported. Methotrexate was associated with dry eye (p=0.03).

Conclusion Ocular symptoms are frequent in IBD patients, but are nonspecific and rarely associated with ocular inflammation. Systematic ocular symptoms assessment is of poor value for diagnosing ocular inflammation in clinical practice in IBD patients.

• T019 / 2686

Intermembranaceous spaces of human optic nerve intracanal part

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Purpose Purpose of research - to reveal laws of structure and distribution of intermembranaceous spaces of optic nerve intracanal part.

Methods 43 bone blocks including optic canal with located in them membranes (dura, arachnoidea, pia), ophthalmic artery of people aged from 26 weeks of prenatal development till 75 years were histologically studied. The structure of optic nerve membranes and intermembranaceous spaces in the cranial, transitive and orbital compartments of optic canal were established. The received data were compared to optic canal MRI results of 27 patients (54 optic canals) aged from 2 months till 75 years on the "VISTA" MP-tomograph 1 T intensity of magnetic field.

Results Wide, uniform, continuous intermembranaceous spaces are characteristic for optic canal cranial compartment, medially and laterally of optic nerve they are more expressed. In optic canal orbital compartment subdural space is the narrowest, non-uniform on MRI and bone blocks research. The subarahnoidal space is most expressed in cranial compartment of canal laterally of optic nerve above of it, and on MRI medially of nerve it is absent or narrow, non-uniform, faltering crack (the similar data is received on histologic research). In transitive optic canal compartment there are separate fragments of subarahnoidal space or its absence in different directions from optic nerve (according to histologic research - above of nerve). In orbital compartment this space in the most cases is closed above and below of optic nerve (by results of research of bone blocks - on all circle of optic nerve).

Conclusion The laws of intermembranaceous space structure and their distributions in optic canal were revealed. MRI was effective method in study of intermembranaceous spaces of optic nerve intracanal part.

• T020 / 4486

CD34 marks angiogenic tip cells in human vascular endothelial cell cultures: a new model to study mechanisms of ocular angiogenesis

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Purpose The functional shift of quiescent endothelial cells into tip cells that migrate and stalk cells that proliferate is a key event during sprouting angiogenesis. Unfortunately, a model of tip cells in vascular endothelial cell cultures is lacking.

Methods We employed the sialomucin CD34 to isolate a small subset of elongated endothelial cells with filopodia from endothelial cell cultures and tested if these cells had properties similar to tip cells in vivo at the functional and molecular level.

Results As predicted by our hypothesis, CD34+ endothelial cells had low proliferation activity. The CD34+ phenotype was upregulated by VEGF-A and downregulated by TNF-alpha and DLL4, three mechanisms known to regulate the tip cell phenotype in vivo. Real-time qPCR and microarray data analysis of the CD34+ cells identified increased expression of all known genes previously associated with tip cells in vivo. Genome-wide mRNA profiling analysis of CD34+ cells demonstrated enrichment for biological functions related to angiogenesis and migration, whereas CD34-negative cells were enriched for functions related to proliferation

Conclusion Our findings suggest that cells with virtually all known properties of tip cells are present in vascular endothelial cell cultures, and that they can be isolated based on expression of CD34. In addition, we characterized the transcriptome of these cells and identified many novel genes with potential significance for angiogenesis. This novel strategy may open alternative avenues of research that may help to understand the molecular processes and functions in angiogenesis in general and of the specialized endothelial tip cell in particular.

• T021

Blood basement membrane alterations in human retinal microaneurysms during aging

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Purpose Different studies indicates that the presence of retinal microaneurysms, dilations of the capillaries which often develop as gross outpouchings of the vessel wall, appears during human aging. However, little is known about the mechanisms involved in the development of these structures. The aim of this study was to examine whether basement membrane protein expression and organization changes during the formation of retinal microaneuryms.

Methods Human retinas were obtained from 17 donors: 14 old-donors and 3 middle-aged donors. Basement membrane proteins (collagen IV, laminin, fibronectin, nidogen), perlecan and MMP-9 expression were analyzed in paraffin sections and whole-mount formalin fixed retinas using immunohistochemistry and laser-confocal microscopy. The structure of basement membrane was analyzed by TEM.

Results Microaneurysms were present in all the retinas obtained from old donors but were absent in the retinas obtained from midle-aged donors. Microaneurysms were classified as Type I (early stage) and Type II (advanced stage). We observed that all basement membrane proteins increased its expression in Type I microaneurysms, but they disminished in Type II microaneuryms. In addition, MMP-9 was strongly expressed in microaneurysms producing basement membrane disorganization.

Conclusion Collagen IV, laminin, fibronectin, nidogen and perlecan were increased in Type I microaneurysm basement membrane. A concommitant expression of MMP-9 could explain the disorganization of blood basement membrane components.

• T022

Normative data for macular thickness by Spectral Domain OCT in healthy children.

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Purpose To evaluate normal values of macular thickness and macular volumen in children without any known retinal disease, using Spectral Domain Coherence Tomography.

Methods This study envolved 323 eyes from 323 pediatric patients (138 male,185 female) with ages between 3 and 14 years. All patients underwent a detailed eye examination, including best corrected visual acuity, cover test, slit lamp and fundus examination and refraction after pupillary dilation. Spectralis OCT scanning were performed by the same operador on all subjects.

Results The 323 subjects had a mean age of 8,3 years (3-14) and the average spherical equivalent value was 0,08 ± 0,14 (-0,06, 0,22).Foveal thickness was 217,08 ± 3,23 (214, 220) for children aged 3-5, 219,16 ± 3,27 (216, 222) for children 6-8 , 215,25 ± 2,97 (212, 218) for children between 9-11 years, and 222,83 ± 3,53 (219, 226) for subjects aged 12-14 years. There was no significant difference with age o gender. Macular volume values are also presented.

Conclusion Our study reports normative data for macular thickness in healthy pediatric patients with SD-OCT . Values obtained may be useful in screening for retinal disease in childhood.

• T023

Choroidal thickness measurements in children using Spectral-Domain OCT

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Purpose The aim of this study was to assess changes in choroidal development in normal children with no refractive error.

Methods Forty children age from 3 to 14 ages with refractive error from 0-1.5 aspheric equivalent and absence of ocular pathology, were evaluated to assess changes in choroidal thickness during development. Seven measurements were taken in a good quality vertical scan: the first was through the fovea and the others in 400 microns steps to nasal and temporal sides (3 each side). Measurements were taken using the manual caliper provided by the software of the device, a Spectralis OCT (Heidelberg, Germany). All measurements were performed by 2 independent observers.

Results Reliable measurements of choroidal thickness were obtainable in 96 % of eyes examined.Mean (SD) choroidal subfoveal thickness was 287.17±70.85 for children aged 3-6, 297.14±66.95 for children 7-10 and 314.70±72.07 for subjects aged 11-14 years. Measurements were lower at the nasal edge 256.05±73.29 compared to 283.50±70.93 at temporal one. There was no difference between sex.

Conclusion Choroidal development during childhood can be assessed by Spectral OCT using manual caliper. Mean choroidal thickness increases with age in childhood and temporal thickness is higher than the nasal one .

• T024

Measurement of scleral curvature using anterior segment optical coherence tomography

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Purpose To work out a way to measuring radius of scleral curvature using anterior segment optical coherence tomography (OCT).

Methods Twenty four volunteers were enrolled. With OCT, horizontal and vertical images centered on the visual axis and four images centered on the upper, lower, nasal, and temporal limbus were obtained. To evaluate tangential radius of curvature, we used each nasal and temporal OCT image and calculated the radius of a circle, which passes by three points of scleral surface at 1, 2 and 3 mm from the limbus. To evaluate axial radius of curvature, central horizontal, nasal and temporal OCT images were composed to a new one and the radius of a circle, the center of which is on the visual axis and passes by the point of scleral surface at 2 mm from the limbus, was calculated. The differences in radius of curvature were analyzed by the student t-test and correlation between two axial radii of curvature calculated by two different reviewers was measured by Pearson correlation coefficient.

Results The mean axial radius of nasal curvature (13.33 ± 1.12 mm) was significantly longer than that of temporal curvature (12.32 ± 0.77 mm). The mean tangential radius of nasal curvature (15.14 ± 2.63 mm) was also longer than that of temporal curvature (14.18 ± 2.24 mm). The axial radii of nasal (13.33 ± 1.12 mm) and temporal (12.32 ± 0.77 mm) curvature from one reviewer were very close to those (13.01 ± 1.16 mm and 12.33 ± 0.78 mm) from the other reviewer (Pearson correlation coefficients 0.942 and 0.841, $p < 0.001$ in both).

Conclusion Anterior segment OCT is a useful tool in measuring the radius of scleral curvature. Measurement of axial radius of curvature is more accurate than that of tangential radius of curvature, and has a good reproducibility.

• T025

Hypoxia Inducible Factor-1a (HIF-1a) and Heat Shock Proteins 90, 70 (HSP 90, 70) expression in ocular pterygium and normal conjunctiva.

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Purpose Research has shown that HSPs participates in preserving HIF-1a function. In this study, HIF-1a, and HSP90, 70, expression and immunolocalization in ocular pterygium and normal conjunctiva samples was examined.

Methods Fifty nine samples of ocular pterygium and twenty samples of normal conjunctiva, surgically removed, were tested with immunohistochemistry, immunofluorecense and western blot analysis.

Results Between pterygium specimens and normal conjuctiva specimens, significant differences were observed in the expressions of proteins HSP90 (p=0.002), HIF-1a (p=0.048). No significant differences were found in the expressions of HSP70 in ocular pterygium when compared to the normal conjunctiva.

Conclusion These data provide molecular evidence that Hypoxia-Inducible Factor-1a and HSP90 may have a role to play in pterygium pathogenesis.

• T026

Comparative endonasal analysis of the inferior lateral wall of the nasal fossae in adults with and without epiphora

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Purpose The development of endonasal dacryocysto-rhinostomia is associated with the advent of nasal video endoscopia which enables a perfect visualization of the surgical site. As the inferior turbinate bones are close to the lacrimonasal duct orifice at the level of Hasner's valvula, anatomic variations of endonasal structures could be associated with the occurrence of epiphora.

Methods The results of nasal endoscopia between a group of adult patients with epiphora (n=35) and a control group of patients (n=19) without epiphora were compared. The endoscopic examination concentrated on changes of the inferior part of the nasal fossae and particularly on the inferior meatus and inferior turbinate bones. A non parametric Mann Whitney test was performed to compare the findings in the two groups.

Results Neither the edema of the inferior turbinate bones nor the visibility of the inferior meatus were associated with epiphora due to lacrimonasal duct stenosis (avec p >0.05). It appeared that there are major anatomic variations of the nasal fossae between two patients but also between either side of the same patient. The lack of difference observed between the two groups of patients could be due to the major anatomic variations observed in the nasal fossae.

Conclusion No particular correlation between anatomical changes of the lateral wall of the nasal fossae and the existence of lacrimonasal duct stenosis was found. However it remains essential to perform preoperative nasal endoscopy in order to detect a possible cause of lacrimonasal duct stenosis and thus evaluate the feasibility of surgery.

• T027

Long-term nanostructural effects of high radiofrequency treatment on the rabbit skin tissues

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Purpose The purpose of this study was to investigate the long-term effects of high radiofrequency (HRF) tissue-tightening treatment in in vivo rabbit dermal collagen fibrils.

Methods These effects would be measured at different energy and at varying pass procedures on the nanostructural response level using histology and AFM analysis. Each rabbit was into one of seven experimental groups, which included the following: control group, and six HRF group according to three HRF energy (10 W, 20 W and 30 W) and two HRF pass procedures. The progressive changes in the diameter and D-periodicity of rabbit dermal collagen fibrils were investigated in detail over one month post-treatment period.

Results Normal dermal tissues show an irregular collagen network structure, whereas those treated with the HRF tissue-tightening device showed more prominent inflammatory responses with inflammatory cell ingrowth compared to the control as well as a well-aligned collagen network structure at the nanostructural level. This effect showed more prominent with the passage of day after treatment. Although an increase in the diameter and D-periodicity of dermal collagen fibrils was identified immediately after the HRF treatment, a decrease in the morphology of dermal collagen fibrils continued until the proliferative period. The dimensions of collagen fibrils returned to level of the control group at the postoperative 7 days.

Conclusion A multiple pass treatment at low energy rather than a single pass treatment at high energy showed the changes in the collagen fibrils at the nanostructural level.

• T028

Morphormetric changes of optic nerve in experimentally induced type 2 diabetic rats

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Purpose To investigate the morphometric changes of optic nerve and evaluate the effect of restriction of diet in experimentally-induced type 2 diabetic rats.

Methods Thirty Strague-Dawley(S.D.) rats were divided into three groups. At 13-week old age, control group (group A) was performed to just open and close the abdominal cavity and partial pancreatectomy was done in group B and C. Group B(ad libitum) was admitted to intake normal diet and group C(restriction) was restricted to intake from 6 week post-operation until to be sacrificed at 24-week old age. We measured the size of optic nerve, axon, the thickness of the myelin sheath, the ratio of axon per myelin, the histologic findings of the optic nerve in electron microscopy.

Results From the 19th week to 24th week-old-age mean blood glucose (mg/dl) was 99.9±11.10 in group A, 399.8±108.42 in group B and 197 ±83.48 in group C($p<0.05$). Mean axon size (μm2) was 0.699±0.094 in group A, 0.579±0.089 in group B and 0.672±0.023 in group C($p>0.05$). The mean ratio of myelin to axon was 1.155 ±0.121 in group A, 1.667±0.075 in group B and 1.070±0.324 in group C($p<0.05$). Disappearance of regular axonal shape was found in group B and lamellar separation of myelin sheath was found in group C.

Conclusion Experimentally-induced type 2 diabetic rats showed morphometric changes of optic nerve during early diabetes even if strict control of blood glucose was performed.

• T029
Blood-retinal barrier serum ferritin transport in mouse retina

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Purpose The general requirement for iron is due to its involvement in various heme and non-heme-containing enzymes, which are ubiquitously involved in metabolic pathways. Iron accumulation is associated with some degenerative diseases, and in the retina with several retinopathies. Iron transport and cell type involved in iron storage mechanisms in the retina are not completely understood.

Methods The iron content was analysed by EDX. Retina ferritin, TIM2 and Scara5 receptors were studied by means of confocal microscopy, rt-PCR and WB. Horse spleen ferritin (HSF) was intravenously injected in healthy ICR mice and in a murine model of blood-retinal barrier (BRB) breakdown.

Results EDX detected iron in perivascular cell lysosomes that significatively accumulate iron in comparison with other cellular compartments. In the lower pH of lysosomes iron is released from transferrin and transported to the cytoplasm. However, this mechanism cannot explain the referred iron lysosomal accumulation. Recently, ferritin was proposed as a new iron delivery protein. TIM2 and Scara5 receptors, that bind to H- and L-ferritin, were expressed in mouse retina, suggesting that serum ferritin can be transported across the BRB into the retinal parenchyma. HSF was intravenously injected and, as expected, ferritin crossed the BRB, probably through TIM2 and Scara5 receptor binding, and accumulated in perivascular cells. In the presence of BRB breakdown injected ferritin was also found accumulated in TIM2 and Scara5 positive cells.

Conclusion Serum ferritin uptake could represent a new pathway of iron delivery in the retina and points out perivascular cells as a key element in retinal iron storage.

• T030 / 4646
Tear film break-up time evaluation by real-time wavefront aberrometry in adult patients with meibomian gland

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Purpose To evaluate tear break-up time (BUT) with repeated higher order wavefront aberrations (HOA) measurements in adult patients with Meibomian Gland Dysfunction(MGD).

Methods Wavefront aberrations up to the sixth order for a 4-mm pupil were measured in 10 normal subjects (Group 1) and 10 patients with severe MGD (Group 2) with corneal involvement, using the IRX3 (Imagine Eyes, Orsay, France) Hartmann-Shack (H-S) aberrometer. The aberrometry was performed once every second for up to 20 seconds. HOA measurements were performed 3 times in a row. HOA variations were compared with the BUT by the conventional fluorescein method(CFM).

Results There was an excellent correlation between the HOA variation and the BUT recorded by the CFM in both groups. There was also an excellent reproducibility of the HOA measurements in all patients. BUT was significantly decreased ($P<0.005$) in all patients in Group 2 compared to the normal tests subjects(Group 1).

Conclusion Studying the HOA variation is a valuable method for evaluatingboth the quality visionand the BUT in patients with MGD and evaporative Dry Eye.The IRX3 H-S aberrometer can be used for an objective and reproducible assessment of the BUT in the follow-up of patients with severe MGD.

• T031 / 4645
Tear film break-up time evaluation by real-time wavefront aberrometry in normal subjects

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Purpose To evaluate tear break-up time (BUT) with repeated higher order wavefront aberrations (HOA) measurements.

Methods Wavefront aberrations up to the sixth order for a 4-mm pupil were measured in 10 subjects using the IRX3 (Imagine Eyes, Orsay, France) Hartmann-Shack (H-S) aberrometer. The aberrometry was performed once every second for up to 20 seconds. HOA measurements were performed 3 times in a row. HOAvariations were compared with the BUT by the conventional fluorescein method (CFM).

Results In 9 patients out of 10 there was an excellent correlation between the HOA variation and the BUT recorded by the CFM. There was also an excellent reproducibility of the HOA measurements in all patients.

Conclusion H-S aberrometry can be used in our daily practice for an objective and reproducible assessment of the BUT.

• T032 / 4647
Corneal respiratory function by FAD autofluorescence lifetime

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Purpose We intend to develop an efficient method to assess in-vivo the corneal respiratory function in order to diagnose corneal cells dysfunction prior to its pathologic expression.

Methods Metabolic alterations can be assessed by measuring the amount of the metabolic co-factors flavin adenine dinucleotide (FAD) and nicotinamide adenine dinucleotide (NADH). FAD has advantages over NADH, like being present only in the mitochondria. Furthermore, using fluorescence lifetime imaging microscopy (FLIM) we are able to discriminate between its free or protein-bound states.We resorted to a PicoQuant MicroTime 100 (PicoQuant GmbH, Berlin, Germany) coupled to an Olympus BX51 Microscope (Olympus Corporation, Tokyo, Japan). This setup uses a pulsed blue diode laser with a trigger frequency of 40 MHz with an excitation filter of 440±10 nm. Intensity decay curves were processed with SymPhoTime v5.3 Software (PicoQuant GmbH). The instrument response function was acquired to improve data analysis precision.

Results We successfully acquired ex-vivo autofluorescence images of male Wistar rat and Bovine corneas. A bi-exponential decay was observed in both cases with a fast decay around 1 ns and a longer one around 4 ns, which correspond to protein-bound and free FAD, respectively. These results are in accordance with other studies, although there is some controversy regarding FAD lifetimes.

Conclusion We showed that it is possible, with our apparatus, to acquire metabolic images of the cornea using FAD autofluorescence.We intend to modify the instrument optical setup in order to acquire reflectance and fluorescence lifetime images simultaneously for corneal layer identification.

• T033 / 2637
Comparison of viral vectors for gene transfer to corneal endothelial cells

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Purpose Thanks to its anatomical location at the posterior surface of the cornea and its monolayer structure, the corneal endothelium is an ideal target for gene therapy approaches. Lentiviral vectors have been shown by our group to be suitable vectors for the transfer of genes into corneal endothelial cells (EC). Aiming for an alternative to these HIV-based vectors, it was the goal of this study to determine the suitability of non-pathogenic adeno-associated viral vectors (AAV) for gene transfer to EC.

Methods Comparison of protein expression after EC transduction using a lentiviral vector or AAV 2/2 with GFP in murine EC (Balb/C) and in human EC (cell line and primary cells)by flow cytometry.

Results Following transduction of EC using lentiviral vector, kinetics of the protein expression are considerably different compared to gene transfer using AAV. In contrast to AAV with protein expression showing a plateau after two to three weeks, lentiviral transfer results in a very rapid of reporter protein. Moreover, we detected significant differences in transduction rates between human and murine EC lines as well as betweeen human EC lines and human corneas (plateau at 70% versus 50% GFP-positive cells with AAV, versus 90-95% with lentivirus).

Conclusion DNA transfer using AAV vectors seems to be an appropriate alternative to lentiviral vectors for gene transfer to EC. Relating to the cultivation of human donor corneas in eye banks over weeks, translation of AAV from bench to bedside, e.g. to reduce apoptosis in corneas, seems to be a promising approach for future gene transfer into donor corneas.

• T034 / 2237
Coupling innovative imaging: in vivo multilaser confocal microscopy and ex vivo confocal Raman spectroscopy of cornea and skin in nephropathic cystinosis

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Purpose Nephropathic cystinosis is a rare, autosomal-recessive inherited disease, characterized by lysosomal accumulation of cystine crystals in almost all tissues. Aim: to describe an innovative in vivo confocal microscopy (IVCM) of crystals in the skin, the cornea and the conjunctiva as well as raman spectroscopy of the crystals in skin and cornea

Methods A 36 year-old women with advanced nephropatic cystinosis underwent penetrating keratoplasty for severe visual loss and chronic ulceration in her left eye. The only dermatology symptom was skin dryness. Cornea and skin was analysed with IVCM using the innovative multilaser (488, 658 and 785 nm) confocal microscope Vivascope 1500 and the handeld monolaser Vivascope 3000 (MAVIG GmbH). In order to obtain the chemical composition, ex vivo Raman spectroscopy (LabRAM ARAMIS,Horiba Jobin-Yvon,France) was performed on corneal button retrieved during keratoplasty and on a skin sample, both immediately frozen in liquid nitrogen without adjuvant

Results Multilaser and monolaser IVCM showed reflective crystals in the corneal epithelium, stroma, tarsal conjunctiva and forearm skin with the highest resolution obtained at 488nm. Ex vivo Raman spectra were obtained in skin and cornea

Conclusion Combination of IVCM with Raman spectroscopy may improve the diagnosis and follow-up for other metabolic diseases with skin and corneal thesaurismoses like amylosis, Wilson disease, Fabry disease or mucopolysaccharidosis

• T035
Changes in meibography in pediatric blepharokeratoconjunctivitis

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Purpose Pediatric blepharokeratoconjunctivitis is an underrecognized and poorly defined disorder. Few details are known about its underlying etiology because children are less cooperative with intensive examination. Nevertheless the meibomian gland dysfunction seems to play an important role in the etiology. Non-contact Meibography can achieve a non-invasive investigation of the meibomian glands inside the tarsal plates of the eyelids.The purpose of this study was to investigate meibomian gland morphology in pediatric blepharokeratoconjunctivitis by non-contact infrared Meibography.

Methods The study group included 10 children (20 eyes) suffering from pediatric blepharokeratoconjunctivitis. Subjective symptoms of ocular discomfort, conjunctival and corneal involvement were recorded. The lid margins were evaluated and non-contact Meibography was performed. Partial or complete loss of the meibomian glands and the presence of tortuosity were checked.

Results All patients reported ocular discomfort as well as lid margin, conjunctival, and corneal involvement. The mean age of the study population was 8 years (2-16 years) and 60% were female. In 8 children (out of 10) meibography revealed partial or complete drop out of meibomian glands in the upper or lower tarsal plate but more frequently in the lower tarsal plate, also abnormal tortuosity of the meibomian glands in the upper eyelid was found.

Conclusion Our investigations showed that pediatric blepharokeratoconjunctivitis can be associated with drop out or abnormal tortuosity of meibomian glands evaluated with meibography.

• T036 / 4446
Comparison of the anti-inflammatory effects of artificial tears in a rat model of corneal scraping

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Purpose The aim of the present study was to evaluate the safety and tolerance of cationic oil-in-water emulsion on debrided cornea, and to characterize its benefits on the corneal epithelium healing process.

Methods A rat model of corneal scraping was used to characterize the effects of four commercially available artificial tears (Cationorm®, Vismed®, Optive® and Systane Balance®) on the recovery process of the debrided corneas. The upper part of the corneal epithelium was scraped mechanically prior to a 5-day treatment with different artificial tears. At the end of the treatment, the ocular surface was evaluated clinically (corneal fluorescein staining, CFS) and by in vivo confocal microscopy (IVCM). Conjunctival function was assessed by goblet cell count and MUC5AC immunostaining.

Results The four artificial tears were all well tolerated by the debrided cornea. By restoring an adequately hydrated ocular surface environment they promote corneal healing, as evidenced by CFS measurements of the scraped area. In contrast 0.02% BAK solution inhibits the healing process. IVCM analysis of the different layers of the cornea confirmed the benefits of the cationic emulsion (Cationorm®). Interestingly inflammatory cells infiltration in the stroma was at its lower following Cationorm® treatment, while 0.02% BAK treatment resulted in marked inflammation. The different treatments were all able to protect goblet cells function and MUC5AC expression.

Conclusion BAK-free cationic emulsion (Cationorm®) is well tolerated by debrided cornea and allow for a safe healing of the cornea. The findings suggest that Cationorm® have the potential to benefit patients with corneal epithelium disorder.

Commercial interest

• T037

Ocular surface effects of antiglaucoma combination therapies in a rat model of corneal scraping

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Purpose Severity of ocular surface damages in glaucoma patients was shown to be correlated to the number of instilled benzalkonium chloride (BAK) preserved (P) antiglaucoma eye drops. While preservative-free (PF) eye drops reduce iatrogenic toxicity they do not restore the ocular surface. The effects of PF-cationic emulsion of latanoprost (Catioprost®) and BAK-free travoprost combined with P- or PF-timolol formulations were compared to BAK-preserved prostaglandin (PG)/timolol-fixed combinations (FC) in an established rat model of ocular surface injury.

Methods Seven PG/timolol combinations were assessed in a rat model of corneal scraping. The upper part of the corneal epithelium was scraped mechanically prior to a 5-day treatment followed by clinical (in vivo confocal microscopy (IVCM), fluorescein staining) and histological evaluations. Conjunctival function was assessed by goblet cell count and MUC5AC immunostaining.

Results Catioprost®/timolol combinations did not induce toxicity as evidenced by IVCM scoring, both reducing inflammatory cell infiltration greater than BAK-free travoprost/P-timolol combination. In contrast, BAK-preserved PG/timolol-FC presented elevated IVCM scores. MUC5AC staining and goblet cell count demonstrated that BAK-free Catioprost®/PF-timolol is the best tolerated combination.

Conclusion BAK-free Catioprost®/P-timolol is very well tolerated, in contrast to BAK-preserved PG/timolol-FC. The findings suggest that Catioprost® associated with PF- or P-timolol have the potential to benefit glaucoma patients with ocular surface disease.

Commercial interest

• T038

Granulomatous conjunctivitis associated with chronic blepharitis in children

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Purpose To outline the clinical and pathological characteristics of granulomatous conjunctivitis associated with primary chronic blepharitis in children

Methods 23 children presenting ocular rosacea with suspected conjunctival granulomas were examined prospectively. Conjunctival biopsies were performed in 20 patients; for each sample we associated histological study with an immunohistochemistry analysis (CD3, CD4, CD8, CD1a, CD11c, CD68, CD123).

Results Conjunctival inflammation was micronodular, associated with follicles in 4 cases. Conjunctival granulomas appeared as whitish or subtle yellowish nodules. Corneal complications were common (87%), as phlyctenular lesions (43.5%) and neovascularization (69.5%). Epithelioid granulomas associated with giant cells infiltrated the conjunctival matrix of most patients (80%), inflammatory infiltrate only was found for 4 patients. The granulomatous specimens showed peri- and intra-granulomas infiltration by inflammatory T-cells (CD3), with more CD4 cells than CD8 cells, monocytic-derived cells (CD11c) including macrophages (CD68+ CD1a), and less frequently plasmacytoid dendritic cells (CD123). Treatment included topical steroids, lubricants and eyelids care (100%), topical ciclosporine (13%), systemic antibiotics (35%).

Conclusion Granulomatous conjunctivitis is a complication of ocular rosacea in children. The immunopathology of the conjunctiva identified the main cellular actors involved in the granulomatous process. Our results provide a new look on this pathology.

• T039 / 4447

Secreted frizzled proteins in control and keratoconus (KC) tears and corneas

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Purpose To investigate the expression and distribution of Wnt pathway antagonists, secreted frizzled-related proteins (SFRPs), in tears and corneas from control and keratoconus (KC) patients.

Methods Immunofluorescence and confocal microscopy were used to examine the expression patterns of SFRP1, 2, 3, and 5 in paraffin sections of KC (n=11) and control (n=7) corneas. A custom SFRP1 ELISA was developed and used to quantify SFRP1 concentration in basal tear samples collected from KC (n=10) and control patients (n=10). The percentage SFRP1 of total tear protein concentration (%SFRP1) was calculated and compared between KC and control groups.

Results Immunofluorescence showed heterogeneous epithelial SFRP1 expression in all KC corneas compared to low expression in controls. SFRP3 and SFRP5 showed unique patterns of immunolabelling. SFRP3 was localised to epithelial cell membranes and limbal vessels in control corneas; cell membrane and cytoplasmic immunolabelling, and increased expression centrally, was seen in KC. SFRP5 was expressed strongly in the corneal stroma (KC and control). SFRP2 immunoreactivity not obvious in either control or KC corneas. ELISA results showed that tear SFRP1 levels were lower in KC compared to control tears.

Conclusion The pathogenesis of KC remains poorly understood. Our current study shows that SFRP1, 2, 3 and 5 are differentially expressed in control and KC corneas, consistent with previous work, suggesting Wnt signalling involvement in KC. The decreased levels of KC tear SFRP1 contrasts with increased expression in KC corneal epithelium, and may suggest KC-associated differences in tear secretion or tear protein breakdown.Funded in part by Sydney Eye Hospital Foundation

• T040 / 3876

Investigation of bacterial contamination of corneal donors using molecular biology

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Purpose transmission of infectious agents is a major concern for every graft process. Corneal transplantation has been associated to transmission of virus and non conventional agents, but bacterial hazard remains possible in eyebanks. In this prospective study, we investigated the presence of resistant bacteriae in contact with the cornea throughout the whole preservation process.

Methods Samples were taken from donor aqueous humor, conjonctival cul-de-sac and limbus, and from Corneaprep®, Corneamax® and Corneajet® media. Scleral rim was harvested as well after surgery. Bacterial contamination was investigated using direct exam, culture and 16S RNA detection.

Results 164 corneas of 83 donors were included. Cul-de-sacs conjonctivaux (CS). 131 cul-de-sac (79,9%) and 119 limbus (72,6%) were contaminated, from S. epidermidis in 50%. 7 aqueous humors (4%) were positive, 5 with S. epidermidis and 2 with Bacillus. We encountered 34 hemocultures (41%), 6 Corneaprep (4%), 6 Corneamax (4%), 0 Corneajet (0%) and 0 scleral rim (0%) positive.

Conclusion 16S RNA detection did not increase the number of positive samples. 92% of Coag. Neg. Staphylococcus, 19% of S. Aureus, 33% of enterobacteriae, 49% of streptococcus and 75% of enterococcus had an acquired phenotype of resistance to antibiotics. No link between blood contamination and corneal contamination is evidenced. Routine eyebank procedures achieve efficient antimicrobial security.

• T041

Evaluation of limbal stem cell deficiency: a new diagnostic tool based on keratin 13 immunostaining in corneal impression cytology

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Purpose The aim of this study was to develop a validated, reliable and minimally invasive technique for diagnosing limbal stem cell deficiency (LSCD) using immunocytochemical detection of conjunctival and corneal keratins on epithelial cells collected by impression cytology (IC).

Methods After validation of the labelling techniques on a cohort of ten healthy control patients, keratins K12, K13 and K19 were labelled on corneal IC of ten eyes suspected of LSCD. Positive scores for the conjunctival markers K13/K19, combined with the rarity of the corneal marker K12, were diagnostic proof of LSCD.

Results IC is a reliable and noninvasive technique for collecting epithelial cells. The labelling validation phase eliminated K3 labelling due to lack of corneal specificity. Among the patients with suspected LSCD, nine samples were diagnosed with LSCD, which was severe (K12 negative) in eight cases and mild (K12 positive) in one case. One sample could not be analysed due to insufficient cells.

Conclusion The immunocytochemical search for the K13/K19 pair using corneal IC provides a simple and reliable method for diagnosing LSCD, while the level of K12 provides a score of disease severity. On the other hand, we question the corneal specificity of K3 as conventionally established. Finally, to our knowledge, this is the first study detecting K13 on a conjunctival IC specimen as a marker of conjunctival differentiation.

• T042

Identification of factors regulating differentiation and growth of limbal stem cells for corneal surface regeneration

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Purpose To identify factors which are produced by damaged corneal epithelium and which control proliferation and differentiation of limbal stem cells (LSC).

Methods The central cornea in the mouse was mechanically damaged and the cornea or limbal tissue was excised at different time intervals after injury. The expression of genes for a number of growth and differentiation factors in the cornea or limbus was determined by real-time PCR. The effects of these factors on the growth and differentiation of LSC in vitro was tested.

Results It was found that the expression of a number of genes in the central cornea was significantly enhanced already 3 or 6 hours after the cornea damage. Insulin-like growth factor I (IGF-I) which is strongly upregulated shortly after injury, was identified as the main factor responsible for LSC differentiation into cells expressing cytokeratin K12, a marker of corneal epithelial cells. Furthermore, IGF-I enhanced expression of its own receptors in LSC, but it had no effect on LSC proliferation. Another two factors produced by the corneal epithelium, fibrocyte growth factor (FGF) and epidermal growth factor (EGF), supported LSC proliferation without effect on their differentiation.

Conclusion IGF-I was identified as the main factor inducing differentiation of LSC into cells expressing corneal epithelial cell markers. The proliferation of these cells was supported by FGF and EGF.

• T043

Gene transfer of HSV1-specific meganuclease to the murine cornea

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Purpose Recombinant Adeno-Associated virus (rAVV) encoding meganucleases specifically designed to address Herpes simplex virus type 1 (HSV1) reduce HSV1 replication both in vitro and ex-vivo. The main issue of this potential antiviral treatment is the delivery system. To evaluate a vector-free method, we tested an electroporation process to transfer HSV1-specific meganucleases (HSV1-SM) to the murine cornea

Methods Corneal gene transfer was achieved by subconjunctival injection (SCI) of recombinant plasmid encoding either GFP (group 1; n=30) or HSV1-SM (group 2; n=12), followed by electroporation. Mice were sacrified at day (D)1, 3, 7, 13, 35 (group 1) and at D13 and 35 (group 2). Control group consisted in SCI w/o electroporation. Corneal samples were analyzed for the expression of transcripts encoding GFP and HSV1-SM using real time PCR. The results were compared to those obtained following SCI of rAAV encoding either GFP or HSV1-SM

Results For HSV1-SM, SCI plus electroporation induced a stronger expression than SCI alone at D13. In group 1, the expression of GFP transcripts decreased from D1 to D35. However, until D13, their levels of expression were higher than those obtained with the rAAV method ($p<0.002$). Similarly, the expression of HSV1-SM transcripts at D13 was higher than those obtained with the rAAV method ($p<0.002$), suggesting that therapeutic concentration could be optimised with this method. At D35, results were not statistically different between the 2 methods

Conclusion In our hands, with the method we used, we can conclude that SCI of plasmid encoding HSV1-SM with immediate electroporation is an efficient method to improve delivery in short-term but not in long-term when compared to rAAV

• T044

Nicorandil: a new case of corneal ulceration

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Purpose To describe a case of corneal ulceration induced by nicorandil.

Methods A 78-year old woman presented a persistant corneal ulceration (RE), resistant to local treatment. She complained of pain and photophobia and visual acuity was 20/125. Slit-lamp examination revealed epithelial erosion, stroma thinning and folds of Descemet's membrane. Anterior chamber and fundus examination were normal. Neither mechanical nor infectious local causes explained the lesions. The trigger was most likely a cataract surgery, two months earlier. In her past medical history she reported angor treated by nicorandil for 2 years, treatment that has been suspected to impede corneal healing. With the appointment of her cardiologist we decided to stop nicorandil and observed complete resolution of the symptoms and ulceration after a few weeks.

Results Pathogenesis of nicorandil-induced ulcerations is not yet elucidated. Recently it has been hypothesized that during prolonged high-dose treatment with nicorandil, or after increased dosage, nicotinic acid (a metabolite) may accumulate outside the endogenous pool of nicotinamide adenine dinucleotide/phosphate and become abnormally distributed. In case of a rather recent or sustained trauma (surgery in our case), nicotinic acid, thanks to nicotinamide, a potassium channel openers with vasodilatator effects, may ulcerate the epithelial proliferation of the edge of the raw area, ultimately flooding the whole scar. The sequence of events of this case strongly suggests a nicorandil-induced ocular side effect.

Conclusion Attention should be paid to the possible ocular iatrogenic role of nicorandil in cases of unexplained corneal ulceration.

• T045
The effect of infliximab on corneal neovascularization in rabbits

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Purpose To determine the efficacy of topical application of infliximab (TNF-α monoclonal antibody) for the treatment of corneal neovascularization in the rabbit model.

Methods With the subject of 12 rabbits (24 eyes), the corneastroma was sutured to induce corneal neovascularization. 1 week after suture,the corneal neovascularization was confirmed, after which the subjects were divided into 4 groups of 3 rabbits, and the control group was applied sterilized balanced salt solution, and the experiment group was treated with infliximab eye drop of varying concentrations of 1mg/ml, 2mg/ml, 4mg/ml for twice a day for aweek. For each group, the area of corneal neovascularization at day 3 and day 7 were measured and analyzed. At day 7, all eyes were extracted to compare the TNF-α mRNA concentration by reverse transcriptase polymerase chain reaction(RT-PCR) and the VEGF activity of corneal neovascular tissue wasobserved by fluorescence immunostain.

Results The area of corneal neovascularization on day 7 was significantly reduced in all three groups treated with 1mg/ml, 2mg/ml, and 4mg/ml compared to the control group (p=0.043, p=0.027, p=0.01). On day 7 of the treatment,TNF-α mRNA was significantly reduced in all three groups treated with 1mg/ml, 2mg/ml, and 4mg/ml compared to the control group(p=0.038, p=0.031, p=0.022). Also, in the fluorescence immunostain, the reduced expression ofVEGF was confirmed in all three groups compared to the control group.

Conclusion The application of Infliximab is expected to effectively inhibit the corneal neovascularization, and further studies for clinical application shall be necessary.

• T046
The ocular surface drug correction in patients after LASIK

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Purpose Optimization the ocular surface after LASIK

Methods Assessed the ocular surface, tear film and tear production before and after optimization in patients after two-step LASIK in 4 groups. Group 1 (A) - high myopia and low degree of astigmatism - (43), aged 18 to 35 years, group 2 (B) - medium myopia and low degree of astigmatism – (32), aged 18 to 35 years, group 3 (C) - myopia medium or high and medium degree of astigmatism – (37), older than 35 years, group 4 (D) - hypermetropia medium or high and medium degree of astigmatism - (32), older than 35 years. The criteria for preoperative drug correction of refractive surgery to the stage were the following diagnostic blocks: clinical data in diagnosis of dry eye and corneal status, corneal thickness, the definition of clinical refraction, including patient age, antioxidant and immune activity of tears.

Results The use of moxifloxacin 0.5% and tear lubricants (such as preparation containing hydroxypropylguar and sorbitol or hydroxypropylguar) in groups A and B, and the use of tear lubricants (such as preparation containing hydroxypropylguar and sorbitol or hydroxypropylguar) in groups C and D after LASIK reduces residual astigmatism and the number of complications refractive surgery.

Conclusion We found the dependence tear lubricants choice for optimizing the ocular surface after LASIK from the indices of corneal status, corneal thickness, the definition of clinical refraction, degree of astigmatism, including patient age, antioxidant and immune activity of tears.Pathogenetically substantiated using of preparations containing hydroxypropylguar and sorbitol or hydroxypropylguar after LASIK reduces the degree of residual aberrations.

• T047
The role of compliance in optimizing the ocular surface after two-step LASIK

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Purpose Development and evaluation of optimizing the ocular surface after two-step LASIK, based on compliance

Methods Assessed the ocular surface, tear film and tear production before and after optimization in patients after two-step LASIK in 4 groups. Group 1 (A) - high myopia and low degree of astigmatism - (43), aged 18 to 35 years, group 2 (B) - medium myopia and low degree of astigmatism – (32), aged 18 to 35 years, group 3 (C) - myopia medium or high and medium degree of astigmatism – (37), older than 35 years, group 4 (D) - hypermetropia medium or high and medium degree of astigmatism - (32), older than 35 years. The criteria for preoperative drug correction of refractive surgery to the stage were the following diagnostic blocks: clinical data in diagnosis of dry eye and corneal status, corneal thickness, the definition of clinical refraction, including patient age, antioxidant and immune activity of tears, determine of compliance

Results Pathogenetically substantiated the two preparations after two-step LASIK - moxifloxacin 0.5% and hydroxyproylguar and sorbitol in group A, and moxifloxacin 0.5% and hydroxyproylguar in group B provide medium compliance. Using only hydroxyproylguar and sorbitol in Group C and hydroxyproylguar in Group D demonstrated a high compliance.

Conclusion First pathogenetically substantiated the choice of therapy based compliance in patients after two-step LASIK.

• T048
Use of lissamine green before conjunctival impression cytology and flow cytometry in patients with sjögren's syndrome

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Purpose Lissamine Green (LG) is a vital dye that stains damaged epithelial cells in ocular surface disease. Conjunctival Impression Cytology (CIC) is used with flow cytometry, to examine surface epithelial cells. We were concerned that, if used prior to CIC, cell uptake of LG might affect the fluorescent signal during flow cytometry. We therefore studied whether the use of LG before CIC, could cause fluorescence interference.

Methods CIC was performed with two autoclaved Supor semicircular filters applied to the lateral bulbar conjunctiva of 6 patients with Sjögren's Syndrome. LG was eluted from a standard strip with a drop of anaesthetic and delivered into the inferior fornix. Two further filters were applied to the medial bulbar conjunctiva. Cells were recovered by agitation for 1 minute, washed, stained and analysed by flow cytometry.

Results When compared with samples taken before LG instillation, cells isolated from all 6 samples taken after LG instillation, and excited at 630nm, showed an increase in fluorescence at 665nm. Some increased fluorescence was also noted at 680nm but was within the limits of spectral compensation. There was no observable effect of LG when cells were excited at 488nm.

Conclusion Cell uptake of LG is detected by flow cytometry, predominantly in the 665nm channel when excited at 630nm. This persists despite cell washing. Whilst this excludes the use of fluorochromes that emit within this spectrum, the use of fluorochromes excited or emitting at other wavelengths, is feasible after LG staining.

• T049

Lacrymal secretion in the non-affected fellow eye of patients with recurrent unilateral herpetic keratitis

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Purpose To assess the potential impact of unilateral recurrent herpetic keratitis on the tear secretion of the fellow eye.

Methods Patients referred for a recurrent herpetic unilateral stromal keratitis and control patients, age- and sex-matched, with no history of corneal disease. .Dry eye conditions where tested in keratitis patients after a minimum quiescent period of three months. Osmolarity (using the TearLab®), tear break-up-time (TBUT), tear reflex (Schirmer I test), and central corneal sensitivity (using the Cochet-Bonnet aesthesiometer) were assessed in the two eyes of patients and controls. Values were compared using non-parametric tests, and statistical significance was defined as $p<0.05$ (2-tailed).

Results Thirty-five patients (mean age: 52.3 ± 7.3 years) and 35 control subjects (mean age: 52.8 ± 8.5 years) were consecutively included in the study. We found no difference between right and left eyes of control patients. The corneal sensitivity and TBUT was strongly reduced in the affected side (4,85g/mm2 ± 2.0; 4.6sec ± 1.1 respectively) compared to the non-affected side (0.57 g/mm2 ± 0.13 p=0.001; 7.7sec ± 1.4 p<0,001 respectively). The average tear osmolarity in non-affected eyes was higher than the average of the highest values observed in control subjects (316.3 versus 303.8 mmol/L, p=0.0001). Similarly, the average BUT in non-affected eyes of herpetic patients was lower than the average of the lowest values observed in control subjects (7.7 versus 12.2 sec, p=0.0001).

Conclusion This study suggests that unilateral recurrent stromal herpetic keratitis induces dry eye condition in the non-affected eye.

• T050

Wetability and deposits accumulation on anterior surface of blue light-filtering contact lens

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Purpose To evaluate wetability and deposits accumulation on anterior surface of blue light-filtering contact lens after a cleaning process with Multi-purpose Solution Cleaning, Hydrogen Peroxide solution and Lubricant Drops.

Methods A self-controlled trial was carried out in 41 contact lens users who were wearing blue light-filtering contact lens (Profilcon A 52%WC) for 30 minutes per test. Wetability and deposits accumulation on anterior surface were evaluated according to the International Organization for Standardization ISO11980 guidelines. Four conditions were set: a)usual contact lens, b)blue light-filtering contact lens after cleaning process with Multi-purpose Solution Cleaning, c)after Hydrogen Peroxide solution disinfection and d) after Lubricant Drops instillation.

Results Statistically significant differences were not observed within the parameters evaluated among the different cleaning solutions proposed. For a,b,c and d conditions, the percentage of lens that showed very insignificant deposits accumulation(visible after drying tear film) were 25%,34%,20% and 27%, respectively and the percentage of lens that showed not significant deposits (deposits easily eliminated) were 3%,2%,7% and 8%, respectively. Regarding wetability, minor wetability problems were showed and these ones were solved by the blinking in 18%, 29%, 18% and 18% of the cases, respectively, whereas the areas that remained dry on the contact lenses were 4%,0%,5% and 2% of the cases.

Conclusion The wetability and deposits accumulation on anterior surface of blue light-filtering contact lenses is similar for the different cleaning treatment and equivalent to the non blue light-filtering contact lens.

• T051

Observation of dendritic cells in subclinical corneal graft disease using confocal microscopy imaging

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Purpose The aim of this study was to show the applicability of confocal microscopy for the diagnosis of corneal graft disease in presence of masking corneal changes.

Methods The examined group consisted of 12 patients with suspected corneal graft rejection, in which the local state of the cornea caused difficulties in diagnosis. 7 patients was after DALK procedure, 4 after PK, 1 after DSAEK. Local state of corneal transplant included: edema in secondary glaucoma (3 patients), inflammation with ulceration (3 patients), edema in bullous keratopathy (1 patient), edema in keratouveitis (4 patients), haze after inflammation (1 patient). We performed following procedures: slit lamp examination, scans using a Scheimpflug camera (Pentacam, OCULUS), confocal microscopy in vivo (Rostock Cornea Module, Heidelberg Engineering Retina Tomograph III).

Results In a slit lamp examination, uncharacteristic macroscopic changes were described - focal turbidity, endothelial deposits and edema. In an examination with the Scheimpflug camera an increased thickness and haze in the posterior stroma was reported. In order to search for microstructural evidence of rejection underwent corneal confocal microscopy which in 11/12 cases showed infiltration of dendritic cells. These cells were located at well-defined depth (where the adhesion of the corneal transplant) and was not appearing in other parts of the cornea.

Conclusion In vivo confocal microscopy is a useful method for the detection of corneal transplant disease also in presence of local changes masking rejection symptoms. This examination is characterized by high sensitivity and ranges in this study of about 92%.

• T052

Risk factors for contact lenses related microbial keratitis: a prospective multicenter case control study

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Purpose MMK remains a rare complication of CL wear, but is of interest because it is both a major cause of new cases of MK in the population, and the only sight-threatening complication of an otherwise safe method of vision correction. The aim of the study is to identify risk factors and to put into perspective the individual risk and the societal burden of CL-related MK patients.

Methods A prospective multicenter case-control study was conducted in 16 French University Hospitals on all lenses wearers presenting with MK between July 2007 and December 2011. Patients had a complete ophthalmological examination and were interviewed by a 50 items anonymous "questionnaire" to determine subject demographics and lenses wear history. The CL related MK subpopulation (Case) was compared to healthy CL wearers (Control).

Results 684 CL related MK and 599 healthy CL wearers were included. Patients wearing soft contact lenses had a higher risk for MK, as compared as rigid lenses wearers (Relative risk, 4.1 ; $p < 0.001$). Among soft lenses, daily disposable CL (RR, 1.8 ; $p = 0.01$) and 2 weekly replacement CL (RR, 2.1 ; $p < 0.001$) had an increased risk of MK than monthly replacement CL, respectively because of some lacks in basic rules of hygiene (absence of hand washing) and the absence of a professional supervision for daily disposable CL and the overtaking of the deadline of renewal for 2 weekly replacement CL.

Conclusion With the increasing avaibility of CL, notably through internet or local market, this study serves to highlight the increasingly documented dangers of freely available CL without professional supervision and of the lack of information about the basic rules of hygiene and the basis of CL care and handling.

• T053

Observation of dendritic cells in corneal graft disease in keratoconus patient after deep anterior lamellar keratoplasty using confocal microscopy imaging

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Purpose The aim of this study was to present the applicability of corneal confocal microscopy for the early identification and monitoring of treatment efficacy in corneal graft disease.

Methods In the 45-year-old patient after transplantation because of keratoconus, suspected of graft rejection was performed the following tests: basic slit lamp examination, corneal scans using a Scheimpflug camera (Pentacam, OCULUS) and corneal confocal microscopy in vivo (Rostock Cornea Module Heidelberg Retina Tomograph III Engineering). The study was performed on admission and one week and two weeks after the implementation of local steroids.

Results In a slit lamp examination, uncharacteristic macroscopic changes were described - focal turbidity, endothelial deposits and oedema. In an examination with the Scheimpflug camera, endothelial deposits were seen as highly hiperreflective structures reaching the level of the endothelium to the posterior of the corneal stroma. These symptoms are not also unique to transplant disease. In order to search for microstructural evidence of rejection underwent corneal confocal microscopy in which visualized monomorphic intense infiltration of inflammatory cells and dendritic cells, located primarily in the area near the posterior stroma and Descemet membrane. During the steroidotherapy reduction with number of dendritc cells were observed cell infiltration set up to complete disappearance of their normal structure and appearance of the endothelium.

Conclusion Corneal confocal microscopy is a useful method for early detection and monitoring of disease corneal transplant.

• T054

Role of human corneal stroma-derived mesenchymal-like stem cells in immunity and wound healing

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Purpose Mesenchymal stem cells (MSC) are the stromal cells of bone marrow, but they can be also found in other tissues including the cornea. Our goal was to isolate and cultivate human corneal stroma MSC-like cells (CSMSCs) and study their role in immunity and wound healing.

Methods Corneal buttons were harvested from cadavers (according to the Guidelines of the Helsinki Declaration). The isolated stromal cells were cultured ex vivo in human serum containing medium. Fluorescent microscopy, FACS and gene array analysis, as well as standardized in vitro differentiation assays were performed to investigate the stemness and phenotype of the CSMSCs. To investigate the immunosuppressive function of these cells, mitogen activated lymphocyte reaction and activation by pro-inflammatory cytokines were used.

Results According to the definition of the ISCT, the most important MSC markers (CD73, CD90 and CD105) were highly expressed on the surface of the CSMSCs with the absence of endothelial or hematopoietic cell markers. The CSMSCs were able to differentiate into fat, bone, cartilage tissues and close wounds within 24 hrs in vitro. They could suppress the proliferation of activated peripheral blood lymphocytes and secrete suppressive cytokines upon pro-inflammatory activation.

Conclusion We demonstrate a method for isolating and cultivating MSC-like cells from human corneal stroma. The ex vivo data suggest that these cells may have a role in wound healing and immunological processes in the eye that can possibly be used in future treatments of ocular diseases and corneal stroma injuries.

• T055

Tear film proteins attached to soft contact lenses

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Purpose Contact lenses (CLs) float on the tear film that is the outer 7-8 µm liquid layer on the cornea. Proteins can adhere to the surface of CLs. Adhered proteins are the agent for irritation and in case of long wear time and poor hygiene, possibly also for keratitis; as the proteins may serve as an anchor for bacteria to attach to.We have isolated and identified such adhered proteins from the CL surface.

Methods Soft CLs from 3 non-atopic human individuals were collected. 1-day, 14-days and 30-days lenses were examined.Adhered proteins were removed in denaturing lysis buffer and separated on two-dimensional polyacrylamide gels that were silver stained. Spots of interest were excised and subjected to in-gel tryptic digestion prior to liquid chromatography - tandem mass spectrometry analysis.

Results Equal amounts of proteins (20-40 µg) were separated on 2D-gels. Protein patterns appeared more intense but with similar patterns with longer wear-period.A fraction of the observed silver stained protein spots were successfully identified with tandem mass spectrometry. Identified proteins included: lactoferrin, lysozyme C, lipocalin-1, mammaglobulin, beta-2-microglobulin, prolactin-inducible protein, immunoglobulins, polymeric immunoglobulin receptor, zinc-alpha-2-glycoprotein, cystatin-S, cystatin-SN, secretoglobulin family 1D member 1 and serum albumin.

Conclusion Adhered proteins from CLs were isolated and identified. The protein composition resembles the protein composition in tears. The combined techniques of 2D-gel electrophoresis and mass spectrometry is proven to be a suitable tool to examine proteins adhered to CLs. Proteins from a single set of CLs can be analyzed.

• T056

Epidemiology of microbial keratitis: A review of 508 cases

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Purpose To describe epidemiological and microbial characteristics of infectious keratitis

Methods The infectious agents of microbial keratitis remains frequently undetermined. We conducted a prospective study to evaluate systematic screening for bacterial, viral, fungal and amoebic pathogens. All patients referred to the participating ophthalmology departments in France from April 2006 to April 2012 had a microbial keratitis that were analyzed by corneal scraping and contact lens and contact lens care testing if patients wore contact lens. The standardized protocol for laboratory investigations included cultures (standard, culture of amoeba and amoeba-based culture of pathogens), and PCR (16s, 18s, mycobacterium, universal fungal, amoeba, HSV, ZVZ, CMV, mimivirus and sputnik).

Results 508 cases of microbial keratitis were included, the average of age was 49.4 years (SD: 23.2), the sex ratio 1:1. Predisposing risk factors were identified in 71.1% of patients: the most frequent was the contact lens wear in 41.2% cases, then ocular trauma and ocular surface disease (8.2% each), ocular surgery (7.5%) and multifactorial in 6.3 %. Among the 508 included patients, an infection was diagnosed in 185 cases (36.4%): 62% on corneal samples, 28% on contact lens and contact lens care and 10 % on both. On corneal samples, 78.5% were caused by bacteria (Pseudomonas aeruginosa was the most frequent), 3 % by mycobacteria, 10.5% by virus, 6% by fungus and 2% by protozoa.

Conclusion Microbial keratitis was rare without risk factor and contact lens wear appear to be the most important risk factor. Microbiological agents responsible of infectious keratitis remain essentially bacterial.

• T057

The contribution of tear osmolarity measurement to ocular surface assessment in soft contact lens wearers

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Purpose To determine whether tear osmolarity using the TearLabTM Osmolarity System contributes to the assessment of the ocular surface in contact lens (CL) wearers.

Methods Data were collected from 44 CL wearers (28 tolerant and 16 intolerant) and 34 healthy subjects. Every patient underwent a thorough ophthalmic examination and tear osmolarity test, conjunctival impression cytology and meibomian lipid sampling. Symptoms, break-up time (BUT), tear osmolarity, conjunctival expression of HLA-DR and meibomian fatty acid composition were evaluated.

Results Tear osmolarity was significantly higher in the controls compared to tolerant and intolerant CL wearers ($p=0.0007$). Flow cytometry results expressed in antibody-binding capacity (ABC) units and percentage of positive cells revealed a significant difference between intolerant CL wearers group and control group ($p<0.0001$). Moreover, impression cytology analysis showed similar values in the tolerant CL wearers and the control group. BUT was significantly shorter in intolerant and tolerant CL wearers subjects than in healthy subjects ($p<0.0001$), whereas there was no significant difference in meibomian fatty acid composition ($p=0.98$) between groups.

Conclusion CL wear is responsible for ocular surface alterations whose patterns are very similar to those reported in dry eye syndrome. However, the yield of tear osmolarity with TearLabTM in assessing ocular surface disorders in CL wearers deserves further investigation.

• T058

Quality of vision in patients with herpetic keratitis

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Purpose Patients with history of recurrent herpetic keratitis very often complain about their vision despite normal visual acuity (VA). The purpose of this study was to assess the optical aberrations and the quality of vision of the affected eye in patients with unilateral recurrent herpetic keratitis with preserved VA, and to compare these results with those of the non-affected eye.

Methods Patients (n=15) with unilateral recurrent herpetic keratitis and an normal VA (Best corrected VA≤0 logMAR) were included in this study. Corneal optical aberrations of both eyes were assessed using dynamic skiascopy with OPD Scan II® (Nidek™). Wavefront analysis was performed during a quiescent period of the herpetic disease. The fellow eye was used as control. A blinded examiner retrospectively analyzed all the datas.

Results The root mean square was significantly increased for high order aberrations ($p=0.004$) in the affected eye and particularly for trefoil and tetrafoil ($p=0.004$ and 0.02, respectively). In addition, The modulation transfer function (area under the curve) and the Strehl's ratio were significantly lower in the affected eyes compared to the non affected eyes ($p=0.02$ and 0.02).

Conclusion Our data show that herpetic keratitis induces wavefront abnormalities which could explain visual discomfort reported by patients with normal VA. A prospective study including more patients should provide further informations on the rate and the clinical significance of these optical aberrations.

• T059

Assessment of the improvement of the quality of vision after Meibopatch© treatment, with OQAS and Hartmann-Shack aberrometry in patients with meibomian gland dysfunction

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Purpose To assess optical quality before and after treatment with Meibopatch© (eyelid-warming device) in patient with mild and severe Meibomian gland dysfunction.

Methods The Meibopatch© was applied for 5 minutes twice a day for one month to 20 eyes of 10 patients who exhibited dry-eye symptoms (OSDI), decreased tear film break-up time (TFBUT) due to altered meibomian gland secretions. We examined TFBUT, meibomian gland secretions, dry-eye symptoms, and assessed optical quality with OQAS (MTF and OSI) and Hartmann-Schack (RMS) aberrometry before, 15 days and 1 month after treatment.

Results We have observed a significant improvement of the BUT, OSDI, Meibomian gland secretion quality, MTF and OSI after treatment.

Conclusion The Meibopatch © eyelids warming device improved dry-eye symptoms, TFBUT and meibomian gland secretion quality. Our study showed also a significant improvement of both MTF and OSI.

• T060

Whole exome sequencing identifies a mutation for a novel form of hereditary benign intraepithelial dyskeratosis

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Purpose To identify a gene for a novel, autosomal dominant form of hereditary benign intraepithelial dyskeratosis (HBID) in a Caucasian French pedigree using deep sequencing technology.

Methods A 7-member family with two affected individuals (6-year-old proband and his mother) with corneal lesions was ascertained. The proband presented with bilateral complete corneal opacification with dyskeratosis, and circumferential corneolimbal neovascularization. Cutaneous features of palmoplantar hyperkeratosis as well as laryngeal dyskeratosis were associated with the ocular phenotype. Histopathology studies of cornea and vocal chord biopsies showed dyskeratotic keratinization. Next generation sequencing with mean coverage of 50x using the Illumina Hi Seq and whole exome capture processing was performed. Sequence reads were aligned, and screened for single nucleotide variant and insertion/deletion calls. In-house pipeline filtering analyses and comparisons with public databases were performed. cDNA expression studies were conducted using systemic and ocular tissues.

Results A novel missense mutation M77T was discovered for the gene NLRP1 which maps to chromosome 17p13.2. This mutation was de novo in the proband's mother, followed segregation in the family, and was not found in 800 control DNA samples. NLRP1 expression was determined in adult cornea.

Conclusion A de novo mutation in NLRP1 segregated with HBID in a non-Native American family. The gene product is implicated in inflammation, autoimmune disorders, and caspase-mediated apoptosis. This is the first identification of a causative gene for a form of autosomal dominant HBID.

• T061

Prospective study of a new matrix therapy agent (RGTA) for the treatment of neurotrophic ulcers

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Purpose To evaluate the efficacy of a new matrix therapy agent (RGTA, Cacicol®), an analogue of heparan sulphates, for management of severe neurotrophic keratopathy.

Methods We carried out a prospective, single-centre, uncontrolled study of 11 eyes in 11 patients, presenting corneal neurotrophic ulcers, despite use of preservative-free artificial tears for 15 days. Mean age was 58 years. All patients had corneal anaesthesia. RGTA treatment was instilled in the morning,as the fist eyedrop, on alternate days. Main outcome measures were for each patient healing of the corneal surface and best corrected visual acuity during and after treatment.

Results Eight patients displayed complete healing of the ulcer, after a mean period of 8.7 weeks (range; 1 to 22 weeks). Mean ulcer area decreased significantly, from 11.12% to 6.37% (p=0.0479) in the first week, to 1.56% (p=0.0054) at one month. Treatment failure was observed in three cases, requiring amniotic membrane transplantation in two patients and penetrating keratoplasty in one patient. At the end of the study, none of the patients displayed a significant improvement in visual acuity. None of the patients reported pain or discomfort during instillation of RGTA eyedrops.

Conclusion This heparin mimetic, which may stimulate extracellular matrix healing, may be a possible, non-invasive, alternative therapy in severe neurotrophic keratopathy. However, randomized studies are necessary.

• T062

Polymeric membranes for corneal epithelium engineering based on chitosan and structural proteins

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Purpose To develop chitosan hydrogel scaffolds for corneal epithelium cultures.

Methods The hydrogel scaffold in the form of a membrane was obtained from chitosan-natural linear polysaccharide derived from chitin from crustacean shells. It is anti-bacterial, biocompatible, biologically inert, stable in the natural environment and safe for human. Chitosan films containing keratin and collagen were cross-linked with genipin, a naturally occurring and nontoxic agent compound found in the gardenia fruit extract. Corneal epithelial cells were seeded on chitosan hydrogel scaffold and were cultivated for 14 days in standard condition using DMEM/F12HAM medium with 3T3 fibroblast co-culture.

Results Mean number of cell layers was 5,2 (3-8). Immunostaining for cytokeratin 3 and 12,protein p63, connexin 43 was performed to confirm origin of the epithelium and presence of low differentiated cells.

Conclusion Genipin crosslinked chitosan hydrogel seems to be a promising material for further clinical tests directed towards the development of implantable corneal epithelial cells

• T063

Ocular granulomatosis associated with brimonidine treatment. Does brimonidine have an effect on human macrophages and dendritic cells in vitro?

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Purpose Conjunctival and episcleral granulomas with uveitis have been reported as a side effect of antiglaucomatous topical use of brimonidine tartrate. We postulated that brimonidine is implicated in this inflammatory process and studied its effects on the antigen presenting cells (APCs) cytokines production.

Methods Conjunctival and episcleral granulomatous lesions were immunohistochemically analyzed for CD3, CD4, CD8, CD1a, CD11c, CD68, and CD123.Macrophages and dendritic cells (DCs) were generated from peripheral blood monocytes of healthy donors and of patients who presented uveitis and granulomatous ocular infiltration induced by brimonidine topical treatment. APCs were respectively exposed to preserved and unpreserved brimonidine tartrate suspension(0.012%),0.005% benzalkonium chloride (BAK) and lipopolysaccharides (LPS). APCs Th1/Th2 cytokines production was measured in supernatants by multiplex flow cytometry.

Results The granulomas consisted predominantly of CD4+ T-cells and APCs, i.e. epithelioid macrophages CD 68+ and myeloid DCs CD11c+.Comparative exposure of APCs to unpreserved or preserved brimonidine tartrate formulations, or BAK alone, induced similar amounts of pro (IL-6 or TNF-α) and anti (IL-10) inflammatory cytokines. Brimonidine tartrate and BAK reduced the LPS-stimulated production of IL-6, TNF-α and IL-10.

Conclusion The histhopathological analysis of the conjunctiva and the episclera identified the main cellular actors involved in the granulomatous inflammatory process. By altering the APCs IL-10 production, brimonidine tartrate will affect induction of tolerance by DCs and allow initiation of immune response leading to granulomas formation.

• T064

Quantification of tear film thickness in healthy subjects using ultrahigh resolution OCT imaging

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Purpose Dry eye syndrome is a highly prevalent disorder that can lead to severe visual impairment. A major challenge in the management of the disease is that signs and symptoms are poorly correlated. As such there is a major need for new innovative techniques to diagnose the disease.

Methods We have realized a high-resolution Fourier domain optical coherence tomography (OCT) system for the measurement of tear film thickness. As a light source we used a Ti:Sapphire laser with a bandwidth of more than 150 nm. A total of 26 healthy subjects were studied. Tear film imaging was started immediately after blinking and continued for 20 seconds thereafter.

Results The tear film was on average 4.8 ± 0.9 µm and could be quantified in all subjects. Over the 20seconds time period no significant reduction in tear film thickness was observed. In some subjects, break-up of the tear film could, however, be observed. The intra-individual variability from frame-to-frame was low and typically below 10%.

Conclusion Our data indicate that the human tear film thickness can be quantified using high-resolution OCT. The technique may have considerable potential in the management of dry eye patients.

• T065

The role of Confocal Microscopy in evaluation and treatment of infectious keratitis

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Purpose To evaluate the role of in vivo confocal microscopy (IVCM) in the diagnosis and treatment of infectious keratitis.

Methods 24 patients with keratitis were examined by slit-lamp biomicroscopy and IVCM (HRT). All IVCM examinations were assessed for inflammatory activity and potential etiology. After obtaining baseline cultures, patients were treated as bacterial (10), viral (5), fungal (8) or Acanthamoeba (1) related keratitis based on clinical findings and IVCM.

Results Primary outcome was clinical improvement, secondary outcome was correlation between IVCM findings and final culture. In 23 cases (9 bacterial, 5 viral, 8 fungal and 1 Acanthamoeba) clnical improvement was observed within 21 days whereas 1 patient worsened. In bacterial suspected group cultures were positive in 7 cases (70%), in viral none of the cultures were positive. Despite typical clinical image and IVCM findings and clinical improvement on adequate medication in fungal and Acanthamoeba suspected groups cultures remained negative.

Conclusion Our study suggests that IVCM along with clinical evaluation can be a useful tool in early diagnosis and guided treatment of patients with infectious keratitis, until definitive culture results are available. However, a prospective clinical study is recommended to further study the role of IVCM in infectious keratitis.

• T066

Corneal cross-linking and Ferrara ° intracorneal rings for the treatment of progressive keratoconus : About 23 cases

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Purpose Keratoconus is a noninflammatory corneal ectasia which results in progressive visual loss due to the appearance of irregular astigmatism and myopia. We present the results obtained in patients treated with cross-linking and intracorneal ring implantation.

Methods This prospective study involved 23 eyes of 17 patients with progressive keratoconus (stage 2 and 3). All patients underwent a combined treatment by cross-linking. and intracorneal rings (Ferrara °) implantation 3 months later.Uncorrected and corrected visual acuity, spherical equivalent, minimum, maximum and mean keratometry were measured preoperatively and 12 months after implantation.

Results At 12 months, improvement in uncorrected and best corrected visual acuity was found, with a gain of 1.6 lines . We found a statistically significant reduction in mean keratometry (1.21 D, P = 0.017) and maximum keratometry with a reduction of 1.969 diopters (P = 0.007). Reduction of minimum keratometry (-2.58 D) and spherical equivalent (-1.711 D) were also statistically significant ($p<0.05$).

Conclusion This new therapeutic approach seems attractive in the management of keratoconus to postpone the time of corneal transplant.

• T067 / 2636

Severe corticoresistant Mooren Ulcers: management with Rituximab and peripheral lamellar graft

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Purpose Mooren's ulcer is a rapidly progressive, painful, ulcerative keratitis which affects the peripheral cornea. We report 6 severe cases of Mooren Ulcers (4 patients) with corticoresistance favourably responding to Rituximab infusions.

Methods Retrospective Case series

Results Despite systemic intensive steroid (4/4 patients), and Cyclophosphamide (2/4 patients) therapy, the 6 cases of Mooren's ulcers progressively spread circumferentially and centrally. Perforation occurred in 4/6 affected eyes, treatment included conjunctival resection and peripheral corneal graft. Rituximab biotherapy was associated with the stabilisation and the healing of the corneal lesions. Systemic steroid therapy was tapered then stopped in all patients within 2-4 months following rituximab therapy.

Conclusion Rituximab, an anti-CD20 monoclonal antibody, has been successfully used off-label for treatment of Severe corticoresistant Mooren's Ulcer.

• T068 / 3877

Surgical approach in corneal perforations and deep ulcers

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Purpose Outcomes of patch grafts in corneal perforations and deep ulcers.

Methods For the study 184 patients (follow-up at least 6 months) were qualified: 57men and 127 women, mean age 61,7,±19,1 years. 198 procedures (112 in corneal perforations and 86 in deep ulcers) were performed. We applied grafts with diameter from 2,5 to 5 mm with oversize of 0,5 – 1 mm. Visual outcomes and corneal surface stability were analysed

Results In 175 eyes we achieved stabile corneal surface, 23 grafts were failed due to graft melting. Among 175 eyes improvement of VA was achieved in 89 eyes, 58 required further procedures of penetrating keratoplasty or cataract surgery. The best visual outcomes were achieved in peripheral ulcers or perforations, central changes usually required further management or were connected with poor prognosis for good vision. 28 eyes due to dry eye, no light localization or retinal detachment (3 eyes) were disqualified to other procedures

Conclusion Patch grafts are useful to restore vision and maintain corneal integrity.

• T069

Postoperative astigmatism induction - femtosecondlaser-assisted penetrating keratoplasty vs penetrating keratoplasty

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Purpose To compare postoperative astigmatism outcomes of femtosecondlaser-assisted 110°-cut PK (FLPK) with conventional PK (PK)in keratoconus patients.

Methods 62 keratoconus patients were divided into 2 groups: FLPK-32 patients, PK-30 patients. Procedures were done with femtosecondlaser-assisted 110°-cut with outer diameter of donor's cornea 8.0 mm, in conventional PK donor's graft diameter was also 8.0 mm. Postoperative astigmatism, BCVA, endothelial cell loss were evaluated.

Results Follow-up was at least 6 months. Postoperative astigmatism was lower in FLPK group (2,1±0,5D versus 4,19±1,7D in PK group, p<0.05). BCVA was respectively 0,59±0,1 and 0,55±0,1, endothelial cell loss 30,4±8,3% and 34,1±7,8% respectively.

Conclusion Femtosecondlaser-assisted surgery results in lover astigmatism level

• T070 / 4648

Assessment of angle and anterior chamber changes after keratoplasty

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Purpose To quantify angle and anterior chamber changes after corneal transplantation using Visante OCT®

Methods In this retrospective study, Visante OCT® examinations were performed in patients, awaiting keratoplasty, preoperatively(J-1) and one month postoperatively(M+1). The anterior chamber depth(ACD), the angle-opening distance at 500µm(AOD), the trabecular-iris space area at 500µm(TISA) and the scleral spur angle(SPA) in the temporal and nasal quadrants were measured. Patients were classified based on their surgery: the surgery was penetrating keratoplasty(PK group), it was descemet's stripping automated endothelial keratoplasty(DSAEK group).Preoperative and postoperative measurements were compared using signed rank test of Wilcoxon.

Results Twenty patients were evaluated: fifteen(75%) in the DSAEK group, five(25%) in the PK. Mean anterior chamber depth width increased from 3,31mm(SD 0,69) to 3,35mm(SD 0,341) after PK(p=1) , and from 3,32mm(SD 0,666) to 3,44mm(SD 0,591) after DSAEK(p=0,719).In the temporal quadrant, after DSAEK, mean anterior chamber angle width increased from 0,281mm(SD 0,126) to 0,334mm(SD 0,100)(p=0,03) in the TISA and after PK ,mean anterior chamber angle width decreased from 0,273mm(SD 0,054)to 0,248mm(SD 0,118) (p=0,812).In the nasal quadrant, after DSAEK, mean anterior chamber angle width increased from 0,253mm(SD 0,089) to 0,285mm(SD 0,085)(p=0,207) in the TISA and after PK, from 0,269mm(SD 0,114)to 0,321mm (SD 0,069) (p=0,437).

Conclusion The angle change significantly in the temporal quadrant after corneal transplantation. Larger study need to be perform to confirm the angle changes.

• T071 / 2236

Identification of label-retaining endothelial cells in adult human corneas: a new clue for the existence of endothelial stem cells

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Purpose The lack of self-renewal capacity of human corneal endothelial cells (EC) in vivo was explained by cell cycle arrest in the G1-phase due to cell contact inhibition, TGF-beta signaling, and stress induced premature senescence. Nevertheless, their residual ability to divide in primary culture suggests the existence of progenitor cells, probably located at the endothelial periphery (Whikehart.MolVis2005; He.StemCells2012). Stem cells are slow-cycling cells characterized by their quiescent state in niches and their ability to retain for a long time markers of S-Phase like BrDU or EdU. Aim: to search for the presence of label-retaining EC in human corneas

Methods Label retaining EC were searched by 5-Ethynyl-2'-Deoxyuridine (Click-it EdU) incorporation during long-term culture: 30 days for organ cultured human corneas (n=10) or 15 days for in vitro primary cultured EC (n=5), both followed by a 30-day culture without EdU. Flat-mouted corneas and EC cultures were observed with an inverted fluorescent microscope

Results Label-retaining EC were observed in the peripheral area of all OC corneas, varying from 1 to 50. Numerous label-retaining EC were also present in all primary cultures, always attached to Descemet membrane fragments

Conclusion The presence of label-retaining EC constitutes a new clue for the existence of corneal endothelial stem cells in human. Their apparent scarcity is consistent with the inability of the human corneal endothelium to repair in vivo, but isolation and expansion of these endothelial stem cells or progenitors could allow development of bioengineered endothelium

• T072

Ex vivo test bench for preclinical assessment of intra corneal new medical devices is needed more than ever

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Purpose Intra corneal medical devices (ICMD) currently invade the refractive surgery market, particularly for presbyopia. Proposed to correct a simple loss of accommodation and not a disease, they should have very long-term efficacy and safety objectives. It becomes evident that pre-clinical tests must be highly efficient in determining the balance of benefits and risks. Despite the European directive 93/42/EEC that defines this balance, several CE marked ICMD, with a quasi-cosmetic action, are implanted in healthy human corneas after, at best, non-representative animal experiments. Aim: to demonstrate the urgent need to develop efficient suitable preclinical assessment methods of these ICMD

Methods Exhaustive review of the literature about animal models and human experimentations used until now for ICMD assessment

Results None of the usual animal models of ICMD assessment seemed acceptable for various reasons: primate for ethical reasons (presbyopia is not a disease), rat, rabbits and cats for biological reasons especially because of their spontaneous endothelial regeneration, or financial reason especially for long-term monitoring after implantation in primate, pig, calf or ovines. One ICMD (CE marked since 2005) was tested in 24 rabbits, without any endothelial viability testing, before being implanted in human corneas. Several ICMD (one CE marked since 2009) were never submitted to pre-clinical assessment and were directly implanted in human cornea

Conclusion New pre-clinical assessment, for example ex vivo test bench with very long term stored and monitored human corneas need to be rapidly developed and validated in order to improve patient safety

• T073

Improving DSAEK donor grafts cut using microkeratome motorization and pressure monitoring

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Purpose in the world, most of the DSAEK donor corneas are prepared using the anterior chamber (AC) and manual microkeratome from Moria. Pressure within the AC, rapidity and regularity of the manual movement directly impact on the thickness and reproducibility of the cut. Our aim was to develop and validate a simple microkeratome motorization and pressure monitoring liable to improve cut quality

Methods we developed a turntable with programmable speed rotation and a sterilizable device to connect a digital pressure gauge (Ahlborn, Germany). After deswelling, organ cultured human corneas were cut with the Moria microkeratome. Cutting speeds from 3 to 10 sec were assessed. AC pressure of 90±5mmHg established by two methods (inflation with a syringe followed by clamping of the pipe, or using a passive high up infusion system without clamping) was continuously monitored and recorded. Central corneal thickness was measured before and after each cut with a US pachymeter (SP1000 Tomey). Endothelial viability was determined with the triple Hoechst/Ethidium/Calcein labeling coupled with image analysis of the whole endothelial surface immediately after the cut (IOVS 2011.52:6018)

Results during the cut, AC pressure slightly increased (+9%) with the passive infusion system whereas it strongly increased (+137%) with the clamping. Impact of pressure maintenance system and cutting speed on lamellar graft thickness and on endothelial viability will be presented

Conclusion automation of the mechanical Moria microkeratome and continuous pressure monitoring may be useful to improve reliability of lamellar grafts preparation and should help standardize the technique

• T074

One year stored corneas: is it possible?

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Purpose To evaluate the endothelial characteristics after very long term organ culture (OC) of human corneas.

Methods Human corneas with initial endothelial cell density (ECD) >2000 cells/mm2 were stored at 31°C in sealed flasks containing 100mL of a commercial medium with 2% foetal calf serum (CorneaMax, Eurobio, France): 6 for 3-6 months (M), 7 for 6-12 M and 5 for more than 12 M. The medium was renewed every 2 M. Transparency was quantified by analysis of modulation and contrast transfer functions. On one half of each cornea, ECD and EC morphology were analysed by image analysis (CellP-Olympus, and SambaCornea-TribVn) after alizarin red staining and flat mounting. On the other half of the cornea, EC differentiation status (NaK ATPase, ZO-1, JAM-1) and proliferative capacity (Ki67, Click-it EdU) were studied by immunostaining in flat mounted corneas (He, MolVis2011;17:3494 and He, StemCells2012 in press). Epithelial cells and stroma were observed by histology on cross sections stained with Hematein/Eosin/Safran and by transmission electron microscopy

Results Corneal transparency and ECD decreased after very long-term OC, but were partially preserved. ECD was about 1200, 800 and 400 cell/mm2 after respectively 3, 6 and 12 months. Morphology and differentiation of residual EC remained nevertheless almost preserved. The epithelium lost its multilayered organization

Conclusion Corneal cells, particularly EC, can survive for a very long time in the rustic environment of OC, suggesting that they are well equipped against environmental stress and cell death. The improvement of storage process and/or storage medium could potentially allow very long term storage without significant attrition of graft quality and therefore provide corneas suitable for graft

• T075 / 3437

Rabbit, rat and pig corneas: main characteristics and storage in organ culture

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Purpose Except for primates, animal models of corneal are far from human. Animal models of corneal storage are virtually non-existent. Aim: to update the main characteristics (especially for endothelial cells (EC)) of the cornea of 3 easily available animals, as well as their ability to be stored in organ culture (OC)

Methods 30 corneas of 6 month-old Large White pig, 20 of 10 week-old California rabbits and 10 of 8 week-old Lewis rats were investigated. Macroscopic data: 1/ horizontal and vertical diameters (digital calliper), 2/transparency (analysis of modulation and contrast transfer functions), 3/ corneal thickness (CT) (ultrasound pachymetry). Microscopic data: 1/ histology on Hematein-Eosin-Safran stained cross sections and ultrastructure, 2/ EC density (ECD) and morphometry, 3/ EC proliferative status (Ki67 and 5-Ethynyl-2'-Deoxyuridine incorporation (Clik-it EdU)), differentiation status (Na+/K+ ATPase, ZO-1, JAM-1), and existence of stem cells (Nestin, ABCG2, Telomerase). Fresh corneas were organ cultured in 2 commercially available media. CT was measured every 2h during 6h, then every 12h. Transparency and EC survival was determined after 2, 3 and 4 days of OC

Results We constituted a complete database of ex vivo corneal characteristics of the 3 species. ECD, polymorphism and polymegathism were higher than in human. CT increased rapidly (up to 3 times) in both OC media, resulting in biconvex tissues with almost complete loss of transparency and significant endothelial folding. EC survival decreased especially in folds

Conclusion Corneas of the 3 animals cannot be stored more than 2 to 3 days in OC media designed for human. Specific media should be developed to obtain reliable models of animal corneal OC

• T076 / 3436

Big bubble technique dissection plane: histological and ultrastructural comparative analysis on both white and clear margin dissected corneas

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Purpose Pneumodissection or 'big-bubble' technique (BBT) is used to separate Descemet's membrane (DM) and stroma in both deep anterior lamellar keratoplasty and Descemet's membrane endothelial keratoplasty. It has been reported that BBT may produce two typer of bubble outlines: clear or white margin. It seems that the components of the posterior lamella obtained with each bubble rims also differ. Our aim is to compare BBT dissection plane using histological and electron microscopy (EM) analysis on eye-bank corneas.

Methods BBT was carried out on donor corneas unsuitable for transplantation for reasons other than corneal disease.Corneoscleral discs were mounted on an artificial anterior chamber and BBT was carried out using a 27G needle. 5 samples which had a bubble with white margin and 5 with clear margin were fixed in formalin and sent for histology followed by EM.

Results Samples in which the edge of the bubble had a white margin showed variable residual stroma adherent to DM. When the edge of the bubble was clear no residual stroma was seen attached to a bare, smooth DM. The anterior lamellae of the cases without residual stroma were also analysed. These showed no evidence of DM elements excluding the unlikely possibility of intra-Descemet's dissection plane. The findings were confirmed by EM in all cases. These showed intact banded DM in all posterior lamellae but only those with a white bubble outline had attached residual stromal collagen.

Conclusion In eye bank corneas the histological elements of the posterior lamella dissected using BBT can be predicted depending on the margin of the bubble obtained. Assumptions that pneumodissection in BBT routinely bares DM need to be revisited.

• T077

Impact of photodynamic inactivation (PDI) on bFGF, HGF, KGF, TGFß1 and VEGF secretion of keratocytes in vitro

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Purpose Photodynamic inactivation (PDI) may eliminate the microorganisms from the infected cornea by damages caused through free oxygen radicals, or even by supporting different stages of activation of keratocytes and inflammatory cell response. The purpose of this study was to determine the impact of PDI on bFGF, HGF, KGF, TGFß1 and VEGF secretion of keratocytes in vitro.

Methods Primary human keratocytes were isolated by digestion in collagenase A (1 mg/ml) from human corneal buttons, and cultured in DMEM/Ham's culture medium supplemented with 10% FCS. Keratocytes underwent illumination (670 nm) for 13 minutes following exposure to 100 nM concentration of photosensitizer chlorin e6 (Ce6) in the culture medium. One day after treatment, bFGF, HGF, KGF, TGFß1 and VEGF release of the cells was determined using enzyme-linked immunosorbent assay (ELISA).

Results One day after PDI, the secretion of bFGF was 1.58, of HGF 1.61, of KGF 0, of TGFß1 2.83 and of VEGF 9.01 pg/µg protein. The secretion of bFGF decreased ($p=0.007$) significantly one day after PDI, compared to controls. In HGF, KGF, TGFß1 and VEGF secretion no significant changes could be detected. Using Ce6 or illumination only, bFGF, HGF, KGF, TGFß1 and VEGF secretion of keratocytes did not change significantly.

Conclusion As a short-term effect, PDI decreases bFGF release of keratocytes in vitro. The altered secretion of these factors may play a role in the activation of keratocytes following PDI.

• T078

Expression of stromelysins 2 and 3 in rabbit corneal epithelium upon UV radiation

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Purpose Stromelysins belong to the group of matrix metalloproteinases (MMPs). These enzymes degrade many extracellular matrix proteins in the basement membrane, including proteoglycans and laminin, but are unable to cleave the fibrillar collagens. Activated stromelysin, via its capacity to catabolize proteoglycans, is likely to help reestablish transparency by returning the proteoglycan ratio to normal during remodeling. Purpose of this study was to investigate the effect of UVA and UVB rays on the expression of stromelysin 2 (MMP-10) and 3 (MMP-11) in the corneal epithelium.

Methods In the first group of rabbits the corneas were irradiated with UVA lamp (365 nm, once a day during 4 days, and a dose per day 1.01 J/cm2). In the second group of rabbits the corneas were irradiated with UVB lamp (312 nm, once a day during 4 days, and a dose per day 1.01 J/cm2). Stromelysin 2 and 3 were examined on cryostat sections immunohistochemically by using sheep polyclonal anti-MMP-10 and anti-MMP-11 antibodies.

Results Our immunohistochemical results showed that UVA rays did not change the expression of both stromelysins studied in the corneal epithelium. In contrast, UVB rays induced the increased expression of stromelysin 2 and 3 in corneal epithelial cells.

Conclusion Even if further studies are necessary, our results point to the suggestions that increased stromelysins after UVB irradiation can participate in remodeling processes during corneal wound healing.

• T079

Corneal biomechanics after corneal cross-linking for keratoconus

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Purpose To assess corneal hysteresis (CH) and corneal resistance factor (CRF) in keratoconic eyes before and after corneal cross-linking (CXL) with riboflavin/ultraviolet-A and to evaluate the correlation between these biomechanics values and central corneal thickness (CCT).

Methods 22 eyes of 12 patients (mean age 25.3±5.9) were evaluated before and 1, 6 and 12 months after CXL. At each visit best corrected visual acuity (BCVA), CCT , CH and CRF using ocular response analyzer-ORA (Reichert Ophthalmic Instruments, Buffalo, NY) were assessed. Data were analyzed using Friedman and Spearman tests.

Results BCVA, expressed in LogMAR, significantly improved 1 year after CXL (0.31±0.05 vs 0.27±0.04, $p<0.05$). Both CH and CFR significantly improved 1 month after surgery (6.26±0.96 mmHg vs 7.93±1.05 mmHg and 4.70±1.2 mmHg vs 6.90±1.13 mmHg, $p<0.0005$ and $p< 0.0001$ respectively), than progressively decreased and at 12th month no difference was found when compared to basal values (6.28±0.48 and 4.74±0.36 respectively). Significantly CCT reduction was found after CXL (472.17±22.59, 459.1±21.68, 465.36±19.59, 465.65±16.47 µm, $p<0.001$). Significantly direct correlations were found between preoperative CCT and both 1 year postoperative CH and CRF ($r=0.85$ and 0.86 respectively, $p<0.001$ for all variables).

Conclusion CH and CRF significantly improved 1 month after CXL but returned to basal values after 1 year, despite a reduced CCT. CXL exerts a transient positive impact on ORA measurements, but further studies are needed to assess why the results is not stable over time. Moreover, preoperative CCT could be a predictive factor for biomechanics values 1 year after CXL.

• T080

Gelatinous drop like dystrophy (GDLD) in a Sudanese patient

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Purpose Gelatinous drop-like corneal dystrophy (GDLD) (OMIM #204870) is an early- onset, autosomal recessive corneal dystrophy, reported globally. It presents in the first decade of life with bilateral, mulberry-like or gelatinous lesions, due to amyloid deposition in the superficial cornea.

Methods A 50 year old Sudanese patient was diagnosed for GDLD. The patient had penetrating keratoplasty in the right eye. The tissue was processed for light and electron microscopy. A DNA sample was screened for 333 sequence variants in 13 corneal dystrophy genes by Asper Ophthalmics Ltd, followed by confirmatory sequencing.

Results The GDLD cornea contained deposits of amyloid fibrils at the sub-epithelial region and in various parts of stroma. The deposits were Congo red positive and showed apple green birefringence under polarized light. The growth of amyloid fibrils was associated with large splits between lamellae, a reduced diameter of collagen fibrils and degeneration of keratocytes. A homozygous c.355T>A mutation in exon 1 of the TACSTD2 (M1S1) gene was identified, not present in dbSNP, predicted to cause a pathogenic amino acid change (p.Cysl19Ser in NCBI entry NP_002344.2).

Conclusion The cornea of this GDLD patient with a novel c.355T>A mutation in exon 1 of TACSTD2 showed degeneration of the corneal epithelium, Bowman's layer, stroma and keratocytes. Deposits of amyloid were found in the sub-epithelium region, Bowman's layer, and stroma. Acknowledgement: Supported by National Plan for Science and Technology, KSU, Riyadh.

• T081

The correlation between central corneal thickness and endothelial cells in healthy patients and in patients with cataract or primary open angle glaucoma

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Purpose To compare the endothelial cells parameters and central corneal thickness (CCT) in four different groups of patients, to find the correlation between the corneal endothelial cell density (ECD) and the cell size, percentage of regular hexagonal cells, CCT and age in all four groups.

Methods All patients (104 eyes) were devided into 4 groups: patients with cataract, with primary open angle glaucoma (POAG), young healthy people and older healthy people. Specular microscopy was performed, endothelial cells parameters were analyzed (ECD, the percentage of regular hexagonal cells), CCT was measured.

Results There were 47 (45%) male, 57 (55%) female. Average age was 59 (± 23.8) years. In the POAG group average CCT was 553 (± 32) µm, ECD 2484 (± 482) cell/mm2, hexagonal cells 60% (± 10%). In the cataract group CCT was 540 (± 64) µm, ECD was 2633 (± 430) cell/mm2, hexagonal cells 60% (± 10%). In young healthy subjects average CCT was 555 (± 43) µm, ECD 2940 (± 345) cell/mm2, hexagonal cells 66% (± 10%), in the older healthy patients group average CCT was 545 (± 39) µm, ECD 2394 (± 416) cell/mm2, hexagonal cells 64% (± 10%).

Conclusion The ECD is higher in thicker corneas. In young subjects ECD was higher than in elderly patients. In males the percentage of regular hexagonal cells was higher than in females. There was no statistically significant difference in CCT and ECD between the gender. We have found very weak statistically significant direct relationship between ECD and CCT. There was no statistically significant difference in CCT and percentage of hexagonal cells in corneal endothelium in all groups.

• T082

Three year visual outcomes and correlation with graft thickness in eyes following descemet stripping automated endothelial keratoplasty (dsaek)

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Purpose To describe 3 year visual outcomes and correlation with graft thickness in eyes following Descemet Stripping Automated Endothelial Keratoplasty (DSAEK).

Methods Retrospective case series of 106 consecutive eyes that underwent DSAEK. We recorded clinical characteristics , best-corrected visual acuity (BCVA) and serial measurements of central graft thickness and total central corneal thickness using anterior segment optical coherence tomography over a 3-year follow-up. Correlation analysis of preoperative and postoperative graft thickness with BCVA at 1, 2 and 3 years were performed.

Results Mean age of recipients was 64.5 years (± 11.8) years. The median preoperative logarithm of the minimal angle of resolution (logMAR) BCVA was 0.71. There was significant improvement in post-operative BCVA at 1-year (median improvement in BCVA 0.41, P<0.001), but no significant improvement in BCVA after 2 year post operatively (P=0.563). Likewise, median central graft thickness significantly decreased post-operatively over the first year (190um vs 166 um, P<0.001), but no significant reduction of graft thickness after 2 years post-operatively (P=0.17). There were no correlations between preoperative graft thickness and BCVA logMAR at 1 year (Spearman=-0.187; p= 0.069), 2 year (Spearman= -0.049; p= 0.650) or at 3 year (Spearman=-0.068; p= 0.614). There were also no significant correlations of logMAR BCVA with post-operative graft thickness by AS-OCT at any time point.

Conclusion Visual acuity significantly improves after DSAEK over the first year postoperatively. However, no correlation can be found between both preoperative and postoperative graft thickness and BCVA over 3 year follow up.

• T083

Distribution of the central corneal thickness in adult residents of Lithuania

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Purpose To determine the distribution of the central corneal thickness by age and gender in Lithuanian population.

Methods Lithuanian residents in the age of 18 and senior, who were registered with the primary health care institutions (PHCI) of different Lithuanian cities and regions participated in the survey. Data including age, gender and measurement of central corneal thickness (CCT) of all tested persons was registered. CCT of each eye was measured by using the ultrasound contact pachymeter. The results were statistically analysed by SPSS 17,0 program.

Results In total 1650 residents of Lithuania were tested, including 688 (41, 7%) men and 962 (58.3%) women. The average age among men was 57.31 ± 0.61, and among women - 53, 63 ±0.74. The average CCT of individuals by age groups equalled to: 18-29 (550,8 ±2,8 µm), 30-39 (557,5±1,9 µm), 40-49 (551,3±1,8 µm), 50-59 (544,0±1,9 µm), 60-69 (544,2±2,1 µm), 70-79 (535,1±1,9 µm), and 80+ (530,1±1,1 µm)(p=0,000, p<0,05). The central corneal thickness of the tested men and women by different age groups (under 40, from 40 to 60 years of age, and over 60) was calculated in percentiles. Corneas of persons under 40 are thicker than of persons in the age between 40 and 60, and corneas of the tested senior persons over 60 are thinner in comparison with other age groups.

Conclusion The average CCT among Lithuanian residents in general is 544,6± 0,7 m, 545,0±0,8 m of men, and 544,4±1,1 m of women. The thickest cornea among Lithuanian residents was measured in individuals under 40. In senior persons it becomes thinner by each decade from 2 to 8µm.The central corneal thickness has no relevance to gender.

• T084

Efficacy of amniotic membrane transplantation (AMT) on corneal surface in bullous keratopathy eyes

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Purpose To determine the effect of cryopreserved amniotic membrane transplantation (AMT) on a patients with bullous keratopathy in pseudophakia eyes.

Methods This retrospective study included 5 eyes (5 patients) with bullous keratopathy in pseudophakia eyes presenting with intractable pain or discomfort (photophobia, tearing and foreign-body sensation). A transplantation of sutureless temporary cryopreserved amniotic membrane was performed on all eyes suffering from bullous keratopathy. The average duration of the follow-up was 14.1 months +/- 1.6 (SD) (range 12 to 16 months).

Results After the AMT was established a significant improvement. We observed complete corneal epithelial healing in all eyes. Sixty percent of the 5 eyes had improvement of the ocular discomfort soon after the first postoperative day. Pain relief was obtained in 80% of patients.

Conclusion The AMT was efficient, safe, and successful method of treatment for intractable pain with chronic bullous keratopathy. Future studies comparing AMT to other methods of treatment of bullous keratopathy would help to better define the role of AMT in ocular surface disease and perhaps further elucidate the mechanisms by which this therapy works.Keywords: Amniotic membrane transplantation, pseudophakia, bullous keratopathy, intractable pain, discomfort

• T085

Keratoconus screening based on data of the high resolution anterior segment OCT Casia 1000

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Purpose Anterior segment OCTs are more and more used in clinical practice for evaluation of corneal disorders. The goal of the study was to derive an automatic screening method for diagnosis of forme fruste and early keratoconus based on data extracted from the OCT CASIA-1000 (Tomey Inc., Japan).

Methods From the Casia-1000 we exported the following raw data: anterior and posterior surface dioptric power data, anterior and posterior surface elevation data, pachymetric data (central, thinnest + X-Y-position). These data were decomposed into Zernike base of radial degree 6 and single indices and combinations (compound index 1 and 2) were tested for specificity and sensitivity (ROC analysis, area under curve). Ninety eyes of 45 patients were included in this study (1 eye each with clinical manifest signs of keratoconus the other without clinical signs of keratoconus each) and 48 eyes of 48 normals as reference.

Results For the single indices the tilt and coma component of 1st and 2nd radial degree showed the best discriminance level between normal and suspects/keratoconus (area up to 0.74/0.86). Compound index 1 considering anterior and posterior surface coma of 1st and 2nd radial degree and pachymetry yielded a discriminance level of 0.821/0.953 and compound index 2 without considering pachymetry showed 0.799/0.935, respectively.

Conclusion The single indexes do not seem do provide better discrimination between normals and suspects/keratoconus compared to the literature data for corneal topography (e.g. Klyce, Maeda, Smolek) or Tomography (Belin&Ambrósio). But in contrast, especially compound index 1 shows an excellent performance. These results have to be validated in a larger case series comparing Casia-1000, TMS and Pentacam.

• T086

Efficacy of gas permeable scleral lenses in refractory severe dry eye syndrome

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Purpose Modern scleral lenses have shown their efficacy in severe ocular surface diseases such as Stevens-Johnson syndrome. Their geometry allows hydration and protection of the cornea and of the limbus. This study determined the efficacy of modern scleral contact lenses in severe eye dry syndrome.

Methods A retrospective single-center study was conducted in patients with severe refractory dry eye syndrome, who were fitted with SPOT™ scleral lenses (LAO, Thonon, France). At inclusion and after 3 months of daily wear, the following parameters were assessed: Ocular Surface Disease Index (OSDI) score, NEI Visual Function Questionnaire-25 composite score (NEI VFQ-25), best-corrected visual acuity, slit lamp examination, number of associated drugs and tolerability.

Results The files of 10 patients (9 women and 1 man) with a mean age of 58.4 years (40-80 years), were reviewed. Dry eye was related to Sjögren syndrome (6 patients), ocular cicatricial pemphigoid (3 patients) and graft versus host disease (1 patient). Lens fitting failed in 1 case. Improvement of quality of life scores (OSDI and NEI NFQ-25) was remarkable in seven patients out of the nine fitted patients. Mean OSDI and NEI VFQ-25 scores improved from 73.5±16.8 to 35±24.2 (p=0.002) and from 49.0±21.0 to 70.5±18.4 (p=0.045), respectively. Best corrected visual acuity improved by 3.2±4.3 Snellen lines. Mean follow-up was 12.6±3.8 months. No serious adverse events attributable to the scleral lenses occurred.

Conclusion Scleral lenses are a promising therapeutic in patients with severe refractory dry eye syndrome. The results can be spectacular with a dramatic improvement of patients' quality of life. Difficulties in manipulation represent the main disadvantage.

• T087

Boston Keratoprosthesis (Type I): visual prognosis and complications

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Purpose to describe the functional results and sight threatening post-operative complications of Type I Boston Keratoprosthesis.

Methods retrospective descriptive study of Boston Keratoprosthesis patients from two European eye centers.

Results A total of 66 eyes were included for analysis. Mean follow-up time was 28 months. Majority of patients had more than 2 penetrating keratoplasties, primary clinical diagnosis are presented. Mean preoperative best corrected visual acuity was 2.05, mean best ever achieved post-operative best corrected visual acuity was 1.16 and final mean postoperative best corrected visual acuity was 1.47 . The most common sight-threatening complications were as follows: retroprosthetic membrane, retinal/choroidal detachment, infectious keratitis, endophthalmitis, peripheral retinal occlusive vasculitis and prosthesis extrusion. Management of complications are discussed.

Conclusion 95 % retention rate with overall improvement in visual acuity demonstrates that Type I Boston Keratoprosthesis is a good alternative to cases of multiple graft failure due to various primary clinical diagnoses. Complications must be detected early on and managed accordingly to ensure success of the procedure.

• T088

Ukraine implantation results of collagen-based bioengineered substitutes of donor corneal allografts in rabbits

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Purpose Ukraine Implantation Results of Collagen-Based Bioengineered Substitutes of Donor Corneal Allografts in Rabbits

Methods Bioengineered corneal substitutes (BCS) were fabricated by cross-linking porcine type I collagen with carbodiimide and N-hydroxysuccinimide as described by Liu et al., 2006. BCS refractive indices were measured using an Abbe refractometer. The mechanical properties were evaluated by their ability to tolerate interrupted sutures placed during deep lamellar keratoplasty performed on isolated rabbit eye. BCS were then implanted into one cornea each of 8 rabbits and followed-up for 12 months.

Results Our BCS had refractive indices of 1.24-1.3 (human cornea 1.37-1.38). They tolerated placement of 12 interrupted sutures well. New technique of BCS "sutureless" implantation was elaborated. When implanted into rabbit corneas, the BCS remained stably integrated and optically clear during 12 month follow-up. Grade 1.5 haze (scale 0-4) was observed in 2/8 eyes during the 1st postoperative week. In one eye, the haze resolved. In the 2nd eye, the grade 1 haze remained. Light microscopy confirmed good integrity of the BCS and absence of inflammation.

Conclusion Our current data suggest that the BCS fabricated in Ukraine by cross-linking collagen is a good alternative to human donor corneas, if medical grade porcine collagen is used. The new "sutureless" implantation technique may decrease BCS damage and accelerate its epithelialisation

• T089

Laser subepithelial keratomileusis (LASEK) versus femtosecond sub-Bowman keratomileusis (FSBK) to correct myopic astigmatism

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Purpose to compare the safety and efficacy of LASEK versus FSBK to correct myopic astigmatism

Methods a retrospective pilot study of 846 consecutive eyes (427 FSBK and 419 LASEK + Mitomycin C). Inclusion criteria was astigmatism ≥ -1.50 D. Uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), sphere and cilynder were examinated preoperatively and at 3 months after surgery. Enhancement rates were also evaluated.

Results both techniques showed similar safety and efficacy indexes (efficacy in LASEK group was 0.9 ± 0.2 and in FSBK group was 0.88 ± 0.2, p= 0.3; safety in LASEK group was 1.0 ± 0.1 and in FSBK group was 1.02 ± 0.1, p= 0.8.Three months after surgery, astigmatism was similar in both groups: -0.52 ± 0.6 in LASEK group and -0.54 ± 0.6 in FSBK group (p= 0.6). The sphere was higher in LASEK group than in FSBK group(0.24 ± 0.7 D, LASEK group; 0.12 ± 0.5 D, FSBK group) p= 0.005. BCVA and UCVA were slightly better in FSBK group (BCVA in FSBK group: 1.02 ± 0.1. BCVA in LASEK group: 0.9 ± 0.2; p= 0.0001. UCVA in FSBK group was 0.9 ± 0.2. UCVA in LASEK group was 0.86 ± 0.2; p=0.03. Enhancement rates were higher in FSBK group, 97 eyes (22.62%), than in LASEK group, 65 eyes (15.51%), p= 0.01.

Conclusion LASEK and FSBK show similar safety and efficacy when used to correct myopic astigmatism ≥ -1.50 D. Postoperative BSCVA was slightly higher after FSBK, probably because it was also higher preoperatively, but the safety and efficacy indexes showed no significant differences between groups. Nevertheless there is a higher retreatment rate after FSBK . This might be due to the more comfortable post-operative recovery of this technique.

• T090

Causes of intracorneal ring segments explantation

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Purpose To illustrate the causes of intracorneal ring segments (ICRS) explantation in patients with ectatic corneal disease.

Methods We performed a retrospective of 92 eyes in which ICRS were implanted between 2007 and 2009. Two types of ICRS were implanted during this period: in 42 eyes (45.7%) INTACS ring segments were implanted, and in 50 eyes (54.3%) KERARING implants were used. In all cases a femtosecond laser was used to create the corneal channels where the implant was inserted. We analyzed the incidence of explantation of both types of ICRS and the causes

Results An explantation of the ICRS was needed in 10 cases (10.9%): 8 INTACS and 2 KERARINGS. In all cases the cause of the explantation was the segment extrusion. Interestingly, we found that the ICRS extrusion was related to the contact of the extremity of the segment with the vertical corneal incision in all cases.

Conclusion Based on our results, the main reason of ICRS explantation is the segment extrusion. The contact between the extremity of the segment and the corneal incision area seem to facilitate the segment extrusion. KERARINGS seem to be much better tolerated than INTACS.

• T091

Ability of keratoconus match index and keratoconus match probability in the differenciation of forme fruste keratoconus and healthy corneas

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Purpose To compare Keratoconus Match Index (KMI) and Keratoconus Match Probability (KMP) of the Ocular Response Analyser (ORA) between forme fruste keratoconus and normal corneas and estimate the sensitivity and the specificity of KMI in discriminating forme fruste keratoconus from healthy corneas.

Methods The study population of this retrospective comparative case series was divided into 2 groups: 8 forme fruste keratoconic eyes (FFKCN) and 36 healthy eyes. Every patient underwent a corneal topography, and a biomechanical evaluation with the Ocular Response Analyser. KMI and KMP were compared between the 2 groups. KMI and KMP results from an individual eye are compared to average values from 5 clinically classified populations in a normative database: Normal, Suspect KCN, Mild KCN, Moderate KCN, and Severe KCN. The software determines which population the measurement result best fits.

Results The mean KMI 0.67 for FFKCN and 0.928 for control eyes. There was a statistically significant difference between the 2 groups (P = 0.05). For a threshold of 0,8, KMI had a sensitivity of 63% with a specificity of 72%. For a threshold of 10,7mmHg, the CH had a sensitivity of 75% and a specificity of 66,7%. According to the KMP, corneas of the control group match best with the normal group in 64% of the cases. According to the KMP, corneas of the FFKCN group match best with the normal group in 34% of the cases, with the suspect group in 35% of the cases, with the mild, moderate or severe group in 31% of the cases.

Conclusion Sensitivity and specificity of the KMI is not greater than those of CH and CRF. The classification proposed by the KMP is not accurate and does not allows the screening of FFKCN.

• T092

Influence of intraocular pressure on the photorefractive keratectomy for myopia correction. a numerical analysis

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Purpose To analyze the effect of the intraocular pressure (IOP) on the refractive correction achieved by the Photorefractive Keratectomy (PRK) surgery using a biomechanical model of the human eye.

Methods A three-dimensional finite element model of the human eye was used to simulate the PRK surgery. A hyperelastic constitutive behavior was assumed for all the tissues of the model. Simulations of PRK surgery for five levels of myopia (2, 4, 6, 8 and 10 diopters) at three physiological healthy values of IOP (10, 15 and 21 mmHg) were performed and the post-surgical diopters were estimated.

Results For low and medium values of IOP (10 and 15 mmHg), the computed results were close to those used by clinicians and defined without considering the IOP, while undercorrection was predicted for the highest value of IOP (21 mmHg) in the 8 and 10 diopter correction cases.

Conclusion From these results, we suggest that IOP should be considered in the determination of the depth of ablation, in addition to other factors.

• T093

Combined treatments for keratoconus: a numerical approach

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Purpose To compare the effects of two combined treatments, corneal collagen crosslinking (CXL) and insertion of intrastromal ring segments (ISRS), for the treatment of keratoconus, using a biomechanical model of the keratoconic cornea

Methods Numerical simulations of both treatments are performed using a biomechanical model of a human keratoconic cornea. Then, simulations of the combination of the two treatments are performed: first CXL and afterwards, ISRS insertion; firs ISCRS insertion and afterwards, CXL.

Results After the numerical simulation, the following effects are observed: the CXL causes a stiffening of the corneal tissue; the insertion of ISRS induces a flattening of the central area of the cornea causing a hyperopic effect and a decrease of the anterior chamber depth (ACD), as our clinical outcomes confirm. The insertion of ISRS achieve higher effect when the CXL treatment is previously performed.

Conclusion The combination of the two treatments, collagen CXL and ISRS insertion, achieve a regularization of the shape of the cornea. According to the outcomes of numerical simulation, collagen CXL must be performed before the insertion of the ISRS in order to achieve better results.

• T094

Usefulness of the optical coherence tomography Spectralis® anterior segment module in the diagnosis and monitoring of corneal pathology

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Purpose The Spectralis® Anterior Segment Module that offers Spectral-Domain Optical Coherence Tomography (SD-OCT) Heidelberg Engineering, is a sign of the revolution who are suffering OCT teams nowadays. The aim of our study is to analyze the usefulness of optical coherence tomography of anterior segment in the diagnosis and monitoring of different corneal diseases.

Methods Some ophthalmologists explored their patients from department of cornea and ocular superfie under slit lamp and later with the OCT Anterior Segment Module. The Spectralis SD-OCT offers high quality images of cornea and anterior segment, without any contact and comfort for the patient. Because it is installed on a slit lamp is very intuitive and easy to use, so no special training is required.

Results We present several cases where we used optical coherence tomography of anterior segment in the diagnosis of different corneal diseases: degeneration, infections, dystrophies... and also in following various surgical procedures such as intrastromal corneal rings, keratoplasty, lamellar corneal graft and amniotic membrane coatings.

Conclusion We believe it is a useful diagnostic tool in every department of cornea, refractive surgery and ocular surface diseases to document, make measurements and studies of evolution and, especially, to evaluate the surgical results.

• T095

Adapting a dermatological multi-laser fluorescent confocal microscope for ophthalmology applications

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Purpose To adapt for ophthalmology the only multi-laser fluorescent confocal microscope available on the market and initially developed for dermatology (Vivascope 1500, MAVIG, GmbH). The arm that maintains the microscope in contact with the skin was too rigid and imprecise, and the disposable plastic window placed at the interface between the tissue and the microscope objective was too large. Both were not convenient for high quality corneal and ocular adnexa imaging

Methods We designed specific stands to create a take-down interface between the confocal microscope, his dermatological arm support and an ophthalmology examination table comprising a 5 degrees of freedom stand (Zeiss, Germany). A male guide rail was machined in polyoxymethylene and permanently fixed on the confocal microscope to avoid repetition of assembly and disassembly. Two females guide rails machined in aluminium 7075 were fixed on the dermatological arm support on the one hand and on an ophthalmological stand on the other hand. Rails were blocked with simple screws. We also designed a new adapter to receive disposable caps already available for corneal confocal microscopy. A lateral camera allowed live visualization of the objective/eye contact

Results These new interfaces allowed easy and solid fastening of the confocal microscope on each arms of the two specialties providing optimal conditions for clinical examination. The new ophthalmology arm allowed a precise positioning of the contact objective on the patient eye

Conclusion Thanks to theses adaptations, the first multilaser fluorescent confocal microscope is now usable by ophthalmologists, and opens a completely innovative field of exploration

• T096

Revisiting corneal storage using a bioreactor: proof of concept

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Purpose Cold storage (CS) or organ culture (OC) for corneal storage, have not been dramatically improved since the 70'. Basically, they consist of immersion of the cornea in a sealed vial or viewing chamber filled with storage medium containing macromolecules for permanent (CS) or sequential (OC) deswelling. None respects the corneal physiology (higher pressure to the endothelial side associated with a retrocorneal fluid circulation), resulting more or less rapidly in endothelial cell (EC) death, stromal swelling and Descemet folding (for OC) that accentuate EC death. In the past, several artificial chambers were built or patented, mainly for toxicology experiments and never with a view to improve graft storage. We developed a corneal bioreactor (BR) that reconstitutes both pressure and continuous slow medium renewal in order to improve corneal storage

Methods The BR (patented) comprised sterile endothelial and epithelial chambers closed with transparent windows to allow easy controls (transparency, thickness, detection of interfaces, and EC count) from both sides. Adjustable fluid flow and pressure (15-30 mmHg) in the endothelial side were maintained by a disposable infusion system connected to a microsolenoid valve controlled by a pressure sensor and a microcontroller. Furthermore, the height of the epithelial window could be adjusted to aplanate the cornea for femtosecond laser cut

Results The BR maintained a stable gradient of pressure during at least 5 weeks with a controlled flow. A few hours after insertion of the cornea in the BR, transparency improved and thickness and folding decreased and were maintained without deswelling molecules

Conclusion The BR could improve corneal storage in eye banks

• T097

Sub Bowman's keratomileusis for the correction of anisometropia after penetrating and lamellar corneal surgery

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Purpose To report the use of Sub Bowman's Keratomileusis (SBK) in the treatment of anisometropia subsequent to Perforating Keratoplasty (PK) and Deep Anterior Lamellar Keratoplasty(DALK).

Methods Three patients with compound myopic and hyperopic astigmatism after PK and DALK were submitted to SBK.Treatments were conducted under topical anaesthesia. Femtosecond laser (IntraLase FS., AMO Inc, CA, USA) was used to create a superiorly hinged anterior lamellar flap at 100 microns in a 7.75/8 mm zone. The flap was lifted and a customized wavefront ablation was performed in two cases with the Star S4IR (CustomVue, AMO Inc., CA, USA), and in one case with Technolas z100 (Zyoptix Custom Wavefront, Bausch & Lomb Inc, NY, USA). The flap was then replaced, and the interface was irrigated. Minimum residual pachimetry value was estimated not inferior to 400µm.

Results Postoperative controls at 1 and 3 months showed a reduction of anisometropia up to 70% with residualspherical equivalent (SE) not superior to 2.50 diopters

Conclusion Sub Bowman's Keratomileusis has been shown to be safe and effective to reduce anisometropia in patients who have previously undergone to PK and DALK.

• T098

Corneal hystomorphology and myopic regression in patients after LASIK in the long follow-up period

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Purpose To estimate the ultrastructure of various layers of a cornea, refraction result and quality of visual functions at the patients after operation LASIK, in the long follow-up period.

Methods The investigated group included 22 patients (44 eyes). Middle age was 31 year (from 23 to 39). The postoperative period - from 4 to 10 years. Patients before operation had myopic refraction of various degrees. Standard methods of research including pachymetry with "Visante OCT", keratotopography with "Pentacam", "Atlas", confocal microscopy with Confoscan 4 (Nidec Tech., Japan).

Results Visual acuity after operation without correction was 1,0 and more only in half of cases (22 eyes). In the presence of initial high myopia, the thickness of a cornea at patients in 10 years after LASIK has returned to preoperative values. The thickness of a corneal flap practically in all cases made the value planned before operation. Epithelial layer has increased no more than by 30 microns.

Conclusion In the remote postoperative period substantial growth of a thickness of a cornea in the central part is observed. Changes occur at all stoma levels. The increase in a thickness of a cornea first of all is connected with morphology of the interface between a flap and a corneal bed.

• T099

Corneal ectasia after excimer surgery and the mandelbrot B. fractal theory in ophthalmology

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Purpose To investigate corneal ectasia after LASIK surgery by using the Mandelbrot B. fractal theory in ophthalmology.

Methods We reviewed our consecutive 55012 cases of excimer-laser surgery including LASIK (48910 eyes) and PRK (6102 eyes). We used MEL-60, MEL-70 and MEL-80 excimer laser ("Carl Zeiss Meditec") and microkeratomes LSK-Evolution 1, 2 and 3 ("Moria") for LASIK. Follow-up period was up to 14 years. The age of all patients was from 18 to 74 years. Some of them had hyperopia with sphere-equivalence (SE) up to 6,5D, and the others had myopia with SE from –1,0D to –18,0D.

Results There was NO corneal ectasia in the PRK and the hyperopic LASIK groups. 38 eyes (0,08%) had corneal ectasia after myopic LASIK (46294 eyes). There were 8 eyes with previous radial keratotomy, 8 eyes with subclinical keratoconus and 22 eyes with normal cornea (0,048% of all myopic LASIK) among the eyes . Pre-op parameters of these eyes were the followings: central K - 44,37±1,09D, CCT - 530,4±34,4 microns, SE – 5,90±3,36D. Fractal theory allows to explain post-op corneal ectasia phenomenon.

Conclusion There are NO optical methods to predict corneal ectasia after LASIK surgery. But the risk factors of this complication were the followings: steep cornea (more than 44,0 D), corneal scars after previous corneal surgery (e.g. anterior radial keratotomy etc.), corneal topography irregularity and probably very thin residual corneal thickness. Myopic LASIK surgery can provoke post-op corneal ectasia development in the long follow-up period. We described post-op myopic LASIK cornea as a "odd" ("curious") attractor according to the Mandelbrot B. fractal theory.

• T100

Graft thickness and visual acuity after automated endothelial keratoplasty

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Purpose Endothelial keratoplasty has become the standard of care for endothelial disease. Descemet Membrane Endothelial Keratoplasty (DMEK) gives superior visual results but poses several surgical challenges, compared to Descemet Stripping Automated Endothelial Keratoplasty (DSAEK). Graft thickness was advanced as a reason for this difference. Ultrathin-DSAEK, with a double microkeratome pass has been proposed to maintain the advantages of both DSAEK and DMEK. The purpose of this study was to evaluate the possible correlation between visual acuity (VA) and central graft thickness in DSAEK.

Methods A preliminary retrospective study was conducted on 42 patients who underwent DSAEK: 26 operated on with a single microkeratome pass with a 350 microns (µm) head, and 16 with a double pass using a 200 µm head. Pre- and post-operative VA, and post-operative central corneal graft thickness measured by OCT and Scheimpflug imaging were collected with at least 6 months follow-up.

Results The overall mean of graft thickness was 127.25 ± 40µm. The overall mean VA was 0.16logMAR. 38% of patients had at least 0.1logMAR VA. Graft thickness was 136.8 ± 43.4µm with a single microkeratome pass compared to 111 ± 30µm with a double pass ($p<0.05$). Considering the overall cohort, we had a correlation between graft thickness and VA ($p<0.05$), but also between the pre and post-operative VA ($p<0.05$). We had no correlation between graft thickness and VA in the double pass subgroup. No difference was found between the single and the double pass subgroups for VA.

Conclusion There is no clear correlation between graft thickness and visual acuity. Other factors may come into account such as scarring of the interface, or the stage of endothelial failure.Preoperative VA could be a prognosis factor.

• T101

Functional and biomechanical changes in keratoconic corneas after implantation of intracorneal ring segments 5 and 6mm in diameter

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Purpose To determinate biomechanical and functional changes in human keratoconic corneas after triangular section ring implantation in two designs.

Methods Retrospective study of biomechanical properties of 46 patients (60 eyes) with keratoconus undergoing surgery Keraring® intracorneal ring segments divided into two groups according to 5 or 6 mm of diameter. Surgical technique to made the channel was with IntraLase femtosecond laser. UCVA and BSCVA were measured and biomechanical factors provided by the device ORA before surgery and postoperatively one month, 3 months and 6 months.

Results After surgery, we obtained a significant increase ($p<0.05$) of the biomechanical parameters (CH and CRF) mean (0.87±2.59)mmHg for CH and (-0.015±2.06)mmHg for CRF.This improvement is not homogeneous during the postoperative follow-up in two groups in diameter. We found increased of CH top with rings of 6mm. The variations found in the CRF, are not significant at the descriptive level with any of the designs ($p>0.05$).At baseline- 6 months, the improvement in BSCVA (LogMAR) is 0.13 in 5mm diameter respect to 0.07 in 6mm in diameter.Among the changes in CH and BSCVA (LogMAR), there is a significant inverse correlation with 6mm rings at baseline-1 month period ($r=-0.442$) and 1 month- 3 month period 0.007 ($r=-0.511$). No significant correlation was detected between CRF and BSCVA.

Conclusion Intracorneal rings improve corneal biomechanics. The CH undergoes improvement in postoperative follow up with any of the ring designs, while the CRF is not affected significantly with any of the types. 5mm rings further improve best corrected visual acuity. This improvement is not related to changes in the biomechanical properties.

• T102

Interest of endosaver® using on endothelial graft

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Purpose To describe characteristics of a delivery device of endothelial graft using in endothelial keratoplasty procedure (Descemet Stripping Endothelial Keraplasty, DSAEK) and to report clinical results.

Methods 20 patients are including in our prospective non-randomised study. Patients were benefited of a DSAEK by an experienced surgeon. The dissection of the endothelial graft were realised after removal epithelium and cutting a cornea anterior hat of 350µm by a microkeratom (Moria France). Grafts are inserted by the Endosaver® (Ocular System Inc USA) by a 4 mm incision and applied by a buffering of a air bubble in the anterior segment after a peripheral iridotomy. Authors reports experiences with this device and the density of endothelial cells after 6 month.

Results Any failure of the graft was reported. The diminution of endothelial cells was correlated to the thickness of the graft and situated between 26% and 31% depending on pachymetry (50-120 µm and 120-150µm).49% of patients had more than 20/40 at 6 month.

Conclusion our study showed the interest of Endosaver® on endothelial grafts to reduce the incision and the diminution of endothelial cells on DSAEK.

• T103

The current practice and researches of orthokeratology in China

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Purpose Orthokeratology is account for 200,000 wearers in current China. In past ten years, orthorkeratology experienced "up-down-up" fortune. This article presents the evidence about what leads to the twists and turns of orthokeratology in China. And it sketches the update researches of orthokeratology in clinical safety and its on myopia retardation.

Methods Based on survey of twelve orthokeratology clinics and consulting work for government, it illustrated both the healthy part and illness part of fitting, wearing and related vision care service administration in the past tens years. Through summary of the research work, the clinical safety of orthokeratology and its on myopia retardation research both laboratories based or clinic based were presented.

Results Orthokeratology was first released in China in late 1990s. It quickly spread over China. But very soon, reports of high rate of complications began appeared, and the safety of Orthokeratology was questioned by both ophthalmologists and the public, and dropped to dead margin. After ten years researches and cautious monitoring from safety administration, the ortho-K practice is backing up. The data from ten ortho-K clinics proved its safety and efficacy. The author showed their clinical and laboratories study around corneal contour and relative peripheral refractive status in myopia retardation.

Conclusion The Orthokeratology not only brings backs to life but in very fast growing trend in current China. The key for its success in clinical safety and efficacy comes from the qualified fitters and scientific monitoring. Although evidence showed myopia retardation with ortho-k among young myopes, whether its mechanism comes from relative peripheral refractive hyperopic changes is still under debate.

• T104

Cis-urocanic acid eye drops are safe and well tolerated in healthy adults – results from a randomised phase 1 clinical study

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Purpose Cis-urocanic acid (cis-UCA) is an endogenous small molecule of the skin. Preclinical data suggest that topical cis-UCA could be used as an anti-inflammatory treatment in ophthalmology. We investigated the safety, tolerability and pharmacokinetics (PK) of cis-UCA in healthy adults in a randomised, double-blind and placebo-controlled phase 1 study.

Methods The 37 subjects in 3 groups received either 0.5% or 2.5% cis-UCA eye drops, or placebo. In part I, the eye drops were administered on one eye 3x in one day. In part II, the same subjects received the same eye drops on both eyes 3x a day for 14 days. Clinical evaluations included complete physical examination and safety laboratory tests, physical examination of the eyes, and ocular comfort rating by 5 parameters.

Results Both cis-UCA eye drops were safe and well tolerated throughout the study. None of the ocular safety parameters differed between cis-UCA and placebo. Of the ocular comfort rating, only burning of the eyes was significantly higher with cis-UCA than with placebo; however, this reaction was mild, transient and infrequent in all cases. PK analysis showed that 2.5% cis-UCA eye drops may be absorbed after repeated ocular dosing, as 7/12 subjects in this group had low cis-UCA levels (< 10 µg/ml) in the urine. However, plasma cis-UCA levels were negligible.

Conclusion The observed good local and systemic safety and tolerability of cis-UCA eye drops warrants further clinical studies in patients with inflammatory ocular diseases.

Commercial interest

• T105
Monochromatic aberrations in children and youth in different cycloplegic conditions

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Purpose The aim of the study was to quantify low and high order Zernike aberrations in children and youths as well as to investigate influence of fogging and cycloplegia on the refraction and aberrations measurement.

Methods KR-1W Topcon aberrometer was used to measure aberrations in refractometer and aberrometer mode. Children were examined three times. First examination in whole group was performed after fogging stimulus used once - in first of three continuous measurements, second after fogging stimulus performed for each measurement and third after pharmacological cycloplegia with 1% Tropicamid. Second and third measurements were performed in selected group of children.Totally 556 schoolchildren and 74 young sportsmen aged from 6-to-18 years were investigated. Average age was 13.87, SD 2.29 in large group and 11.33 years, SD 2.7 in smaller group.

Results We found significant differences in spherical refraction measured after pharmacological cycloplegia compared to that after fogging. Refraction after cycloplegia was more hyperopic. There were higher differences in high hyperopic children. There were no differences between fogging and cycloplegic measurements in myopes higher then -2.00 D.. Aberrometry has given more myopic results then refractometry. Cylinder values were almost the same. Keratometer readings were the same in all measurements conditions. We found similar levels of high order aberrations in myopic, emmetropic and hyperopic children. There was no noticeable symmetry in high order aberrations between right and left eye.

Conclusion Both methods of low order aberrations measurement are similar. Optical parameters of cornea do not depend on the cycloplegic status. Low order Zernike aberrations strictly correspond to the refraction error.

• T106
Clinical and therapeutic aspects of vernal kerato conjunctivitis in Algeria

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Purpose To evaluate clinical aspects, specific sensitization, epidemiological and therapeutic characteristics of vernal keratoconjunctivitis (VKC)

Methods Retospective clinical case series included 300 VKC patients,between may 2008 and may 2012, data included patients and family histories,results of ocular surface exams, allergic tests and response to corticosteroids assocated to mast stablizers (NAAGA) treatment.

Results The majority of VKC patients were male(67%), 36% of limbal forms, 56% of corneal complications,15 keratoconus associated, a skin prick tests and specific serum IgE was positive in 58% and 64% of patients respectively. therapeutic results were good in 73% cases, satisfactory with frequent relapses treated with corticosteroids in 21% cases, 5% of steroid dependent and 1% of several unresponsive forms

Conclusion Vernal keratoconjunctivitis,very common in our climate remains a severe form by they corneal complications and diffficult managment.

• T107
Comparison of decellularization methods for human corneal lenticules

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Purpose Human or animal thin corneal lenticules (L) have been used as biological carrier to experimentally reconstitute tissue-engineered grafts. Decellularization of the stroma proved to reduce immune rejection after allografts in animals. Aim: to assess different decellularization methods of human corneal L.

Methods Stromal L were prepared with a Moria microkeratome on human organ cultured corneas mounted on an artificial anterior chamber. After desepithelialization, an anterior L was obtained with a 90 µm head and a posterior one with a 110 µm head. Four physical methods (sonification at 37 kHz for 45 minutes (min), 3 freeze/thaw cycles in liquid nitrogen, heating at 50°C for 60 min, and hypoxia) and four chemical methods (75% ethanol for 2x10 min, 0,1% sodium Dodecyl sulphate for 24 hours (h), 4M urea for 4h, and 29% NaCl for 24h) were tested. Efficiency and safety were assessed by determining: 1/mortality of the keratocytes using the Hoechst-Ethidium-Calcein triple labelling (Pipparelli, IOVS2011;52:6018), 2/alteration of the stroma using transparency measurement (analysis of modulation and contrast transfer functions), and collagen fibres analysis by transmitted electron microscopy (TEM), and 3/elimination of the cell debris using a staining of cell cytoplasm (Dioc 6) and TEM.

Results 75% ethanol and hypoxia triggered complete keratocytes mortality with minimal alterations of the stroma. None of the methods eliminated dead cells debris. Combination with the sonification helped fragmenting cells

Conclusion Two simple and rapid methods allow complete decellularization of human corneal L. The ability of these Lt to promote endothelial cells adhesion and proliferation is under investigation.

• T108
We don't graft as many endothelial cells as we think (Part 1): what early post-operative endothelial cell counts tell us

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Purpose The decrease of endothelial cells density (ECD) after penetrating keratoplasty (PK), is calculated form ECD given by eye banks (ebECD) and post-operative specular counts. To better understand the difference between both counts, usually considered caused by EC mortality, we have introduced a new concept of viable ECD (vECD) experimentally determined with a triple staining of viable and dead EC. We demonstrated that vECD just before graft was lower than the ebECD by 12+/-9% (IOVS 2011.52:6018). The aim of this prospective study was to measure post PK ECD as early as possible in order to compare it with vECD and deduce the true post op EC mortality

Methods Standard ebECD were determined 48h before graft with a validated analyzer (Samba cornea) on a minimum of 300 EC. Postoperative central ECD were determined by a non-contact specular microscope (Topcon SP2000P) with manual determination of contours of the maximum of EC. Thirty-four PK done by the same surgeon (>1000 PK) were analysed at D5, D15, and M1. Non-parametric tests for paired data were used

Results All PK were uneventful. ebECD (n=40) was 2585(482) cells/mm² (mean(SD)). Postoperative ECD at D5 (n=22), D15 (n=29), and M1 (n=33) were respectively 1850(386), 1655(285) and 1650 (408) cells/mm² and were lower than ebECD ($P<0,05$). They corresponded to apparent EC loss of respectively 28%, 36% and 36% compared to ebECD

Conclusion ECD at D5 is dramatically lower than ebECD but subsequent decrease seems low. Results are consistent with the vECD that we previously noticed and suggest that EC mortality triggered by surgery and perioperative events may only minimally contribute to the decrease of ECD

• T109

We don't graft as many endothelial cells as we think (part 2): comparison of cell loss after autograft and organ cultured allograft in the same patient

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Purpose Reasons for endothelial cell density (ECD) decrease after corneal grafts remain unclear. We recently demonstrated that eye bank ECD (ebECD) overestimates the pool of viable EC really grafted to patients (Pipparelli.IOVS2011;52:6018) because standard ebECD cannot take account of acellular areas or area covered by dying EC. Autograft is a very rare situation where ECD can be easily determined by specular microscopy just before graft and almost all grafted EC are living. Aim: to compare EC decrease after simultaneous autograft and organ cultured (OC) allograft in the same patient

Methods A 71 year-old woman presented with pseudophakic corneal edema in left eye and amblyopic right eye with a normal cornea. She underwent two penetrating keratoplasties (PK): autograft of the left eye and allograft of the right eye with an OC cornea. Follow-up at day (D)1, 5, 15, 20 and 30 comprised slit lamp examination and non-contact central specular microscopy (Topcon SP2000P)

Results Both grafts were uneventful. For the allograft, ebECD 48h before graft was 2787 cells/mm^2 and postop ECD decreased of 39%, 40%, 40% and 43% at D5, 15, 20 and 30. For the autograft, pregraft specular ECD was 2017 cells/mm^2 and postop ECD were 1941, 1934, 1924, 1909 and 1900 cells/mm^2 respectively at D1, 5, 15, 20 and 30

Conclusion This exceptional case confirms a dramatic discrepancy between ebECD and very early postop ECD, likely to be explained mainly by an overestimation of the true EC pool of viable cells by standard eye banks count, rather than by overmortality due to peri-operative events, since almost no early cell loss is observed during autograft

• T110

Cornea innervation: from physiologic to drug-induced recovery

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Purpose To review the role of corneal innervation both in normal conditions and pathology and provide update on new therapeutic strategies considering cornea nerve fibers as a pharmacological target.

Methods A review of the available literature has been performed and insights on new drugs summarized.

Results The cornea is the most densely innervated tissue in the human body and the integrity of the nerve fibers is crucial in maintaining its refractive and protective power. A lot of ocular and systemic diseases - as well as ocular surgery - can adversely affect corneal nerves and consequently impair their function, with vision loss as a possible consequence. However, current standard treatment regimens do not consider cornea nerve fiber impairment as a therapeutic target, but the current strategy is to face symptoms. In the recent years, the number of published papers concerning this new therapeutic approach has been growing.

Conclusion This report reviews cornea innervation impairment of any kind and the main attributes of therapeutic agents which could be useful in improving corneal nerve recovery stimulating nerve regeneration.

Commercial interest

• T111

Influence of culture time on maintenance of limbal epithelial progenitors in the explant culture system

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Purpose To assess the influence of culture time on maintenance of limbal epithelial progenitors in the explant culture system.

Methods Limbal epithelial cells were cultured from 2-mm2 human limbal explants in cholera toxin-free medium with no feeders for 9-21 days. Expression of differentiation and progenitor markers was assessed by immunochemestry and RT-PCR. The clonal growth ability of cultured epithelial cells at each time of culture and with murine 3T3 feeders or human corneal stromal feeders was evaluated by determining colony forming efficiency (CFE).

Results The average number of cultured cells obtained after 7, 14, and 21 days was, respectively, 500, 60489, and 195949. Expression of broad spectrum cytokeratins, CK3, CK19, vimentin, p63, and ABCG-2 was observed at all culture time points by immunocytochemistry and RT-PCR. Epithelial colonies were observed at 9, 11, 14 and 18 of culture but not at 21 days, both with murine 3T3 feeders and human corneal stromal feeders. Higher number of colonies was obtained when limbal epithelial cells were cultured with murine 3T3 feeders than with human corneal stromal feeders. The highest number of colonies was obtained at 14 days of culture with murine 3T3 feeders. The average cell Feret diameter (µm)/circularity for clones obtained from 11-, 14-, and 18-day primary cultures were, respectively, 38.4/0.76, 34.2/0.80, and 45.7/0.72 ($p<0.0001$). The average percentage of p63+ small cells was, respectively 2.6%, 4.7%, and 1.3% in clones obtained from 11-, 14-, and 18-day primary cultures ($p=0.002$).

Conclusion In the explant culture system, limbal epithelial progenitors are better preserved after 2 versus 3 weeks of culture.

• T112

Targeting host kinases for the treatment of herpes keratitis

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Purpose Herpes keratitis (HK) is a common cause of blindness in the developed world. A large number of HK cases are refractory to antiviral agents and ultimately result in permanent corneal damage. The purpose of this study is to identify new therapeutic targets against HSV and to assess their antiviral potential in tissue culture experiments, as well as in more sophisticated models of HK. Specifically, we focused on the involvement of ataxia telangiectasia mutated (ATM) and its downstream target Chk2 in facilitating productive HSV infection in corneal epithelium.

Methods We used human corneal epithelial cell lines – hTCEpi and HCE – as in vitro models of corneal HSV infection, and also developed an ex vivo model of acute corneal epithelial infection, where explanted human and rabbit corneoscleral buttons were infected and maintained in organ culture. We are currently utilizing an in vivo mouse model of ocular herpes to further validate our findings. Small molecule inhibitors of ATM (KU-55933, wortmannin, caffeine) and Chk2 (Chk2 inhibitor II), as well as RNAi against ATM and Chk2, were used to inhibit these two kinases. We used plaque assays and qPCR to assess the infectious particle production, genome replication, and transcriptional activity of HSV in corneal epithelium.

Results Small molecule or RNAi-mediated inhibition of ATM or Chk2 greatly suppressed the replication and transcription of the viral genome, as well as the infectious particle production. This was observed in the tissue culture models and, importantly, in organotypically explanted human and rabbit corneas. Results of the animal studies will also be presented.

Conclusion This study identifies two host kinases – ATM and Chk2 – as potential novel therapeutic targets against herpes keratitis.

• T113

Biocompatible of human acellular cornea matrix

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Purpose The aim of this study was to construct a rabbit anterior cornea replacement with an acellular human cornea matrix (AHCM) as a scaffold

Methods Cornea was taken from the enucleated eye from patient with melanoma of choroidea. Before the decellularization process, human corneas were washed 3 times in sterile phosphate buffered saline. To remove the hereditary materials, the cornea discs were immersed in a Triton X 100 solution and Ammonium Hydroxide with a solvent/ tissue mass ratio of 20:1 (vol./wt.). AHCMs were transplanted into the right corneas of 9 Chinchilla rabbits. The superficial corneas of the right eye of the rabbits were excised with a 6-mm punch. AHCM lamellas (150 mm, 6 mm diameter) were made using a microkeratome. AHCM were transplanted and fixed with 10-0 nylon into rabbit corneas. All rabbits received topical levofloxacin eye. The non-operated, contralateral eye was used as a positive control. Follow-up clinical examinations included slit-lamp examination to assess corneal optical clarity, neo-vascularization and degradation of grafts. After post-operative 8 weeks, rabbits were euthanized respectively and the corneal specimens were examined by H&E staining

Results After lamellar implantation of the AHCM, all animals survived without infections or other complications during the follow-up period. The transplanted AHCM could be recognized in the rabbit corneas at 8 weeks after operation, with no neo-vascularization and inflammation or any other rejection signs in or around the transplanted disks, as demonstrated by H&E staining. H&E staining showed that the implants were well integrated within the host corneas, with cells infiltrating the transplanted disks.

Conclusion Acellular human cornea matrix has a good biocompatible properties after lamellar keratoplasty

• T114

Epithelial thickness and structure in patients with congenital aniridia after COMET procedure

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Purpose To evaluate epithelial structure after COMET procedure in patients with congenital aniridia.

Methods 17 patients (20 eyes) with congenital aniridia underwent COMET procedure. Subjects were 13 women and 4 men, in 4 patients surgery was bilateral. Indication was aniridia related Limbal Stem Cell Deficiency (LSCD).Mean follow-up was 13 months (6 to 26). Analyzed data included OCT assisted epithelial thickness measurement and structure assessment by confocal microscopy

Results Mean epithelial thickness performed in 5 different points was 52,2±14,3 µm in successful cases, 88,1±42,4 µm in failed cases with recurrent conjunctival ingrowth

Conclusion Analysis of epithelial structure and thickness could be useful in postoperative care in patients with congenital aniridia after COMET procedure

• T115

Treatment of ligneous conjunctivits with subconjunctival fresh frozen plasma (ffp): about three severe cases

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Purpose Ligneous conjunctivitis is a rare type of chronic membranous conjunctivitis. It is inherited as an autosomal recessive disorder, with low plasminogen levels reported in both homozygous and heterozygous individuals

Methods we describe the clinical features and response to subconjunctival FRESH FROZEN PLASMA (FFP) in three patients with severe ligneous conjunctivitis with a mean follow-up of 12 months, among 15 patients followed in our department for the past 10 years.

Results All our cases had bilateral ocular involvement except. They were all treated with subconjunctival injection of FFP after resection of the membranes. Topical heparin and rimexolone application was continued 1 month after surgery. As the case 2 presented a corneal perforation during the course of the disease, he was also treated with multiple inlay amniotic membrane graft.

Conclusion FFP shortens the treatment period, reduces the probability of mid-term recurrences and is a good alternative to a long-term topical treatment with Heparin and steroid.

• T116

Cultivating oral mucosa epithelial transplantation (COMET) followed by penetrating keratoplasty (PK) in ocular surface reconstruction

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Purpose Efficacy of COMET and subsequent PK in patients with limbal insufficiency combined with stromal corneal haze after corneal burns

Methods 15 patients (16 eyes)who underwent corneal burns with vascular conjuctival pannus and stromal involvement underwent autologous cultivated oral mucosa epithelial transplantation. Cellular material was obtained from buccal mucosa, tripsinized, and settled on the previously prepared culture dishes. Cultures was carried on denuded amniotic membrane in presence of inactivated with mitomycin C 3T3 fibroblasts. At least 12 month after epithelium restoration patients underwent PK. Corneal surface stability and visual acuity were evaluated.

Results 6 month after last step of the surgery 68,7% of eyes had transparent cornea without reccurent revascularization, 31,2 % of eyes developed vascular pannus again with vascular ingrowth on the transplanted cornea (in 2 cases visual axis was involved), in 62,5 % of eyes visual acuity increased from mean 0,01 to 0,3.

Conclusion COMET combined with PK effectively improves ocular surface stability and quality of vision.

• T117

Comparative study of three exophthalmometers and computed tomographic biometry

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Purpose Accurate and reproducible exophthalmometry is recognized as having a great importance in the clinical setting. However many variations are described among the different commercially available exophthalmometers.

Methods In this prospective study, 3 exophthalmometers (Luedde's, 2 mirrors Hertel's, and 1 prism Mourits' exophthalmometers) were compared to tomodensitometric biometry by 2 observers, for 60 patients. Data recorded were the external prebicanthal segment (EPBCS), the inter-orbital distance (IOD) and the axial length of the globe (AL). Intraobservers and interobservers reproducibility were evaluated, using intraclass correlation coefficient (ICC) and Bland and Altman method.

Results Concerning agreement between EPBCS measurements and CT-scan biometry, ICC for Luedde's instrument was 0.59 and 0.64 respectively for the 2 observers, for Hertel's exophthalmometer: 0.63 and 0.72 and for Mourits'exophthalmometer: 0.94 and 0.87. Intraobserver and interobservers reproduciblities were high, particularly for Mourits' exophthalmometer, concerning EPBCS and IOD measurements. Moreover, Bland and Altman charts showed that Luedde's instrument induced underestimation of the readings, Hertel's exophthalmometer overestimated small values and underestimated high values, and Mourits' exophthalmometer slightly underestimated the readings compared to CT-scan biometry.

Conclusion We showed a greater accuracy with 1 prism Mourits' exophthalmometer, whereas Luedde's instrument has a moderate agreement with CT-scan biometry and Hertel's exophthalmometer intermediate results. Intra- and interobservers reliability were good. International selection of reliable exophthalmometers should be defined for clinical practice and studies.

• T118

Use of wide field digital retinal imaging (RET CAM II) in paediatric retinal diseases

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Purpose To report our experience using the RetCam II to evaluate retinal pathology and morphology in children who did not cooperate for standard examination and to follow them by monitoring changes and development of the diseases

Methods We reviewed charts of 107 consecutive uncooperative children with fundus abnormalities that were photographed using the RetCam as a routine part of patient care.Since 2004 detailed diagnostic examination with use of RetCam II was performed in children with ocular tumors, vitreo-retinal dysplasia, hereditary retinal dystrophies, ROP, congenital abnormalities of optic disc, retinal haemorrhages in shaking injury, neuroretinitis. All eyes were dilated with 1% tropicamide. 0.4% oxibuprocaine drops were used prior image acquisition. A blefarostat was used to keep the eye lids wide apart during the examination.The children were directed to lie supine, under sedation.

Results The authors report cases series: 7 cases of Ret Cam imaging (2 siblings with gyrate atrophy of the choroid and retina after reduction of plasma ornithine with diet; 1 Pedler's coloboma with overlay of the peripapillary retina,2 cases with retinal haemorrhages in shaking injury in the acute phase and until the bleeding reabsorption,1 infant with early onset autosomal dominant hereditary rod-cone dystrophy , 1 optic nerve glioma extending to the retina, 1 case with chorioretinal dysplasia in systemic disease.

Conclusion In this study analysis of RetCam digital images allowed to evaluate objectively, to determine exactly the areas of the disease, and to estimate changes and worsening.In our cases series the wide-field digital ophthalmic camera provided a new tool for the evaluation and precise documentation in paediatric retinal disease.

• T119

Lyme borreiosis with ocular manifestations during childhood period

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Purpose Lyme borreliosis (LB) is the most common human tick-borne disease in the Northern hemisphere. The various ophthalmologic manifestations of Lyme borreliosis (LB) during childhood period are discussed in this study.

Methods Six children with LB-associated ocular manifestations were treated between 2000 and 2010 in the ophthalmology department of Strasbourg University Hospital (an endemic area). Medical history, ocular and systemic clinical findings, determinations of antibodies related to Borrelia as well as exclusion of other causes were diagnosis criteria.

Results Two uveitis, Two abducens palsies, one optical neuropathy and one orbital myositis associated with LB were diagnosed. Systemic findings, such as arthritis, rash, or erythema migrans were mentioned in all cases. Two children also complained about severe knee arthritis. Determination of antibodies was positive in all patients. All patients were treated by antibiotics adjusted to individual circumstances and some of them (two uveitis and one optic neuropathy) also had anti-inflammatory treatment. Resolution of ocular signs, without any relapse, was observed in all patients within two to twelve weeks.

Conclusion For any unexplained ocular symptom, even for children, LB should be taken into account especially in endemic areas. Such patients should undergo serological testing. If the clinical presentation is suggestive of LB, a course of oral antibiotics should be used. All in all, permanent defects are extremely rare during childhood period, even following long-term manifestation at an early age.

• T120

Vincristine-induced unilateral ptosis

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Purpose To report the ocurrence of an unilateral ptosis in a 2-year-old girl treated by vincristine for a vaginal rhabdomyosarcoma.

Methods Our young patient developed a vaginal rhabdomyosarcoma and had been treated by chemotherapy (Ifosfamide-Vincristine-Actinomycine) when an unilateral ptosis occurred 7 days after the fifth vincristine dose (1.5 mg/m2). At that time, cumulative vincristine dose was 4.50 mg. Neither oculomotor dysfunction nor anisocoria were present. Neurological and systemic examinations were otherwise unremarkable. Laboratory testing and thoracic-cervical-cranial scan were normal. Other causes of ptosis were excluded. Despite vincristine dose was reduced by a third, ptosis slightly increased after the 2 subsequent injections but decreased between cures. Ptosis disappeared at day 78 and no recurrence was noticed after the treatment continuation at the same dose.

Results Neurotoxicity is a well-known complication of vincaalkaloids. Bilateral ptosis is relatively common but reported cases of vincristine-induced unilateral ptosis are infrequent. In our young patient, occurrence of the ptosis during treatment, increase during new infusions of vincristine and exclusion of other aetiologies are forceful arguments to consider the role of vincristine in this side effect. The use of pyridoxine or pyridostigmine were suggested to treat vincristine-induced cranial neuropathies but to date, the benefit remains unproved. Adaptation of treatment regimen must be done. In our case dose reduction allowed disappearance of the ptosis.

Conclusion Even if unilateral ptosis is rare among vincristine-induced neurological complications, ophthalmologists must be aware of this diagnosis.

• T121

Bilateral non-arteritic ischemic optic neuropathy due to excessive use of transdermal estrogen by transgender patient

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Purpose Nonarteritic anterior ischemic optic neuropathy (NAION) is a common, visually disabling disease. It is usually due to a hypotensive perfusion insufficiency leading to infarction of the optic nerve. Only very rarely, NAION has a thromboembolic etiology. A transgender patient with a sequential bilateral NAION related to excessive use of transdermal estrogen is described.

Methods A 44 year-old male to female transgender patient developed acute painless visual loss in the right eye (RE) followed by the left eye (LE) 2 months later. She underwent a full ophthalmic exam and an extensive etiological work-up.

Results Visual acuity (VA) dropped to perception of light in the RE and, 2 months later, to 3/10 in the left eye. Fundoscopy showed a swollen disc in both eyes in the acute phase, which evolved into pallor later. CT-brain revealed old ischemic areas unrelated to VA loss. A diagnosis of bilateral sequential NAION was made. Predisposing risk factors, though both well controlled, were diabetes and arterial hypertension. Thrombophilia screening and cardiac work-up were negative. When estrogen levels of 60 times the normal value were measured, the patient admitted to overdose with transdermal estrogen to enhance her female characteristics. Such high estrogen levels are very thrombogenic. It is highly likely that it caused the cerebrovascular accidents and also triggered the bilateral sequential NAION.

Conclusion NAION only rarely has a thromboembolic etiology. However, careful history taking is warranted to exclude modifiable risk factors in the poorly treatable NAION to prevent affection of the second eye and/or the central nervous system.

• T122

Jugular venous thrombosis secondary to idiopathic myelofibrosis: a rare cause of bilateral papilledema

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Purpose Idiopathic myelofibrosis is a chronic myeloproliferative disorder in which the bone marrow is progressively substituted by connective fibrous tissue.This is due to an increase of the fibroblast growth factor, produced by the megakaryocytes. Among its signs and symptoms, we can find extramedullary hematopoiesis with hepatosplenomegally, anemia, weight loss, bone pain, infections or coagulopathy.Bone marrow biopsy shows different degrees of fibrosis and nests of megakaryocytes.Patients receive mainly symptomatic treatment and,sometimes,chemotherapy.

Methods We present the case of a 65-year-old woman diagnosed with idiopathic myelofibrosis.She complained of bilateral loss of vision after suffering a right internal jugular vein thrombosis.Her best corrected visual acuity was 20/40 in the right eye and 20/200 in the left eye.She developed a severe bilateral papilledema and macular edema, as well as retinal hemorrhages and peripapillary cotton wool spots.

Results The patient was treated with systemic steroids and anti-platelet therapy, showing great improvement, with a final visual acuity of 20/25 in the right eye and 20/30 in the left eye.The macular edema was recovered, along with the visual fields.The papilledema was significantly reduced after the treatment.She is now being treated with heparin and her visual acuity remains stable.

Conclusion Jugular thrombosis is an uncommon cause of papilledema. Idiopathic myelofibrosis often causes platelet disorders which may lead either to thrombosis or easy bleeding.Ophthalmologists should be aware of internal jugular vein thrombosis as a possible cause of bilateral papilledema in patients suffering from diseases that can cause blood coagulation abnormalities.

• T123

Optical coherence tomography: a window into the brain of schizophrenic patients

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Purpose Our study aims to assess peripapillary retinal nerve fiber layer (RNFL) thickness, macular thickness and volume, and optic nerve head (ONH) measurements in patients affected by schizophrenia

Methods 30 schizophrenic patients (mean age 44.5 +/- 10.9 years) were enrolled. They were compared with 30 age-matched controls. In all subjects, peripapillary RNFL thickness, ONH measurements, macular thickness and volume were measured by optical coherence tomography (OCT). The eye studied was the right eye

Results Schizophrenic patients showed an statistically significant reduction of the overall peripapillary RNFL thickness (95.1+/- 13.4 µm) compared with those values observed in control eyes (103.3+/-9.0 µm) (p=0.008, Student t test). We also observed reduced peripapillary RNFL thickness in superior quadrant in schizophrenic patients (114.7+/-18.0 µm) when compared with controls (127.3+/- 14.4 µm) (p=0.004, Student t test). Cup/disk area ratio (cases: 0.45 +/- 0.31; controls: 0.26 +/- 0.27 p=0.002, Mann-Whitney U test), cup/disk horizontal ratio (cases: 0.67 +/- 0.22; controls: 0.48 +/- 0.23 p=0.003, Student t test), cup/disk vertical ratio (cases: 0.60 +/- 0.24; controls: 0.44 +/- 0.23 p=0.003, Mann-Whitney U test) and cup area (cases: 1.32 +/- 1.09; controls: 0.73 +/- 0.82 p=0.001, Mann-Whitney U test) were statistically increased in schizophrenic patients.

Conclusion Schizophrenia patients showed a reduction in peripapillary RNFL thickness evaluated by OCT and an increase in some measurements of ONH. These findings suggest that as previously observed in neurodegenerative disorders, neuronal degeneration could be present in the

• T124

Contribution of MRI in cases of isolated mydriasis: description of neurovascular conflicts.

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Purpose To study the contribution of MRI (sequence FIESTA) in the analysis of isolated and persistant mydriasis.

Methods Prospective single center study (November 2010 to March 2012) including patients with unilateral mydriasis (pure intrinsic Cranial Nerve III palsy) without life-threatening pathology. Complete ophthalmological, systemic and neurological examinations were performed. All patients with any symptoms of extrinsic CN III palsy (diplopia, ptosis or ophthalmoplegia), with tonic pupil (pilocarpine diluted test positive), use of toxic or drug taking, sign of focus at neurological examination have been excluded. Our patients underwent cerebral MRI: images acquisition were performed on a GE 3T MRI, protocol included FIESTA and 3D TOF sequences.

Results Five patients were included (20 to 41 years), 2 women. They presented with a single non reactive, isolated and persistent mydriasis with a pilocarpine diluted-test negative. For all, an obvious relationship between CN III and its adjacent Posterior Comunicating Artery (PCA) was demonstrated through FIESTA sequences with MPR images (3 real neurovascular conflicts in Root Entry Zone, 1 before cavernous sinus, 1 compression between PCA and dorsum selae). No saccular aneuvrysm or tumors were found.

Conclusion Thanks to MRI, we explained the symptoms for all the five patients, because of anatomical features, including neurovascular conflicts. If it has been described previously for facial and trigeminal nerves, no neurovascular conflict between CN III and PCA has been demonstrated before. The contribution of MRI in the study of anisocoria seems to be considered, and could help for diagnostic of a pathology tagged idiopathic.

• T125

Relationship between retinal nerve fiber layer thickness and the duration and severity of parkinson disease

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Purpose To determine in patients with Parkinson disease (PD) the correlation between peripapillary retinal nerve fiber layer (RNFL) thickness and macular thickness and volume, with the duration and severity of the neurological disorder.

Methods 102 eyes corresponding to patients affected by PD were compared with 97 eyes of age-matched controls. In all individuals peripapillary RNFL thickness, macular thickness and volume were measured by optical coherence tomography (OCT).

Results We found statistically significant differences in all parameters of peripapillary RNFL thickness between Parkinson patients and controls. In all quadrants RNFL thickness was significantly lower in PD patients ($p = 0.017$ in temporal RNFL and $p < 0.001$ in the other quadrants). Nevertheless, macular thickness and volume did not reveal any statistically significant reduction in PD patients when compared with controls ($p>0.05$). Furthermore, we found a significant inverse correlation between disease duration (years) and disease severity measured by Unified Parkinson's Disease Rating Scale and overall peripapillary RNFL thickness ($p=0.002$ and $p <0.001$, respectively), indicating that the more years of illness or greater UPDRS score, the lower peripapillary RNFL thickness.

Conclusion PD patients showed a statistically significant reduction in peripapillary RNFL thickness evaluated by OCT in terms of evolution and severity of PD. That means that the further evolution of PD, the lower average peripapillary RNFL thickness. Our results suggest that RNFL thickness measured by OCT might be used as a biomarker of PD severity progression or even as an indicator of good response to long-term treatment.

• T126

Three-dimensional geometries representing the retinal nerve fiber layer in multiple sclerosis, optic neuritis, and healthy eyes

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Purpose To represent and interpret the three-dimensional geometry and distribution of the axonal damage to the retinal nerve fiber layer (RNFL) in patients with multiple sclerosis (MS) compared with healthy subjects. To analyze alterations in RNFL morphology in eyes of MS patients with or without previous episodes of optic neuritis (ON).

Methods MS patients (n=122) and age-matched healthy subjects (n=108) were enrolled in this observational cross-sectional study. The Spectralis OCT system (Heidelberg Engineering) was used to determine the circumpapillary RNFL thickness in both eyes of each participant. The 768 RNFL thickness measurements provided by the Spectralis OCT were used to evaluate thickness measurements in MS patients with or without antecedent ON and to design a three-dimensional reconstruction of the RNFL thickness representing the mechanobiologic tissue response to neurodegeneration caused by MS and ON episodes.

Results RNFL thickness was decreased in MS patients, and higher in the MS group with previous ON. Statistical analysis and three-dimensional RNFL reconstruction revealed greater damage to the ganglionar cells in the superonasal RNFL area in MS eyes (101.77 µm in MS vs 125.47 µm in healthy subjects) and in the inferotemporal RNFL (119.05 µm in healthy eyes vs. 149.26 previous-ON MS eyes) in MS eyes with previous ON.

Conclusion The three-dimensional representation of RNFL thickness based on measurements provided by the Spectralis OCT allows physicians to better observe damage in the temporal areas, especially in patients with previous ON.

• T127

Retina thickness measurements provide a sensitive and specific diagnostic tool in Parkinson's disease

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Purpose To test the diagnostic ability of optical coherence tomography (OCT) for the detection of Parkinson's disease (PD). Retinal thickness depends in part on the retinal pigment epithelium, one of the principal tissues producing levodopa.

Methods PD patients (n=111) and healthy subjects (n=200) were enrolled. The Axonal application of the Spectralis OCT was used to obtain the circumpapillary RNFL thickness and retinal measurements in each participant. Two linear discriminant functions (LDF) were developed, one using RNFL parameters and another LDF using retinal thickness. A validating set (120 eyes from healthy individuals and 66 eyes from PD patients) was used to test the performance of both LDFs in an independent population. Receiver operating characteristic (ROC) curves were plotted and compared between both LDFs and with the standard parameters provided by OCT. Sensitivity and specificity were used to evaluate diagnostic performance.

Results The Retinal LDF combines only retinal parameters and provided the best performance: 31.1 + 0.02 x Temporal Outer - 0.2 x Superior Outer + 0.16 x Nasal Outer - 0.2 x Inferior Outer - 0.06 x Superior Inner + 0.05 x Foveal thickness. The largest areas under ROC curve were 0.902 for Retinal LDF and 0.845 for RNFL LDF. At 95% fixed specificity, the Retinal LDF yielded the highest sensitivity values.

Conclusion Measurements of retinal thickness obtained with Spectralis OCT had a very good ability to differentiate between healthy and PD individuals. Based on the area under the ROC curve, the Retinal LDF performed better than any single parameter or diagnostic test used for PD.

• T128

Axonal loss in multiple sclerosis: a morphological and functional analysis of retinal nerve fibbers

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Purpose The main purpose of this work was to study the retinal nerve fibber layer (RNFL) atrophy by optic coherence tomography in different subtypes of multiple sclerosis (MS) patients and to compare these results with electrophysiological examinations.

Methods Fifty eight patients were included, 43 suffered from a relapsing-remitting MS and 15 suffered from a progressive MS. We studied all eyes according 2 groups, MS eyes with a history of acute optic neuritis (MS-ON eyes, n=39) and MS eyes without history of optic neuritis (MS-non ON eyes, n=76). Electrophysiological exams were performed in all MS patients: (1) visual letter acuity (Snellen Charts), (2) visual evoked potentials, (3) pattern electroretinogram and (4) perimetry (Metrovision France). Retinal nerve fibber thickness were measured by Optical coherence tomography (OCT; fast RNFL thickness protocol).

Results The rate of MS-ON eyes and MS non-ON eyes were not different between the 2 subtypes of MS ($p>0.05$, Fisher test). Progressive MS demonstrated a mean value decrease of RNFL thickness particularly in inferior quadrant compared to relapsing-remitting MS (respectively, 92.9 um and 98.7 um for mean value, $p= 0,04$; 117.7 um and 127.4 um for inferior RNFL thickness, $p=0,05$). An increased P100 latency and decreased P50 and N95 amplitude were noted in MS-non ON eyes compared to MS-ON eyes (respectively $p=0,013$; $p=0,026$ and $p=0,003$).

Conclusion This study seemed to illustrate a potential axonal loss in MS patients through these structural and functional differences between progressive MS and relapsing-remitting MS optic nerves. The N95 amplitude of non-affected eyes measurement appeared to be a new index to diagnose early progressive MS.

• T129
Extraocular blood flow in multiple sclerosis (MS) patients

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Purpose Buckground: Multiple sclerosis is autoimmune disease which is often associated with vascular dysregulation syndrome (VDS), mediated by endothelin-1 (ET-1). Vascular dysregulation syndrome can lead to diminished blood flow in eyeball arteries. The aim of this study is evaluation of retrobulbar hemodynamics in multiple sclerosis (MS) patients.

Methods Material of this study consisted of 76 eyes of 38 MS patients (8 males and 30 females, mean age 39,38 years, range : 22-56 years, SD: 10.02) which were recruited from Neurology and Epileptology Department. The healthy controls consisted of 52 eyes of 26 patients (3 males and 23 females, mean age: 36.26 years, range: 19-55 years, SD: 10.88). No patients in the active stage of the disesses. The peak systolic (PSV) and-diastolic (EDV) blood flow velocities, indicators of peripheral vascular resistance such as Gosling Index (PI) and Pourcelot Index (RI) of the ophthalmic artery (OA), lateral short posterior ciliary arteries (LSPCA) and central retinal artery (CRA) were measured in each eye, using color Doppler imaging (CDI). In order to compare examined eyes between two groups we used analyze of variance (Unianowa). Additionaly, we analyzed the obtained values of blood flow in patients who received immunomodulation therapy and in patients who passed neuritis optica in history.

Results Statistically significant disturbances in the examined eyeball arteries were found in CRA and OA. The affected parameters were: diminished PSV velocity in CRA and OA; EDV in CRA (border of statistical significance); PI, RI in OA and increased EDV in OA.

Conclusion This study suggests that in MS eyes may exists of retrobulbar hemodynamics impairment.

• T130
Retinal circulation and intracranial pressure in idiopathic intracranial hypertension

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Purpose Idiopathic Intracranial Hypertension (IIH) is associated with moderate to severe papilledema (PE). Cases of central retinal vein oclusion identified in IIH suggest that PE can obstruct venous flow. The aim of this study was to evaluate the effect of intracranial hypertension on venous circulation and to determine the correlation between vascular caliber and intracranial pressure level.

Methods In this retrospective multicenter study, we included 8 patients with newly diagnosed IIH. Fundus photography were performed before and after lumbar puncture at various time points. The images were aligned with i2k pro© software. Arterio-veinous ratio (AVR) was measured by a dedicated software.

Results Immediately following lumbar puncture these was decrease of the diameter of the central retinal vein. In 4 patients, an associated decrease in venous tortuosity was observed. For all patients, AVR increased immediately after lumbar puncture. This was due to the combined effect of a decreased venous diameters and an increase of the arterial caliber.

Conclusion Venous diameters may be an interesting indicator of PE evolution. Fundus photography are a non-invasive, convenient method to investigate and monitor IIH which may be useful in a variety of setting, including neurosurgery units. A prospective study is necessary to confirm these results.

• T131
A new technique of noninvasive evaluation of the intracranial pressure with retinal vessel analyzer

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Purpose One of the clinical signs observed at the funduscopic examination of the eye of the intracranial hypertension patients, apart from the papillary edema is the reduction, even the disappearance of the spontaneous pulsatility of the retinal vessels..A new device, Retinal Vessel Analyzer (Imedos) now makes it possible to measure negligible variations of the vascular diameter (arteriolar and venular) . We thus measured the retinal vascular pulsatility found among patients having a benign intracranial hypertension (BIH) which we compared with a control population.

Methods We included 6 patients presenting a benign intracranial hypertension. For each participant, an examination with RVA was carried out right before the lumbar puncture (J0) then at 1 month (M1) and 3 months intervals (3M). We compared these results with a control population (n=76).

Results The mean venous pulsatility found at the 76 controls was 5,07m ± 1,57. Our 6 patients presenting a BIH, had a venous pulsatility that was lower than 0,5m at D0 ($p < 0,05$), lower than 0,8m± 0,52 at M1 ($p < 0,05$) and between 0,5 and 3m at m3. All the 6 patients had an abnormal measurement of the intracranial pressure . It was not found a correlation between the value of pulsatility and the value of the intracranial pressure

Conclusion The variation of the vascular diameter, measured by RVA, is an indirect reflection of the vascular transmural pressure.Our results show that even in the case of a moderate BIH it exist an early, identifiable repercussion at the level of the retinal vascular network quantifiable by RVA.This reduction in the venous pulsatility can be explained by an increase in the intravascular pressure and/or by a parietal remodeling, especially at the later stage.

• T132
Persistence of treatment effect of idebenone in Leber's Hereditary Optic Neuropathy

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Purpose To establish the long term benefit of oral idebenone 900mg/day in the treatment of Leber's Hereditary Optic Neuropathy (LHON).

Methods Patients who participated in a 24-week, multi-centre (3 sites), double-masked, randomized, placebo controlled trial (RHODOS) were re-assessed at a single visit by means of Visual Acuity (VA) using ETDRS charts.

Results Eighty-five patients were enrolled in the RHODOS study: 55 treated with idebenone (900mg/day) and 30 with placebo. At the end of the 24 week treatment period, the VA for patients randomized to placebo deteriorated. In contrast, in patients treated with 900mg/day idebenone, VA was preserved. In addition, in severely affected patients with off-chart vision at Baseline, only idebenone treated patients improved sufficiently to read at least 1 full line on the ETDRS chart (Klopstock et al., 2011). VA was repeated at a follow-up visit conducted 2.5 years (median) after treatment discontinuation. The difference in VA between placebo and idebenone treated patients was maintained. Specifically, in patients who during RHODOS received idebenone and who on average were protected from vision loss, VA did not deteriorate upon discontinuation of treatment.

Conclusion These findings support the original conclusion that in selected patients with LHON, idebenone has significant therapeutic potential in preventing further vision loss and facilitating vision recovery.

Commercial interest

• T133

An interesting case of Mohr-Tranebjærg Syndrome

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Purpose To describe an interesting rare case of Mohr-Tranebjærg Syndrome, a X-liked recessive syndrome also known as Deafness-dystonia syndrome.Setting: The severity of the symptoms may vary, but they progress usually to severe deafness and dystonia and sometimes are accompanied by cortical deterioration of vision and mental deterioration.

Methods A 24-year-old man with Mohr-Tranebjærg Syndrome underwent electroretinogram (ERG) and visual evoked potentials (VEPs).

Results Fundus examination showed apparently normal retina with pallor of the optic disc. Pattern reversal VEP and flash VEP responses were non-recordable. ERG showed amplitude reduction of the fotopic, scotopic and flicker responses.

Conclusion Full-field ERG revealed generalized retinal dysfunction with reduction of cone and rod responses. The progressive neurodegeneration can be associated with a retinal degeneration.

• T134

Dyslexia and eye movements

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Purpose To analyze the relationship between dyslexia and eye movements.

Methods 22 patients were included in the study, 11 patients have a diagnosis of dyslexia and 11 subjects were used as a control group (normal readers). The age of patients enrolled ranged from 8 to 13 years. All patients underwent careful orthoptic and ophthalmological visit; eye movements were quantified by Ober-2 system. Ocular motility was divided into three phases: stability analysis to while fizating a still target; analysis of fixation pauses, analysis of tracking saccades (left and right horizontal axis); speed reading, saccades and regressions through the reading of a text.

Results The stability analysis on fixating a still target showed a significant ($p<0.001$) difference between dyslexic and control group, outlining an increased amount of loss of fixation in dyslexic subjects (5.36 +/- 2.5 and 0.82 +/- 2.1, respectively). Only two patients in the control group presented a fixation loss while none in the study group presented this defect. Also tracking saccades (left and right horizontal axis) and loss of fixation after saccades did not show significant difference. When the reading time was analyzed, a significant ($p<0.001$) difference was found between the dyslexic subjects and the control group (90+/- 52.0 second and 42 +/- 17.3, respectively). When the regression saccades were analyzed, a significant ($p<0.001$) difference was found between the dyslexic subjects and the control group (52+/- 33.4 seconds and 20.3 +/- 11.3, respectively).

Conclusion This is the first report of some ocular movement difference between dyslexic and healthy subjects detected by using the Ober-2 system. Should our findings be confirmed, this analysis could be added to the work-up of dyslexic.

• T135

Aicardi syndrome with macrocrania

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Purpose to report a case of Aicardi syndrome associated with macrocrania.

Methods Aicardi syndrome is a very rare X-linked congenital disorder. It is characterised by a typical triad of chorioretinal lacunae, agenesis of the corpus callosum and early-onset infantile spasm.

Results A five-month-old girl presented with macrocrania and abnormal visual behavior. She was born in Abidjan (Côte d'Ivoire) and suffered from hydrocephalus. She underwent first ventriculo-peritoneal derivation when she was one-month-old. This derivation was not efficient and her intracranial hypertension worsened.She suffered from local seizures during the two first months of life. Her brain CT scan showed tri-ventricular hydrocephalus and agenesis of the corpus collosum.She was referred to Caen university hospital neurosurgery department in order to have a new derivation. She presented with no ocular pursuit and no light perception. The papillary light reflexes were present.Fundus examination showed bilateral chorioretinal lacunae involving both maculas with clear cut margins.

Conclusion We diagnosed this Aicardi syndrome thanks to the clinical triad. However, Aicardi syndrome is rarely associated with macrocrania.We rewiewed the literature to discuss the wide nosological status of this syndrome and its described associations.

• T136

Postural control in children with early strabismus without amblyopia

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Purpose In healthy subjects, the postural stability in orthostatic position is better when fixating at near than at far distance; increased convergence angle contributes to such effect. Children with strabismus present a deficit in vergence movements. The goal of this study was to evaluate the postural control in children in relation with the vergence angle while fixating at different depths, and also while making active vergence movements.

Methods A TechnoConcept platform (Céreste, France) was used to record postural stability of 11 subjects (M= 11.18 years) with convergent strabismus and 13 (M=11.31 years) with divergent strabismus in 3 conditions: fixation at 40cm, at 2m and active vergence movement between two target at 20cm and 50cm.

Results As for the controls, the standard deviation of medio-lateral body sway decreased with proximity for convergent strabismus but increased for divergent strabismus. Relative to fixation, vergence eye movements caused an increase of medio-lateral body sway for convergent strabismus but decrease for divergent strabismus. Yet, vergence eye movements were associated with the least variance of speed, indicating that less energy is needed to control body sway.

Conclusion We conclude that the fixation depth at which postural stability is best in strabismus is that for which the appropriate vergence angle correspond to the strabismus angle. It might be mediated by preponderant eye movement signals related to the angle of strabismus. Reduction of variance of speed in the active vergence eye movement condition corroborates further such interpretation.

• T137

Visual function improvement after idebenone therapy in Leber hereditary optic neuropathy

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Purpose There is still no therapy for patients with Leber hereditary optic neuropathy (LHON). Recent studies have confirmed the effectiveness of Idebenone for the treatment of specific groups of LHON patients. However, it is still unclear if this treatment can be interesting in all cases of LHON. We wanted to evaluate whether Idebenone therapy in association with vitamin B2 and vitamin C can modify the visual function in non selected LHON patients.

Methods A retrospective review of visual acuity and Goldmann visual field performed in patients referred to the ophthalmology clinic for LHON before and after a therapy with Idebenone (up to 270 mg/day), vitamin B2 and vitamin C.

Results Seventy five patients were included. Mean duration between LHON onset and inclusion was 36 months. Mean treatment duration was 25 months. Twenty seven per cent of patients presented visual improvement. A surface reduction of the central scotoma greater than 30 % was observed in 36.2 % of these patients.

Conclusion There is an effect of Idebenone therapy on visual function of LHON patients. Due to the delay between symptoms onset and beginning of the treatment, improvement does not seem to be due to habituation to low vision. However, Idebenone therapy is unable to correct visual disability in LHON population.

• T138

Analysis of changes in the macula and retinal nerve fiber layer by optical coherence tomography in patients with Alzheimer's disease (AD)

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Purpose To evaluate the usefulness of optical coherence tomography (OCT) in the diagnosis of Alzheimer's disease(AD)Thickness is determined at the peripapillary RNFL and macular volume with OCT, in individuals suffering from AD and compared with a control group.

Methods Prospective study in 40 eyes of 20 patients with Alzheimer's disease and 40 eyes of 20 controls, measuring the thickness of the peripapillary RNFL and macular volume with OCT.

Results The average thickness of RNFL in patients with Alzheimer's disease was 65,28±11,55 microns (53,50 to 87,29), significantly decreased compared to control subjects, which was 107.1 ± 7, 2 microns (94.9 -128.8) (p = 0.0001. Mann-Whitney U test.). Macular volume in patients with AD was 5.6 ± 0.3 mm 3 compared with control subjects: 7.0 ± 0.5 mm3.Peripapillary RNFL thickness evaluated in each of the separate quadrants (superior, inferior, nasal and temporal) is also statistically significantly decreased in patients with AD in connection with control subjects. However, the central foveal thickness (1 mm), thickness macular inner ring (3 mm) and macular volume were significantly higher in AD patients.

Conclusion The AD is the major cause of dementia in the world. Although the entorhinal cortex and hippocampal complex are best known as the sites of early pathology in AD, increasing evidence shows that the eye, particularly the retina, is also affected. The AD-related changes in the retina are associated with degeneration and loss of neurons, reduction of the retinal nerve fibres, increase in optic disc cupping, retinal vascular tortusity and thinning, and visual functional impairment.

• T139

Neurotrophic keratopathy associated with congenital agenesis of the corpus callosum

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Purpose The corpus callosum (CC), with its central position in the cerebrum, has an essential role in relaying sensory, motor, and cognitive information from homologous brain regions across cerebral hemispheres. Corpus callosum agenesis (CCA) is a rare congenital malformation which is caused by an alteration in embryonic development.

Methods We report the case of a 3 year old child who was diagnosed of complete corpus callosum agenesis with a normal karyotype. The neurological findings were spastic tetraparesis with dystonia, several delayed psychomotor and epilepsy. In ophthalmology examination he presented esotropia, bilateral optic nerve hypoplasia, delayed visual evoked potential flash type and altered corneal sensibility in both eyes which is manifested clinically by recurrent corneal ulcers and epithelial disruption associated with stromal edema.

Results After Neurotrophic keratopathy suspected, treatment with autologous serum was decided and response to treatment was favorable in both eyes with closure of ulcers and good management of symptoms.CCA has also been described in association with other ocular abnormalities such as optic nerve hypoplasia, retinal detachments, cataracts, morning glory syndrome, iris and optic nerve colobomas, among many others.

Conclusion In all patients diagnosed with agenesis of the corpus callosum, the possible alteration of corneal sensitibility is a fact that will be suspected to perform early diagnosis and appropriate treatment and follow-up.

• T140

Altered functional connectivity of primary visual cortex in adult comitant strabismus using resting-functional mri

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Purpose Strabismus is not only associated with an abnormal eye position, but also with abnormal eye movement and poor stereopsis, both of which may be associated with high brain function. The aim of this study was to examine the functional connectivity between primary visual cortex and other cortical areas during rest in normal subjects and patients with comitant strabismus using functional magnetic resonance imaging.

Methods Functional magnetic resonance imaging (fMRI) was carried out on ten patients with comitant exotropia and eleven well-matched healthy subjects while all were in a resting state. The primary visual cortex was selected as the region of interest and the resting-state functional connectivities of this area were analyzed.

Results Compared with normal controls, strabismic patients showed that left BA17 had decreased functional connectivity with the right parietal lobe, left middle frontal gyrus, left superior frontal gyrus and right cerebellum, while the functional connectivity of the right BA17 was decreased at the middle frontal gyri bilaterally and the left inferior frontal gyrus. Enhanced connectivity of right BA17 to the bilateral middle occipital gyrus was also identified.

Conclusion These data suggest that functional dysconnectivity between primary visual cortex and other cortical areas may exist in patients with comitant strabismus, and the abnormal connectivity may be associated with abnormal eye movement and loss of stereopsis.

• T141

Comparison of latency of P100 wave in children demonstrating some pathological disorders

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Purpose A goal of the present paper was an assessment of usefulness of latency of P100 wave in describing few pathological disorders in children.The study group comprised 268 children, including 68 with cytomegaly (CM), 59 with myelomeningocele (MM) , 69 with purulent meningitis(PM) and 73 with Down's syndrome (DS). The control group consisted of 592 healthy children.

Methods Registrations were performed using Visual Evoked Potentials for each patient, stored on data bank and evaluated automatically with manual correction. Collected values of P100 wave's latency were analyzed using typical statistical tools (t-test contained in STATISTICA-data analysis software system. StatSoft, Inc. 2011, version 10. www.statsoft.com).

Results The comparison performed in regard to the group-mean latencies of the analyzed P100 wave between the control group and the four studied groups revealed statistically significant differences ($p<0.0001$). There were also statistically significant differences in the mean P100 latency between DS group and CM and PM groups ($p<0.0001$). Evaluation of the mean latencies in three groups (CM, MM and PM) did not reveal statistically significant differences ($p>0.05$).

Conclusion The results show the differences in mean latency of P100 wave between normal subjects and children with pathological disorders. In children with Down's syndrome observed abnormalities were smaller than in other 3 groups.

• T142 / 4477

The use of propranolol in the treatment of periocular infantile hemangiomas

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Purpose Infantile capillary hemangiomas (IH) are the most common tumours of the eyelid and orbit in infants. Despite their self-limited course, IH can impair visual function. Recently, the use of propranolol was found to reduce the size of IH. We will present our own case series of patients with periocular IH treated with propranolol to illustrate these findings.

Methods We conducted a retrospective study on 10 children with IH treated with propranolol. After exclusion of any contra-indication, propranolol was initiated at a dose of 1 mg/kg/d. After 10-14 days, patients were checked again for side-effects. If these were absent, propranolol was increased to 2 mg/kg/d. Further follow-up consists of monthly clinical and photographical evaluations of the IH, monitoring of treatment compliance and tolerance. Success of treatment is defined as stopping growth or reducing size. The response to treatment was rated by 3 blinded, independent observers.

Results The age range at start of treatment with propranolol was between 2 and 19 months (mean 6,8 months). The mean age at stopping propranolol was 14,4 months. The mean duration of treatment was 7,6 months and only 1 patient had to stop treatment because of side effects. Two patients (20%) had a rebound after temporary stop of propranolol. The success rate in our case serie was 100%. Half of the group had excellent results, 30% had a good response and 20% had a fair response. We also obtained objective measures of astigmatism and anisometropia in 6 patients. We report a reduction in anisometropic astigmatism in 5 of these 6 patients.

Conclusion These data support the current perception that propranolol is a highly effective first line treatment for IH with very limited and mild side effects.

• T143 / 4476

Generating human retinal ganglion cells from human induced pluripotent cells in feeder and feeder-free conditions

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Purpose Glaucoma, and other optic neuropathies, results in the loss of retinal ganglion cells (RGCs) and vision dysfunction. Therefore, cell replacement therapy may offer promising treatments to protect the degenerating retina and potentially restore vision function. Although significant progress has been made to generate photoreceptors from stem cells, there has been little advancement in efficiently generating RGCs. Therefore, we have been investigating the optimal conditions for differentiating RGCs from stem cells for cell replacement therapy.

Methods Human induced pluripotent stem cells (iPSCs) were maintained and expanded on feeder layers using previously published conditions. During embryoid body formation, genes and proteins were tested for effects on increasing RGC differentiation efficiency. Differentiated RGCs were identified and quantified using RGC-specific markers including Brn3. Feeder-free conditions were examined for functional equivalence.

Results iPSCs that express stem cell-specific markers were passaged in proliferative conditions and differentiated into RGCs in vitro. Feeder-free cell culture conditions allowed iPSC maintenance without the presence of mouse immunogenicity. iPSCs were found to respond to pro-RGC differentiation signals in similar fashion to rodent embryonic retinal progenitors.

Conclusion These findings will provide valuable insight in our understanding of RGC differentiation and will pave the way to cure retinal diseases. The transplantation of these cells in vivo will elucidate the integration potential of these cells in degenerating retina.

• **F001**

Comparison of three different methods of intraocular pressure (IOP) measurements including properties of the cornea

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Purpose The aim of this study was to show the usefullness of three different methods of Intraocular Pressure (IOP) measurements: Goldmann Applanation Tonometer, Rebound Tonometer and Ultra High-Speed Scheimpflug Technology.

Methods The examined group consisted of 96 patients, 192 eyes (63 females, 33 males of mean age 59,3±19,9 years old). IOP measurements were carried out using Goldmann Applanation Tonometer (GAT), Rebound Tonometer Icare Pro (RT) and Ultra High-Speed Scheimpflug Technology (UHS ST) – "Corvis ST" with pachymetry which automatically took into account of central corneal thickness (CCT) correction. Additionally corneal pachymetry with Pentacam, Oculus were made to considered CCT in GAT IOP value. Statistical analysis was based on the software Statistica 10.0 PL, Statsoft, Poland.

Results Mean IOP measured with GAT was 15,6±3,75 mmHg; GAT with CCT correction 15,7±3,7 mmHg; mean IOP measured with RT was 15,6±3,5 mmHg; with UHS ST 16,1±4,0 mmHg. Mean CCT measured with UHS ST was 543,7±52,7 µm; with Pentacam 547,9±54,0 µm. In comparison, there is significant difference between IOP measured with GAT and GAT+CCT, RT versus UHS ST (P<0,001) and no significant between GAT, GAT+CCT versus RT (p>0,5). Central Corneal Thickness was without differences in measurements carried out with UHS ST and Pentacam. All technics showed correlation IOP with CCT (p<0,05; r~0,3).

Conclusion Applanation Tonometer and Rebound Tonometer can be equal methods of IOP measurements in contrast to Ultra High-Speed Scheimpflug Technology which give significant different values but can be use to take accurate measurements of Central Corneal Thickness

• **F002**

Comparison of intraocular pressure measurements with the reichert pt100, the keeler pulsair intellipuff portable non-contact tonometers and goldmann applanation tonometry

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Purpose To compare the intraocular pressure (IOP) measurements by two portable tonometers, the Keeler Pulsair Intellipuff™ and the Reichert PT100™, with Goldmann applanation tonometry (GAT).

Methods Prospective cross-sectional study conducted on normotensive and hypertensive patients. IOP was measured by the two portable non-contact tonometers and GAT in one eye of each patient in a random order. The Wilcoxon test was used to compare the differences between tonometers, the Spearman correlation test to evaluate the correlation among the methods, and Bland–Altman plots and intra-class Correlation Coefficient (ICC) to evaluate the agreement among the methods.

Results 137 eyes of 137 patients were included. We found an excellent agreement (ICC > 0.75) between PT100™ and GAT and between Intellipuff™ and GAT in normotensive patients. We found a fair to good agreement (ICC 0.67) between PT100™ and GAT in hypertensive patients. The agreement we found between Intellipuff™ and GAT was also excellent in hypertensive patients (ICC 0.83). The differences between the measurements of the two non-contact tonometers and the GAT were significantly correlated to the central CCT.

Conclusion The two non-contact tonometers agree well with GAT in normotensive patients. The Pulsair Intellipuff™ agrees also well with GAT in hypertensive patients.

• **F003**

24-hour intraocular pressure of healthy humans in supine position: rhythm and reproducibility

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Purpose To evaluate the reproducibility over time of 24H intraocular pressure (IOP) rhythm in healthy humans in supine position.

Methods In a sleep laboratory, six healthy young Caucasian male subjects were included in each six weekly 24H sessions of hourly IOP measurements in a control supine position using the pneumatonometer Digilab Modular One . IOP 24H rhythm was modelled using a nonlinear least squares dual harmonic regression analysis. The intra- and inter-subject variability of acrophase, bathyphase, amplitude and IOP values were evaluated.

Results A significant nyctohemeral IOP rhythm was noted in 30/36 (83%) sessions. Nocturnal IOP was significantly higher than diurnal IOP (20.1 ± 0.2 vs. 18.8 ± 0.1 mmHg). Reproducible distribution over 24H of intra-subject acrophase and bathyphase was found respectively in 3/6 (50%) and 4/6 (67%) subjects. Intra-subject means of amplitude were not statistically different between subjects. IOP values at 2:00, 3:00, 4:00, 10:00, 11:00 AM and 2:00 PM and IOP mesor had fair to good agreement between sessions.

Conclusion Most healthy subjects exhibited a nyctohemeral rhythm of IOP with fair reproducible characteristics in supine position. Amplitude is the best reproducible parameter. This result strongly suggests that chronobiological lower IOP therapies could be powerfully studied using paired intra-subject 24H nyctohemeral rhythm data comparison, during repeated sessions overtime before and after treatment.

• **F004**

Relationship between IOP and biomechanical corneal values obtained by ORA

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Purpose To evaluate the relationship between intraocular pressure (IOP) measurements and corneal biomechanical parameters obtained with Ocular Response Analyser (ORA) in healthy subjects.

Methods Sixty-five eyes from 65 healthy subjects were prospective and consecutively selected. All of them underwent a full optometric examination, including central corneal thickness (CCT) and IOP measured with ORA: ORA Goldmann-corrected IOP (IOPg) and ORA corneal resistance-corrected IOP (IOPcc). Pearson correlation coefficients between IOP values and corneal biomechanics parameters obtained by ORA were also calculated.

Results IOP parameters, evaluated by Pearson correlation coefficients were significantly correlated with p<0.001; r=0.826 for IOPcc-IOPg. IOPg was linearly associated with corneal resistance factor (CRF; r=0.619) and with CCT (r=0.579). IOPcc had a linear relationship with CH (r=-0.482); similar results were obtained with CRF and corneal hysteresis (CH; r=0.841), CRF and CCT (r=0.681) or between CH and CCT (r=0.466).

Conclusion IOPcc and IOPg have a positive linear correlation. ORA biomechanics parameters CRF, CH and CCT show also a linear positive relation between them.

• F005

Comparation between Keeler and ORA IOP measurements

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Purpose To evaluate the relationship between intraocular pressure (IOP) measurements obtained with Pulsair EasyEye (PEE) and Ocular Response Analyser (ORA) in healthy subjects.

Methods Sixty-five eyes from 65 healthy subjects were prospective and consecutively evaluated. All of them underwent a full optometric examination, including central corneal thickness (CCT), and IOP measured with both PEE and ORA devices. Differences between IOP measurements between both tonometers were analyzed.

Results Statistically differences were found between IOP measurements of PEE (IOPk) and ORA Goldmann-corrected IOP (IOPg; p=0.001). IOPk and ORA corneal resistance-corrected IOP (IOPcc) were also statistically different (p=0.025). However, no differences between IOPg and IOPcc were found (p=0.952). Mean differences between IOPg-IOPk, IOPcc-IOPk and IOPg-IOPcc (±SD) were 0.71±1.66, 0.70±2.46 and 0.01±1.54 mmHg respectively. Pearson correlation coefficients showed that IOPk, IOPg, IOPcc were significantly correlated (p<0.001): r=0.816 for IOPk-IOPg, r=0.826 for IOPcc-IOPg and r=0.587 IOPcc-IOPk.

Conclusion There are statistically differences between mean IOP values measured with PEE and ORA. ORA tonometer provides higher IOP values than PEE in most of the cases. IOPk, IOPcc and IOPg have, at least, moderate positive linear correlations between them.

• F006

To assess the difference in the corneal biomechanical properties in healthy subjects with and without their contact lenses

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Purpose To assess the difference in the corneal biomechanical properties in healthy subjects with and without their contact lenses.

Methods The study included one eye of 20 healthy subjects who wear monthly, soft contact lenses for a refractive error. The subjects were asked, not to wear their contact lenses during at least 12 hours. The central corneal thickness was measured at least 30 minutes before other examination using an ultrasonic pachymeter. The corneal biomechanical properties and the intraocular pressure (IOP) were measured by ocular response analyzer (ORA). The measurements were repeated immediately with the contact lenses. A student t-test was used to assess the difference between the measurements with and without contact lenses.

Results The mean corneal hysteresis without and with contact lenses were 10.88 ± 1.8 mmHg (9.6-13.7 mmHg) and 10.92 ± 1.7 mmHg (8.5-13.4 mmHg), respectively (p = 0.16). The mean corneal resistance factor was 9.96 ± 1.7 mmHg (7.9-12.6 mmHg) without contact lenses compared with 9.95 ± 2.1 mmHg (7.6-12.3 mmHg) with the contact lenses (p= 0.21)There was no significant difference nor in corneal-compensated IOP neither in Goldmann-correlated IOP, with or without the contact lenses.

Conclusion Our results suggest that ORA-generated parameters are not influenced by the contact lens itself. Further longitudinal studies should be performed to establish the eventual changes of the biomechanical parameters with duration of the contact lens wear.

• F007

IOP management in glaucoma/OHT following intravitreal anti-VEGF injections

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Purpose To determine a protocol for IOP management in glaucoma/OHT cases following intravitreal anti-VEGF injections

Methods Baseline IOP with Icare tonometry, optic disc assessment and automated perimetryIOP post-injection at 5, 15, 30 and 60min.Standard injection technique.

Results Mean baselineIOP was 16.92 mmHg (SD 4.98, 95% CI 14.95 to 18.88). Thirty minutes postApraclonidine 1% administration, mean IOP was 15.71 mmHg (SD 4.58, 95% CI 13.74 to17.67) Paired Student's t-test giving a P value of 0.368 indicated that administration ofApraclonidine 1% prior to intravitreal treatment did not cause a statistically significantIOP reduction in patients with ocular hypertension and glaucoma. Immediately postinjection, mean IOP was 41.54mm Hg (SD 14.1, 95% CI 37.20 to 45.88). Paired T testresults showing a p value < 0.0001 confirmed a statistically significant difference betweenbaseline and immediate post injection IOP. 13 out of 24 (58%) of the study patientsrequired anterior paracentesis post intravitreal injection according to our devisedprotocol.

Conclusion The authors propose the use of theformulated paracentesis protocol for intraocular management in patients with ocularhypertension and glaucoma receiving intravitreal anti-VEGF treatment.

• F008

Persistent ocular hypertension following intravitreal injections of anti-VEGF agents or dexamethasone intravitreal implant

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Purpose To report the rate of intraocular pressure elevation following repeated intravitreal injections (IVI) of anti-VEGF agents or dexamethasone intravitreal implant and to determine the risk factors.

Methods A prospective study of 166 eyes undergoing IVI of ranibizumab (n=126), bevacizumab (n=19), or dexamethasone implant (n=12) was carried out. A total of 886 IVI were performed. The development of ocular hypertension (OHT) following these injections was investigated with respect to number of injections, pre-existing glaucoma, diabetes and YAG capsulotomy.

Results After a mean of 5.34 +/- 5.1 IVI (range, 1-30), 8.4% (n=14) had IOP elevation above 25 mmHg and required medical treatment (3% of them peaked above 30mmHg). Patients with pre-existing glaucoma experienced highter rates of OHT were compared to patients without pre-existing glaucoma (21.7mmHg +/-12.4 versus 17.23mmHg +/-4.5, p=0.06). No significant difference was found in diabetes subgroup (n=40, p=0.32), nor in YAG capsulotomy subgroup (n=12, p=0.8) compared to the control group. The peak of IOP was significatively correlated with the total number of IVI (p=0.01, R=0.19).The mean highest IOP was 17.2mmHg in ranibizumab group, 18.8mmHg in bevacizumab group and 19.9mmHg in dexamethasone intravitreal implant. No difference was found between these molecule subgroups (Kruskal-Wallis p=0.38).

Conclusion Serial intravitreal injections may lead to persistent IOP elevations that require IOP lowering therapies. This risk is correlated with the number of injections and must be checked during the follow-up. Pre-existing glaucoma could be a risk factor but larger prospective studies are needed to verify these results.

• F009

Optic disc torsion direction predicts the location of glaucomatous damage in normal tension glaucoma patients with myopia

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Purpose To characterize optic disc tilt and torsion in normal tension glaucoma(NTG) patients with myopia and evaluate the relationship between optic disc tilt and torsion with the location of visual field(VF) defect

Methods Patients were divided into myopic NTG group (spherical equivalent(SE)≥-2.0 diopters(D) or axial length(AL)≥24.0 mm) and non-myopic NTG group (SE<-0.5 D or AL<24.0 mm). Disc tilt, torsion, and area of peripapillary atrophy(PPA) were measured from disc photographs. Patients were further divided into superior and inferior defect groups according to the location of the VF defect in the pattern deviation map. Logistic regression analysis was used to determine the relationship between tilt ratio, torsion degree, and the VF defect location.

Results Among 225 NTG eyes, 166(73.8%) were myopic eyes. The myopic NTG group was significantly younger(42.85 years) than the non-myopic NTG group(60.73 years). Disc tilt(45.8%) and torsion(75.9%) were significantly more prevalent in the myopic NTG group. PPA area was larger in the myopic NTG group(P=0.057). VF defect location was significantly different between the two groups, with superior defects more prevalent in the myopic NTG group(69.9%, P<0.001). Torsion degree was significantly different in the superior defect group(18.45 degrees) compared to the inferior defect group(-3.81 degrees, P = 0.001). Torsion degree was the only factor related to VF defect location in both univariate(P=0.001) and multivariate logistic regression(P=0.014) analysis.

Conclusion Korean NTG patients had a high prevalence of myopia and young age. Optic disc tilt and torsion were highly prevalent in Korean NTG patients with myopia. The direction of the optic disc torsion may predict the location of damage.

• F010

Structure–function relationship: assessment of macular ganglion cell complex with FD-OCT and standard automated perimetry

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Purpose This study aims to evaluate relationship might exist between new indices of structural damage provided by FD-OCT which analyses macular ganglion cell complex (mGCC) and functional indices collected in standard automated perimetry (SAP).

Methods 102 eyes (56 PAOG and 46 control) benefited a SAP(Humphrey SITA-Standard 24.2, Carl Zeiss Meditec) and an FD-OCT imaging (RTVue 100, macular grid of 7*7mm, Optovue Inc.). We analyse: MD, PSD and VFI for functional analysis, and focal and global losses (FLV and GLV) of mGCC for macular mapping. Statistical regression analysis was used to assess possible structure-function relationship.

Results Glaucoma (66.2±3.5y) results report: MD:-6.25±1.46dB, PSD:5.9±1.1dB, VFI:84±4.7%, FLV:4.84±1.26% and GLV:19.2±2.7%. Controls (61.6±4y) results were: MD:0.36±0.22dB, PSD:1.6 ± 0.1dB, VFI:99±0.5%, FLV:2.04±0.59 and GLV:9.8±2.3%. Structural damage and functional impairment indices may be correlated by linear regression. Correlation is higher in glaucoma group. Strongest relation is between PSD and FLV with determination coefficient (r^2) of 0,63.

Conclusion This study evaluates the possible relationship between new structural and functional parameters in 2 age-matched groups. Linear correlation, greater in glaucoma group, emphasizes a structure-function relationship with a highest determination coefficient of 0,63. This correlation is between focal indices of structural and functional damage (PSD and FLV).New FD-OCT parameters of mGCC provided us a better understanding of glaucoma structural damage. Assessment of structure-function relationship is improved and we find a higher correlation between focal indices.

• F011

Retinal pigmentepithelium (rpe) alterations correspond to retinal nerve fiber layer (rnfl) degeneration in glaucoma

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Purpose A close interaction between neurosensory retina and the retinal pigmentepithelium (RPE) is a prerequisite for normal vision. Glaucomatous damage is characterized by neuroretinal degeneration. As a result, an imbalanced interaction exists. However, there is only limited evidence regarding RPE involvement in glaucoma patients' eyes. This study investigates the correlation between retinal nerve fiber layer (RNFL) thickness and RPE alterations as detected by widefield fundus autofluorescence (FAF).

Methods Peripapillary RNFL thickness was quantified by optical coherence tomography (OCT). The six corresponding retinal areas were defined by a standardized grid and FAF intensity/irregularities were assessed and correlated to RNFL measurements.

Results 84 glaucomatous eyes were investigated. A correlation between RNFL thickness and standardized FAF in the corresponding topographic retina segments was observed. Correlation coefficients ranged between -0.12 to 0.35 and were statistically significant in the temporal inferior central field (r=0.35, p=0.02) and the temporal inferior peripheral field (r=0.31, p=0.04).

Conclusion This study provides early evidence that in glaucoma RNFL degeneration may be accompanied by corresponding RPE alterations

• F012

Correlation of various optic nerve head parameters obtained by 3D non-mydriatic retinal camera and optical coherence tomography (OCT)

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Purpose To evaluate the relationship between various optic nerve head parameters(ONHP) provided by 3D non-mydriatic retinal camera and OCT. Agreement in assessing the disc damage likelihood scale (DDLS) using 3D monitor between trainees and the validity of the DDLS provided by the integrated algorism of 3D retinal camera were also investigated.

Methods Patients(122 eyes from 82 patients) were categorized as normal, glaucoma suspect and glaucoma groups. Stereoscopic images were taken by 3D non-mydriatic retinal camera(Nonmyd WX 3D,Kowa company Ltd.,Japan) and various ONHP provided by the instrument were used. To access the agreement in assessing the DDLS between trainees, initially DDLS score was graded using slit lamp by each observer and then each observer was provide with the 3D image of the optic nerve head using 3D monitor and was asked to re-grade the DDLS according to their findings. OCT was performed to acquire retinal nerve fiber layer analysis and optic nerve head analysis.

Results There was a good correlation between various ONHP obtained by 3D non-mydriatic retinal camera and OCT. The interobserver agreement of the DDLS evaluated through the 3D monitor was excellent(0.91), whereas the interobserver agreement of the DDLS evaluated clinically by slit lamp was substantial (0.80). The DDLS evaluated by the integrated algorism of 3D non-mydriatic retinal camera was not itself satisfactory in the diagnosis of glaucoma. ROC curve shoed that DDLS evaluated using 3D monitor had the best predictive power(0.93).

Conclusion ONHP obtained by 3D non-mydaiatic retinal camera are useful in evaluating patients with glaucoma, however, the integrated algorism of the device to calculate the DDLS needs to be improved.

• F013

To assess circumpapillary retinal arteries and veins thickness (cRAT and cRVT) at optic disc (OD) border and correlate them with circumpapillary retinal nerve fiber layer (cRNFL)

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Purpose To assess circumpapillary retinal arteries and veins thickness (cRAT and cRVT) at optic disc (OD) border and correlate them with circumpapillary Retinal Nerve Fiber Layer (cRNFL).

Methods 123 healthy subjects underwent complete ophthalmologic examination including Cirrus®HD-OCT and GDx-ECC® (both Carl Zeiss Meditec Inc.). We used SLO images of HD-OCT and MATLAB® (Version R2009b, The Mathworks Inc.) to manually identify the OD contour and measure cRAT and cRVT at OD border. cRAT and cRVT data were convolved with a Gaussian window to generate a 64-sector profile.

Results 123 and 118 subjects showed significant intrasubject correlations between the cRNFL thickness profiles of the GDx-ECC and cRVT and cRAT profiles, with Rmean 0.68 (0.96 – 0.03) and Rmean 0.65 (0.92 – 0.02). 26 and 24 of 64 plots showed significant intersubject correlation between cRNFL and cRVT and cRAT profiles (Rmax 0.35 and 0.29). For all vessels together intrasubject Rmean was 0.74 (0.40 – 0.96). Intersubject correlation was significant in 33/64 plots (Rmax 0.37).

Conclusion The individual cRVT and cRAT profiles contain approximately 46% of the individual RNFL profile information. Up to 12% of the intersubject variability of cRNFL might be explained by variations of cRVT or cRAT profiles. Analyzing all vessels together performed even slightly better.

• F014

Asymmetry in hemifield macular thickness as an indicator of early glaucomatous structural or functional progression

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Purpose To evaluate whether asymmetry in macular thickness can serve as an indicator of glaucomatous structural or functional progression utilizing Spectralis spectral domain optical coherence tomography (SD-OCT).

Methods 31 early glaucoma eyes were evaluated in this study. Average macular thickness maps were acquired by posterior pole analysis of SD-OCT and Macular thickness asymmetry between superior and inferior hemifield was analyzed. 16 eyes were classified as asymmetric and 15 eyes were classified as symmetric. Average macular thickness and circumpapillary retinal never fiber layer (cRNFL) were measured by SD-OCT while Visual sensitivity loss was determined by mean deviation (MD) using Humphrey Visual Field Analyzer. All examinations were repeated after 6 months.

Results In asymmetry group, average macular thickness decreased from 280.8±8.2 to 273.3±7.4μm and cRNFL decreased from 80.2±3.4 to 76.8±3.0μm. Both of them became thinner statistically significantly. In symmetry group, neither average macular thickness nor cRNFL had significant change. Visual sensitivity loss did not get significantly worse in each group.

Conclusion Evaluation of asymmetry in macular thickness in early glaucoma eyes may serve as a useful indicator in the progression of glaucomatous changes.

• F015 / 4453

Biomechanical response of lamina cribrosa and prelaminar tissue to an acute induced IOP elevati

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Purpose We decided to investigate the effects of an acute induced IOP elevation on the prelaminar tissue and on the lamina cribrosa in glaucomatous eyes and in healthy eyes by means of an high resolution Spectral Domain (SD) OCT.

Methods We enrolled 10 patients (mean age 70.2 years) affected by primary open angle glaucoma (POAG) and 10 healthy subjects (mean age 70.8 years) as controls. All the subjects were scanned with a SD-OCT with real-time eye tracking at baseline and in the same exact position during IOP elevation performed with an ophthalmodynamometer. The IOP was measured with a Tono-Pen at baseline and during IOP elevation. The SD-OCT images acquired were processed with a computer graphical suite to determine the prelaminar tissue displacement (PTD) and the laminar displacement in the two groups. An analysis of variance was used for evaluating group differences considering statistically significant a $P < 0.05$.

Results Baseline IOP was significantly different in the two groups, with higher values in patients compared to controls: 18.9(4.3) vs. 15.7(2.6) mmHg ($P<0.037$). Mean PTD was significantly lower in glaucomatous eyes compared to healthy eyes: 6.8(13.7) vs. 20.8(17.5) micron ($P<0.039$); whereas LD was similar in the two groups: -0.5(3.7) vs. 0.2(2.0) micron ($P=0.366$), and not statistically different from 0 ($P=0.366$).

Conclusion The study shows that an acute induced elevation of IOP does not induce a detectable movement of the lamina cribrosa anterior surface both in glaucomatous and healthy eyes.On the other hand the displacement of the prelaminar tissue is lower in patients with POAG than in controls.

• F016

Macular ganglion cell-Inner plexiform layer thickness measurement and reproducibility with SD-OCT

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Purpose To evaluate the macular retinal ganglion cell-inner plexiform layer (GC-IPL) thickness with automated detection and analyze the intra and interobservator reproducibility in normal, ocular hypertensive (OHT) and glaucomatous eyes.

Methods A total of 138 eyes were enrolled in 3 goups: normal subjects (n=69), OHT subjects (n=35), and open angle glaucoma subjects (n=34). All patients underwent a complete ocular examination including 24-2 standard automated perimetry, biometry and pachymetry. Each eye had macular scanning using the Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA), 3 times by each of 2 observators, and the ganglion cell analysis (GCA) algorithm provided parameters as average, minimum and 6 sectoral GC-IPL thicknesses. The reproducibility was assessed with intraclass correlation coefficient (ICC), coefficient of variation (CV) and test-retest SD (TRTSD).

Results The mean GC-IPL thickness was 82.27 ± 7.37 μm, 76.84 ± 7.01 μm and 66.16 ± 11.16 μm in normal, OHT, and glaucoma group respectively. The GC-IPL thickness was significantly lower in glaucomatous eyes than in normal and OHT eyes ($p<0.0001$ for all parameters). In the 3 groups ICC ranges were 96.4-99.9 % and 92.5-99.8 %, CV ranges were 0.41-2.24 % and 0.55-1.67 %, and TRTSD ranges were 0.61-2.64 μm and 0.83 and 2.22 μm, for respectively the intraobservator and interobservator reproducibility analysis.

Conclusion To our knowledge this is the first study of GCA algorithm in normal, OHT and glaucomatous eyes. A highly satisfactory reproducibility of GC-IPL thickness measurements using Cirrus HD-OCT is reported. GC-IPL thickness might be promising new OCT parameter for glaucoma diagnosis and follow-up.

• F017

Average nerve width measurement obtained by optical coherence tomography and glaucoma

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Purpose This study will investigate the optic nerve head (ONH) using optical coherence tomography (OCT) and analyze the correlations between neuroretinal rim and optic disc-cup structure in order to apply the finding in glaucoma.

Methods This cross-sectional study enrolled 157 healthy subjects firstly and analyzed one randomly selected eye in each subject. The measurements for ONH parameters, including neuroretinal rim and optic disc-cup structure (disc or cup areas and cup-to-disc ratios), were taken by a single experienced operator. The associations among neuroretinal rim and optic disc-cup structure were determined. Independent parameter was further tested in 25 glaucomatous patients.

Results In healthy subjects, average cup-to-disc area ratio estimated was 0.2827 ± 0.1134 (95% CI; range, 0.263 to 0.302); rim area (vertical cross section), vertical integrated rim area, horizontal integrated rim width, and rim area positively correlated with disc area ($p<0.05$); rim area (vertical cross section), average nerve width, and vertical integrated rim area negatively correlated with cup area ($p<0.05$); and rim area (vertical cross section), average nerve width, vertical integrated rim area, horizontal integrated rim width, and rim area negatively correlated with cup-to-disc ratios ($p<0.05$). In further stepwise regression analysis, average nerve width was not associated with optic disc-cup structure measurements ($p>0.05$, $F<4.000$) in healthy subjects. In glaucomatous patients, average nerve width was positively correlated with the mean deviation (dB) in standard automated perimetry ($p<0.001$, $r=0.709$).

Conclusion Average nerve width (the height of the nerve fiber bundle) is an independent rim parameter, and is helpful for the evaluation in glaucoma.

• F018

Glaucoma diagnostic accuracy : comparison of RTVue-100 and Cirrus HD

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Purpose To compare diagnostic performance of peripapillary retinal nerve fiber layer and macular complex acquisitions in both Cirrus HD and RTVue OCTs.

Methods Observational study. 26 control eyes of 13 patients and 29 glaucomatous eyes of 16 patients were included. Inclusion criteria were : VA>20/25, no retinopathy nor maculopathy, spherical equivalent between -6 and 4 diopters, no recent ocular surgery. Acquisition protocols were : optic disc cube and 200x200 macular cube for the Cirrus. RNFL parameters and the macular complex (retinal ganglion cell and inner plexiform ie GCA) in 6 zones were studied. With the RTVue:3D optic disc plus ONH map then macular map. RNFL parameters and macular complex (retinal nerve fiber plus retinal ganglion cell plus inner plexiforme ie GCC). Statistical analysis : normal and glaucomatous population were compared with a Mann-Whitney test. Area under curve (AUC), sensibility and specificity were calculated for each parameters. Agreement between the 2 OCT for the RNFL was evaluated with a Bland Altman plot

Results there was a difference for all the studied parameters between the two populations (u-test $p<0,01$). AUC ranges from 0,782 to 0,963. for the Cirrus, the best parameters were GCA inferotemporal (AUC=0,955 Se=88% Sp=91%) and inferior RNFL (AUC=0,963 Se=93 Sp=91%) whereas for the RTVue,it was FLV (AUC=0,942 Se=89%, Sp=92%) and average RNFL (AUC=0,935 Se=85%, Sp=96%). There was no statistical differences when comparing those four AUC. There was a moderate agreement between the RNFL values with a biais of 9 micrometers.

Conclusion There is no difference between GCA (Cirrus) and GCC (RTVue) in diagnostic accuracy for glaucoma. Macular parameters have the same performance than peripapillar parameters.

• F019

Scanning laser polarimetry in glaucoma suspects: influence of the lens

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Purpose to compare scanning laser polarimetry (GDx) variable corneal compensation (VCC) and enhanced corneal compensation (ECC) in glaucoma suspects divided on the basis of lens conditions

Methods 339 eyes of 182 consecutive patients were selected and submitted to complete ophthalmic evaluation, automated perimetry (HFA 24-2), scanning laser polarimetry of RNFL with GDx VCC and ECC. Patients were divided into 4 groups if pseudophakic (IOL) or with different lens opacities graded according to LOCS-III (NO/NC 1, 2 or 3). Morphometric parameters as TSNIT average, superior, inferior, nerve fiber indicator(NFI); quality of the image (Q)and typical scan score(TSS) given by the two GDx algorithms were compared applying Wilkoxon signed-rank test and Lin's concordance coefficient. Kruskall-Wallis test was used to compare the 4 groups on the basis of age, intra-ocular pressure (IOP), perimetric indices as mean defect (MD) and pattern standard deviation (PSD),TSNIT,NFI,Q and TSS

Results IOL group was significantly older, with lower IOP and higher MD as compared to the other groups. ECC gave better quality scans, thinner RNFL and higher NFI as compared to VCC. ECC/VCC outcomes were significantly different and concordance was poor to moderate but slightly better with transparent lens than with cataract (NO/NC3) or IOL. IOL and cataract seemed to affect GDx outcomes especially with VCC

Conclusion different lens conditions seemed to influence laser polarimetry outcomes particularly with VCC. ECC as compared to VCC gave better quality scans, thinner RNFL, higher NFI and was less influenced by lens condition. ECC could possibly better reproduce RNFL thickness, giving a more reliable model of early glaucomatous neuropathy

• F020

Reproducibility of retinal nerve fiber layer parameters measured with scanning laser polarimetry in healthy eyes

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Purpose To determine the variability of retinal nerve fiber layer (RNFL) parameters measured with scanning laser polarimetry (SLP) with enhanced corneal compensator (GDx ECC) in healthy eyes.

Methods Eighty-two healthy individuals were prospectively selected. Only one eye per subject was randomly included in the study. All participants had intraocular pressure less than 21 mmHg and normal standard automated perimetry (Humphrey 24-2 SITA Standard). Peripapillary RNFL parameters were measured using the GDxPRO (Carl Zeiss Meditec, Dublin, CA) 3 consecutive times on the same session. Left eye data were converted to a right eye format. The same operator performed all acquisitions with the same device. Intraclass correlation coefficient (ICC), coefficient of variation (COV), and test-retest variability were calculated for all SLP parameters: TSNIT average, superior average, inferior average, TSNIT standard deviation and the nerve fiber indicator (NFI).

Results Mean age was 56.08 ± 9.4 years. The ICC was higher than 0.928 for all SLP parameters. The TSNIT average had the highest ICC (0.967), while the TSNIT standard deviation showed the lowest ICC (0.928). The COVs ranged from 2.4% (TSNIT average) to 21.8% (NFI). Test-retest variability was 6.55 for the NFI and 2.51 for the TSNIT average.

Conclusion The reproducibility of RNFL measurements acquired with the GDxPRO was excellent. Variability was higher for NFI than for other SLP parameters.

• F021

The influence of TSD (topographic standard deviation) and RH (refference height) test/retest variability upon the test/retest variability of the HRT stereometric parameters

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Purpose To investigate the role of TSD and RH inter-test variability upon the variability of the stereometric parametres.

Methods 204 glaucomatous patients underwent regularly complete ophthalmological follow-up for 3 years and HRT3 exam (yearly). The exclusion criteria were optic disc or retinal pathology that might interfere with the detection of glaucoma progression, TSD >30µm and progression of glaucomatous defect on optic disc photography or TCA.

Results TSD inter-test variability <27; no statistically significant correlation between TSD variability and stereometric parameters changes. RH variability ranged between -198 and 187. Correlation analyses revealed a linear dependence between the inter-test variability of RH and stereometric parameters change. The most powerful correlations were observed for: RNFL Thickness (r=0.756, p<0.001), Rim Area (r=0.662, p<0.001), C/D Area Ratio (r=-0.663, p<0.001). The least correlated were Height Variation Contour (r=0.31) and Cup Shape Measure (r=0.07, p=0.3). When RH variability did not exceed 25µm, the correlations with stereometric parameters change were not statistically significant (for Rim Area, r=0.21, p>0.05, for C/D Area Ratio, r=-0.13, p=0.22, for RNFL Thickness r=0.06, p=0.52).

Conclusion At TSD <30, the impact of TSD variability upon stereometric parameters changes is of little relevance. For values >25µm, the variability of the RH is a major factor determining test/retest variability for RNFL Thickness, Rim Area, C/D Area, Rim Volume and Linear C/D. Inter-test variability of RH <25µm is an important criterion for the clinical relevance of stereometric parameters changes.

• F022

Stereometric parameters change vs. HRT Topographic Change Analysis (TCA) agreement in early detection of glaucoma progression

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Purpose To investigate the sensitivity and specificity of the stereometric parameters change analyses vs. TCA in early detection of glaucoma progression.

Methods 81 patients with POAG were monitored for 4 years: GAT (monthly), SAP (every 6 months), optic disc photographs and HRT3 (yearly). The exclusion criteria were optic disc or retinal pathology that might interfere with the detection of glaucoma progression, TSD >30 and inter-test variation of RH above 25 µm for all HRT exams. The criterion for structural progression was considered at least 20 adjacent super-pixels with clinically significant decrease in height (>5%).

Results 16 patients of total 81 presented structural progression on TCA. The most useful stereometric parameters for early detection of glaucoma progression were: Rim Area change (sensitivity 100%, specificity 74.2% for a "cut off" value of -0.05), C/D Area change (sensitivity 85.7%, specificity 71.5% for a "cut off" value of 0.02), C/D linear change (sensitivity 85.7%, specificity 71.5% for a "cut off" value of 0.02), Rim Volume change (sensitivity 71.4%, specificity 88.8% for a "cut off" value of -0.04). RNFL Thickness change (<0) was highly sensitive (82%), but less specific for glaucoma progression (45,2%). The changes of the other stereometric parameters have a limited diagnostic value for early detection of glaucoma progression.

Conclusion TCA is a valuable tool for assessing structural progression in glaucoma patients and its inter-test variability is low. On long-term run quantitative analysis by stereometric parametres change is also very important. The present study shows that the most relevant parameters to detect progression are RA, C/D Area, Linear C/D and RV.

• F023 / 2455

Defects in macular-retinal layer analysis of glaucoma patients compared to normative database

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Purpose High-resolution optical coherence tomography (HR-OCT) enables a quantitative analysis of the configuration of retinal layers. The aim of this study was to analyze the topographic distribution of pathologic thinning of specific macular retinal layers of glaucoma patients.

Methods Macular 3D-scans were recorded with HR-OCT (Cirrus®, Carl Zeiss Meditec). Retinal layers, especially the retinal nerve fiber layer (RNFL) and the retinal ganglion cell plus inner plexiform layer (RGIPL), were automatically segmented with a custom made software (Matlab R2009b®, The Mathworks Inc.). A normative database for the thickness of the RNFL, the RGIPL and the retina was created using healthy subjects (n=84) taking into account for the effects of age. 18 glaucoma patients were compared to the 95% confidence interval of the normative database using the thickness values of RNFL, RGIPL and retina within 65 segments.

Results On average the glaucoma patients showed for RNFL, RGIPL and retina 29.8, 49.4 and 53.9 pathologic segments within the macula. The minimum number of pathologic segments per patient was 5, 24 and 29. The average thickness values for healthy subjects were 32.95 µm (RNFL), 79.02 µm (GCIPL) and 321.46 µm (retina), for glaucoma patients 24.85 µm, 57.46 µm and 281.30 µm, respectively.

Conclusion In our study quantitative analysis of retinal layer thickness based on macular HR-OCT showed a decrease of RNFL, RGIPL and retinal thickness in glaucoma patients. Within our sample all patients had several pathologic segments for all of the analyzed retinal layers. In most of the cases those segments were clustered. Further studies including larger numbers of patients to confirm our findings are advisable.

• F024 / 2456

Manual placement of SD-OCT peripapillary circle scan: possible influence on RNFLT classification and profile shape

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Purpose Automatic classification of peripapillary retinal nerve fiber layer thickness (RNFLT) with Spectral Domain OCT (SD-OCT) using a circle scan centered at the optic nerve head (ONH) is a standard test in glaucoma diagnosis. Possible influences of manual center selection on the double-hump (DH) shape of RNFLT profile and classification have been evaluated.

Methods SD-OCT (Spectralis , Heidelberg Engineering GmbH, Germany) standard circle scans were performed on 17 healthy eyes. Based on the infrared (IR) reflectance image, the center (C) of the circle scan was manually aligned to the ONH center and then shifted half way to the rim and on the rim at 3, 6, 9 and 12 o'clock position. Angle (AHP) and thickness (THP) of the highest peak in the superior and inferior RNFLT profile were calculated. Changes in RNFLT classification were analyzed.

Results Horizontal shift of C significantly affects the AHP. Temporal shift moves the DH together, nasal shift diverges it. Temporal or nasal shift results in higher changes of superior than inferior RNFLT profile. Vertical shift induces a significant difference between THP and AHP. Superior shift increases inferior THP, decreases superior THP and moves the DH slightly to the left. Inferior shift does the opposite. The first temporal shift changed normal RNFLT classification in 15 of 119 sectors: 10 borderline (BL), 5 outside normal limits (ONL). Shifting C further on the temporal rim changed 33 sectors: 9 to BL, 24 to ONL.

Conclusion Extreme decentration of the circle scan center (C) can significantly affect position and height of the RNFLT profile double hump (DH). If the RNFLT DH profile does not match the typical normal shape, decentration of C should be considered as a possible reason.

Commercial interest

• F025

Combined analysis of five observational studies evaluating the efficacy and tolerability of bimatoprost/timolol fixed combination in patients with primary open-angle glaucoma or ocular hypertension

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Purpose To evaluate the efficacy and tolerability of a fixed combination (FC) of bimatoprost 0.3 mg/ml and timolol 5.0 mg/ml (BTFC; Ganfort®) in patients with primary open-angle glaucoma (POAG) or ocular hypertension (OHT).

Methods This was a combined analysis of five prospective, observational studies involving 5556 patients from 830 centres in Germany, Switzerland, Netherlands, Austria and France. All treatment decisions were at the physician's discretion.

Results In the study population, 78% had POAG and the remainder had OHT. Patients were monitored for a median of 14 weeks. Overall, 93% (n = 5164) had received prior therapy; 47% receiving timolol. The most frequent reason for switching to BTFC (in 81% of patients with prior therapy) was insufficient intraocular pressure (IOP) control. Over the treatment period, mean IOP decreased from 21.5 to 16.1 mmHg with BTFC (25% reduction). BTFC reduced IOP in patients previously receiving prostaglandin monotherapy, β-blocker, carbonic anhydrase inhibitor (CAI) and FCs containing a prostaglandin or CAI plus β-blocker. In categorical analyses, physicians rated BTFC efficacy as 'very good' or 'good' in 86% of patients. BTFC tolerability was rated 'very good' or 'good' by 70% of physicians and 65% of patients. Adverse events were recorded for 9.7% (n = 541) of patients: the most common were eye irritation (2.8%) and ocular hyperaemia (2.2%).

Conclusion When used in a real-life clinical setting, BTFC was well tolerated and effective in the management of POAG and OHT.

Commercial interest

• F026

The impact of brimonidine on the loss of retinal nerve fiber layer (RNFL) thickness in glaucoma diabetic patients

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Purpose Brimonidine has proved protective effects on Retinal Ganglion Cells (in animal researches with intravitreal injection), but when used in topical application, its neuroprotective activity has not been unequivocally confirmed. A trail to evaluate potential neuroprotective effect of brimonidine on RNFL in Glaucoma patients.

Methods After a retrospective analysis of 1800 patients data, we selected 98, who revealed a significant RNFL thickness loss (21 had Diabetes). We compared the rate of RFNL loss between the group of 53 patients (100 eyes) treated with brimonidine and 45 (90 eyes) treated with other drugs.

Results In patients with well-controlled intraocular pressure (IOP) there is statistically significant relationship between the use of brimonidine and loss of RNFL thickness ($p < 0.01$) and an annual rate of RNFL loss ($p=0.01$).

Conclusion The potentially neuroprotective effect of brimonidine depends on IOP. The higher than normal IOP will limit this potential effect.

• F027

Effectivness of brimonidin and dorsolamid as additional therapy to beta-blockers-comparable analysis

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Purpose The aim of this survey is comparison of brimonidin and dorsolamid effect as an additional therapy for primary open angle glaucoma patients already treated with beta-blockers.

Methods Primary open angle glaucoma patients treated with beta-blockers and who had unregulated IOP were divided in two groups: the first one was additionally treated with 0,2% Brimonidin, and the second one with 2% Trusopt. The therapy was administered twice a day to all the patients. IOP and visual field changes and progression were followed up in next six months. Analysis and comparison of IOP and computerised visual field was done after 4, 12, 16 and 24 weeks from the treatment beginning.

Results We have followed up 80 patients in total, 40 in the group treated with 0,2% Brimonidin and 40 in the group treated with 2% Trusopt. 48 patients or 60% were women. We didn't noticed any significant differences in visual field defects progression during the six months period between these two groups, but middle IOP decrease was 4.2mmHg in the first and 3.0mmHg in the second; that presents high statistical significance. From 15.6% patients (13 in total; 6 in the 0.2% Brimonidin group and 7 in the 2% Trusopt group) with significant visual field defects at the end of study, 85% (11 patients) had those defects already in the first week, at the beginning of additional therapy.

Conclusion There was no statistically significant difference between these two groups in the visual field defects prevention and progression during six months period of treatment. Middle IOP decrease in these two groups was significant.Key words: glaucoma, optic nerve, 0.2% Brimonidin, 2% Dorsolamid, beta-blockers.

• F028 / 2457

Clinical trial for the evaluation of neuroprotective effects of palmitoylethanolamide: Visual Field and Pattern-ERG

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Purpose To study the effects of palmitoylethanolamide (PEA), a fatty acid ethanolamide, on IOP, visual field and pattern-ERG in glaucoma patients.

Methods 36 glaucoma (POAG) patients treated topically with timolol 0.5% were randomly assigned to either orally PEA 300 mg/die 2 times daily (Group A) or placebo (Group B). The patients had at least 5 VF tests using the Humphrey Visual Field Analyzer (Threshold 30-2) for more than a 2-year period before PEA treatment. At baseline and after 6, 12, 18, 24 months of treatments we evaluated in both groups the change of progression rate of visual field using mean deviation (MD), and pattern standard deviation (PSD). Comparison of means was performed with the paired t-test. The involvement of retinal ganglion cells (RGCs) were investigated using pattern electroretinograms (PERG) recorded twice a year in 36 glaucoma patients over at least 2 years.

Results Significative IOP reduction was observed in the Group A, PEA treated patients (16.94 ± 3.96 vs. 13.8 ± 3.24 mm Hg; $P < 0.001$).A statistically significant difference in the MD was found between the two groups (PEA treated, -2.9 dB±2.93; Placebo treated, -8.55 dB±6.51 P=0.001). Furthermore, the change in PSD reached statistical significance: PEA 2.63 dB ±1.47; Placebo 6.59 dB ±6.51 P=0.002. PERG amplitude decreased significantly ($P<0.01$) in patients treated with placebo compared with PEA. PEA tablets continued to be safe and well-tolerated, with no drug-related adverse events.

Conclusion These findings show substantial clinical benefits of PEA treatment in POAG patients:reduction of IOP as well as significative improvement in visual field and PERG.

• F029

Multiple topical administrations of Ramipril enhance retinal ganglion cell survival after transient retinal ischemia-reperfusion in rats

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Purpose The aim of the present study was to evaluate the protective effects of eye drops the angiotensin-converting enzyme (ACE) inhibitor ramipril on retinal ganglion cells (RGC) in a model of ischemia-reperfusion (I/R) injury in pigmented rat retina.

Methods Retinal I/R injury was induced in adult Long Evans rats by vascular ligation of the optic nerve for 45 minutes, after which reperfusion was immediately established. Rats were treated topically with Ramipril 2% or vehicle eyedrops three times before and after ischemia. Intraperitoneal injection of brimonidine (2 mg/kg) was used as reference. Post-ischemic retinal function was assessed by scotopic electroretinography (ERG) and RGC density by immunofluorescence on retinal flatmounts 8 days after ischemia.

Results In ischemic eyes, no ERG responses could be recorded immediately after reperfusion. They gradually recovered to approximately 75% of baseline 8 days after injury. Recoveries of the b-wave in the Ramipril- and brimonidine groups were better than those in the vehicle group. Severe RGC loss was also observed after I/R injury. However, Ramipril and brimonidine treatments significantly enhanced RGC survival (270.43 ± 87.57 cells/mm2 and 300.65 ± 92.48 cells/mm2), in comparison with the vehicle group (178.42 ± 107.81 cells/mm2).

Conclusion Multiple instillations of ramipril 2% enhanced rat RGC survival and retinal function in the ischemia-reperfusion injury model. This warrants further evaluation of the neuroprotective properties of ramipril in eye diseases.

Commercial interest

• F030

Efficacy and safety assessment of preservative-free latanoprost (T2345) versus Xalatan™ in ocular hypertensive or glaucomatous patients

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Purpose To assess the efficacy on intraocular pressure (IOP) and safety of preservative-free latanoprost (T2345) versus BAK-preserved latanoprost (Xalatan™) for the treatment of open-angle glaucoma (POAG) and ocular hypertension (OHT), through 2 clinical trials (phase II and III).

Methods A pilot phase II, cross-over, 6-week study with plasma samples was conducted in (2x15) patients. In an international investigator-masked, phase III study, 402 patients with POAG or OHT already controlled by Xalatan™ were randomized to receive either T2345 or Xalatan™ for 3 months, after a 5-week run-in period with brinzolamide and a 5-day wash-out period so as to achieve an IOP ≥ 22 mmHg at baseline. The main primary endpoint was the change in IOP at 9:00 am between D0 and D84 in the worse eye. Safety parameters were also assessed.

Results The mean IOP was reduced from baseline to D84 by 36% with T2345 (-8.6 ± 2.6 mmHg) and 38% with Xalatan™ (-9.0 ± 2.4 mmHg). These results met the limits set for non-inferiority of T2345 to Xalatan™. Conjunctival hyperaemia was less frequent on T2345 at D42 and D84 (20% vs. 30% on Xalatan™). Upon instillation, the subjective ocular symptom score was lower on T2345 than on Xalatan™ (p=0.001). The phase II study showed comparable efficacy on IOP of both products during the whole day (8am, 12am, 4pm and 8pm). After instillation, AUC(0-30) was 1086 ± 509 pg.min/mL on T2345 and 1379 ± 784 pg.min/mL on Xalatan™, suggestive of lower plasma concentrations of latanoprost on T2345 treatment (p=0.036).

Conclusion T2345 is the first preservative-free formulation of latanoprost, stable at room temperature, showing a non-inferior IOP lowering efficacy compared to Xalatan™, with improved local tolerance.

• F031

Relative efficacy and safety of preservative-free latanoprost (T2345) for the treatment of open-angle glaucoma and ocular hypertension. An adjusted indirect comparison meta-analysis

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Purpose Adjusted indirect comparison (AIC) were performed to assess the relative efficacy and tolerability of T2345 compared to the other prostaglandin analogs for the treatment of open-angle glaucoma (OAG) and ocular hypertension (OH)

Methods We performed a systematic literature review to identify randomized controlled trials evaluating prostaglandin analogs with or without preservative for the treatment of OAG and OH. AIC were conducted using Bucher's method. The main endpoints was intraocular pressure (IOP) measured at 3 months and hyperhemia or ocular redness

Results Twenty-one studies were included. No statistically significant difference in IOP were found between T2345 and BAK-free travoprost (mean difference and 95%CI 0.47 [-0.58;1.51]), bimatoprost (0.49 [-0.13;1.10]), bimatoprost 0.01% (0.19 [-0.69;1.06]), travoprost (.27 [-0.50;1.03]) and latanoprost (0.40 [-0.02;0.82]). T2345 was found statistically significantly superior to tafluprost (-0.90 [-1.52;-0.28]).For hyperhemia or ocular redness, T2345 was found statistically significantly superior to BAK-free travoprost (odds ratio 95% CI 0.30 [0.14;0.61]), bimatoprost (0.18 [0.10;0.33]), bimatoprost 0.01% (0.27 [0.13;0.56]), tafluprost (0.18 [0.05;0.65]), travoprost (0.25 [0.14;0.46]) and latanoprost (0.52 [0.31;0.86])

Conclusion In terms of efficacy on IOP, indirect comparisons never found T2345 statistically significantly inferior to the others. T2345 was found superior to tafluprost and an almost statistically significant trend was found in favor of bimatoprost for IOP. For hyperemia or ocular redness, T2345 latanoprost was statistically significantly superior to all the others

Commercial interest

• F032

Prostaglandin drug partitioning into contact lens material

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Purpose Patients who take topical ocular hypotensive medications are often instructed to remove their contact lenses prior to instilling the drug. These instructions have been based upon the known affinity that polymeric material has for the most commonly used ophthalmic preservatives. Newer, preservative-free agents, such as Saflutan® (tafluprost 0.015mg/ml), offer no direction to patients concerning contact lens wear.This study was conducted to determine if the possibility arises that tafluprost could partition between the solution phase (drug product formulation) and the contact lens polymeric material, thereby potentially impacting pharmokinetics and efficacy.

Methods Tafluprost 0.015mg/mL and bimatoprost 0.3mg/mL preservative-free solutions were added to single contact lens and incubated up to 2 hours at either 25 or 37 C. After the incubation interval, a 0.20 mL aliquot of product was withdrawn and diluted 10X in mobile phase for determination of drug concentration by reverse-phase ultrahigh performance liquid chromatography (RP-UPLC).

Results Tafluprost and bimatoprost partition from product solution into contact lens material rapidly (within 15 min). At 37 C, for all solution volumes tested, Fsoln for bimatoprost was approximately 2X higher than Fsoln for tafluprost.

Conclusion Both tafluprost and bimatoprost partition rapidly from product formulation into soft contact lens material. Tafluprost (logP = 4.2) is more hydrophobic than bimatoprost (logP = 3.2) and partitions more strongly than bimatoprost into contact lens material. This study demonstrates that contract lens wearers should remove lenses prior to instilling the product formulations. Lenses may be reinserted after drop instillation.

Commercial interest

• F033
Angle closure glaucoma associated with venlafaxine treatment

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Purpose Despite its very weak anticholinergic profile, there are few case reports linking venlafaxine treatment with angle closure glaucoma. One of the principal pathophysiological mechanisms suggested is through supraciliary effusions.

Methods We report a case of an 86 year old patient who presented with progressive symptoms of angle closure glaucoma in her left eye. Venlafaxine treatment had been started one week prior to presentation. Intraocular pressures were initially 22 mmHg in the right eye and 59 mmHg in the left eye. Ultrasound biomicroscopy (UBM) and gonioscopic exams were performed to better identify the pathophysiologic mechanism of her glaucoma.

Results Gonioscopy demonstrated a closed angle in the left eye and a narrow angle in the right eye. Venlafaxine was discontinued and an anti-glaucomatous treatment was started. There was bilateral resistance to 2% pilocarpine at presentation which subsided 48 hours after venlafaxine cessation. UBM demonstrated a plateau iris configuration with absence of supraciliary effusions.

Conclusion To our knowledge, this is the first case describing angle closure glaucoma associated with venlafaxine treatment, where there is a documented bilateral resistance to pilocarpine and an UBM demonstrating a plateau iris configuration with absence of ciliary body effusions. These findings suggest a mydriatic mechanism for our patient's glaucoma. The weak anticholinergic properties and the noradrenergic effect associated with venlafaxine could precipitate angle closure glaucoma without supraciliary effusions in a patient who is at risk for this condition.

• F034
Safety and efficacy of phacoemulsification and intraocular lens implantation in eyes with end-stage chronic angle-closure glaucoma

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Purpose To evaluate surgical outcomes of phacoemulsification and intraocular lens implantation in eyes with end-stage chronic angle-closure glaucoma (CACG).

Methods Patients with medically controlled end-stage CACG (mean deviation, < -19 dB) and clinically significant cataracts were enrolled in this prospective observational study. Standard phacoemulsification and intraocular lens implantation were performed. During at least 6 months of follow-up, changes in visual acuity, intraocular pressure, visual field parameters, and number of antiglaucoma agents used were assessed. Intraoperative and postoperative complications were documented. Multiple regression analysis was performed to identify independent predictors of postoperative visual outcome.

Results Twenty-two eyes of 19 subjects were enrolled. The mean follow-up period was 13.7 months (6–27 months). Corrected visual acuity improved from 0.63 ± 0.50 logarithm of the minimum angle of resolution (logMAR) preoperatively to 0.20 ± 0.31 logMAR postoperatively ($p < 0.001$). Intraocular pressure decreased from 14.05 ± 3.11 mmHg to 10.55 ± 1.79 mmHg ($p < 0.001$). No change was found in visual field parameters or number of antiglaucoma agents used. During surgery, 2 eyes had zonular dialysis and 1 eye had posterior capsule rupture. After surgery, 1 eye required additional trabeculectomy due to uncontrolled intraocular pressure after phacoemulsification. Preoperative visual acuity and mean sensitivities of 4 central points of the visual field were independent predictors of postoperative visual outcome.

Conclusion Phacoemulsification and intraocular lens implantation was performed safely and effectively in end-stage CACG eyes with cataracts.

• F035 / 2458
Case from hell in narrow angle glaucoma patient

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Purpose To present the complicated case of a young man with Bechterew uveitis and secondary glaucoma, who underwent glaucoma implant surgery.

Methods From the age of 8 years he presented with multiple attacks of anterior uveitis of his right eye. Each attack was treated with high dose of corticosteroids, leading to pressure rise. Quickly tampering the amount of steroids lead to reactivation of his uveitis. From 2011 on, he developed intraocular pressures up to 40 mmHg, treated with local drops and acetazolamide.

Results A tube implantation (Baerveldt 350) was performed with good eye pressure for the first 6 postoperative weeks continuing under maximal therapy (due to the Vicryl ligature).After these 6 weeks he developed multiple attacks of hypotony, for what an anterior chamber filling was performed each time with different types of viscoelasticum. After 3 attempts a bleb revision was performed, leading again to a massive intraocular pressure rise. Mainwhile the uveitis remained fairly inactive.

Conclusion Patients with juvenile rheumatoid arthritis often have a very difficult intraocular pressure regulation. Their response to a Baerveldt implantation is really unpredictable. It is either too high or too low.

• F036
Valuation of surgery in combination chamber angle lens

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Purpose To assess the variation of the chamber angle in glaucoma patients postphacotrabeculectomy primary open angle.

Methods Was measured by optical coherence tomography Fourier domain (Spectralis, Heidelberg Germany) the chamber angle in 30 patients diagnosed with primary open-angle glaucoma with cataract surgery combined before and postoperatively, performed with the same protocol and evaluated the difference of the angle pre-and postoperatively.

Results We observed a statistically significant increase in the chamber angle in patients undergoing phacotrabeculectomy

Conclusion The phacotrabeculectomy is a safe and effective procedure with minimal complications and good results of intraocular pressure and visual acuity postoperatively.

• F037 / 4457

Marginally controlled open angle glaucoma and cataract: sequential (1st phacoemulsification,2nd trabeculectomy) versus combined (phacotrabeculectomy) surgery

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Purpose glaucoma patients with borderline controlled intraocular pressure (IOP) may benefit from cataract surgery alone. However it is possible that these patients may need glaucoma surgery at some point in the future. Furthermore the risk of postoperative IOP spikes and the inconvenience of two operations (sequential) should be weighed against the complexity of the combined operation. The purpose of the study is to compare the results of phacotrabeculectomy with trabeculectomy in clear corneal incision pseudophacic eyes.

Methods retrospective study of 31 patients with visually significant cataract and open angle glaucoma with IOP 22-25 mmHg on topical medications. The patients were assigned to either surgical treatment according to their glaucoma severity. 20 patients underwent combined phacotrabeculectomy (two-sites) and 11 patients underwent sequential (1st phacoemulsification(temporal clear corneal incision with intraocular lens implantation), 2nd trabeculectomy). Antimetabolites and adjustable sutures were used in all glaucoma operations. IOP measurements were recorded. Follow up time was 6-18 months (median 12 months).

Results the effect of type of surgical treatment on postoperative IOPs was not statistically significant. Combined phacotrabeculectomy resulted in higher IOPs by 0.97(95% Confidence Interval [-1.6 3.59]) mmHg (p=0.47) versus sequential surgery.

Conclusion in patients with clinically significant cataract and glaucoma with borderline control of IOP the choice of combined (phacotrabeculectomy) versus sequential (1st phaco, 2nd trabeculectomy) surgery can be done according to the severity of glaucoma and based on surgeon's preference and experience.

• F038

Ex-press glaucoma shunt for the treatment of complex glaucoma

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Purpose To assess the safety and efficacy of Ex-PRESSMini glaucoma (EMG) shunt for the surgical treatmentof complex glaucoma.

Methods EMG shunt was inserted in the following cases of complex glaucoma: Failed glaucoma drainage surgery Multiple co-morbidity /high risk (proliferative diabetic retinopathy,neovascular glaucoma, vitreo-retinal surgery, OSD). Surgical procedure was in accordance with published methods.10 cases of complex glaucoma were reviewed retrospectively over aperiod at least 6 months following surgery. The end-points were:intraocular pressure (IOP)number of glaucoma drops usedvisual acuityUnqualified success was defined as IOP < 19 mmHgwithout glaucoma drops, and qualified success was IOP < 19 mmHgwith the use of drops. Complications were noted.

Results 7 cases (70%) were successful at a mean of 6 months postoperatively without drops with a mean IOP of 11.6mmHg (sd 1.6mmHg).3 cases required drops to achieve the target IOP, the meanIOP being 18.7mmHg (sd 0.8 mmHg) with a mean of 1.3glaucoma medications required at 6 months post-operatively. (3.7 pre-op 1.3 post-op, p<0.05)Cases requiring additional topical treatment had ocular co-morbidity.

Conclusion EMG shunt was safe and effective in controlling IOP in complex cases of glaucomaEMG shunt was relatively easy to insert with a minimum of post-operative manipulationsThe IOP was stable and predictable at 6 months; the IOP was reduced significantly at 6 months (p<0.05) with a significant reduction in medications (p<0.05)Multiple co-morbidities were associated with less chance of unqualified successAlthough a small cohort, the experience so far in treating complex cases with EMG shunt has been very encouraging and the study is continuing with more data being collected

• F039

Non penetrating deep sclerectomy versus trabeculectomy in bilateral primary open-angle glaucoma

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Purpose To establish the efficacy and safety of non penetrating deep sclerectomy versus trabeculectomy in primary open-angle glaucoma.

Methods A Prospective randomized trial of fifteen patients (30 eyes) with bilateral primary open angle glaucoma were included in the study. Eyes were randomly assigned to receive deep sclerectomy in one eye and trabeculectomy in the other eye. Outcome Measures included :mean intraocular pressure (IOP), postoperative medications, visual acuity, success rate, and complications.

Results At 12 months, mean IOP reduction was 11.5 +/- 3.5 (sclerectomy) versus 13.2 +/- 4,4mmHg (trabeculectomy) (P = 0.12), and an IOP </= 21 mmHg was achieved in 13 (86,6%) and 14 eyes (93.3%) (P = 0.9), respectively. Complications included two (13,3%) flat/shallow anterior chambers and one (6.6%) hypotony (trabeculectomy), whereas internal iris incarceration was encountered in two eyes (13,3%) (sclerectomy).

Conclusion Deep sclerectomy may provide comparable IOP reduction with fewer complications in management of primary open angle glaucoma.

• F040

Glaucoma surgery in a patient with prominent episcleral vessels

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Purpose We report a case of a patient with dilated episcleral veins of unknown etiology and with secondary open angle glaucoma, who developed ciliochoroidal effusion as result of an early glaucoma filtration surgery.

Methods Observational single case report. A 74-year-old male patient who had undergone sequential trabeculectomy for his both eyes, postoperatively he presented with redness of both the eyes and choroidal effusion, which was not resolved with conservative management (systemic steroid in tapering dose) or surgery. Slit-lamp biomicroscopy revealed dilated episcleral veins and the gonioscopy showed open angles with blood in Schlemm's canal in both eyes.

Results During follow-up, his intraocular pressure (IOP) remained in high thirties in the left eye (LE) and mid-twenties in the right eye (RE) despite anti-glaucoma medications and surgery. Systemic examination was negative for carotid cavernous fistula, low-grade dural arteriovenous fistula, dysthyroid ophthalmopathy or orbital tumor. The chest X-ray excluded any tumor at the apex of lung. Finally, the patient was admitted to the hospital for a right congestive heart failure and he was diagnosed with primary pulmonary hypertension (PPH) confirmed by physical examination, electrocardiogram and echocardiogram.

Conclusion Secondary glaucoma related to dilated episcleral veins is difficult to manage medically and surgical complications are also high. The underlying mechanism by which PPH causes uveal effusion is an increased pressure in the superior vena cava transmitted to the ophthalmic veins and choroidal circulation that lead to the excessively dilated and congested episcleral veins observed in our patient.

• F041

The morphological changes in the eye tissues during implantation drainages for glaucoma surgery

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Purpose to study experimentally the morphological changes in the eye tissues with implantation of different drainages for glaucoma surgery

Methods The experiment was conducted on 15 rabbits (30 eyes) breed «Gray Chinchilla» at the age of 4-6 months, the weight of 2-2,5 kg, without signs of ocular pathology. Animals were divided into 3 groups of 5 animals in each group. Deep sclerectomy and implantation of different drainages for glaucoma surgery was performed in all rabbits. Polymer triangular setons by digel were implanted to rabbits of 1 group, perforated drainages from digel - to rabbits of 2 group, lamellar collagen drainages - to rabbits of 3 group. After 6 months the animals were taken out of the experiment. We fixed enucleated rabbit eyes in 10% formalin solution, produced serial sections of thickness 20 microns, stained with hematoxylin - eosin

Results Histological studies of eyes in the late postoperative period showed that the polymer drainages from digel exist in the intraskleral cavity, the collagen drainage completely resorbed. The cavity is formed in the location of any drainage, but in the case of implantation digel drainage it is surrounded by a capsule. However, all drainage cavities is isolated, i.e. no messages subconjuctival or suprachoroidal space

Conclusion Thus, the drainages does not provide enhanced outflow of aqueous humor from the eye through the anastomosis in the late postoperative period.The reason of this is a fibrosis by intraskleral or subconjuktival level

• F042

Changes in anterior segment after-iridotomy with nd: yag laser for narrow angle measured with spectral domain OCT

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Purpose To evaluate the anterior chamber variations after-iridotomy with Nd: Yag laser in eyes with narrow angle.

Methods Twenty one patients with shalow anterior chamber were studied. Spectral domain OCT (Heidelberg, Germany) was performed before and seven days after laser peripheral iridotomy treatment in all cases. Spetial attention was taken to evaluate angle changes. Main measures were: anterior chamber volumen, central anterior chamber depth and temporal angle wide.

Results Thirty two eyes of twenty one patients , 15 females and 6 males, age average 66.28 years old were measured. The preoperative angle wide at the temporal angle was 25.9 ± 4,8 degrees and postoperative was 27.1 ± 10 degrees. Morphological changes were evident with a deeper chamber and disruption in iris parenchyma.

Conclusion Spectral domain OCT is a potential tool to evaluate changes in anterior chamber in narrow angle someted to iridotomy with Nd: Yag laser. The procedure is effective to increase anterior chamber volumen, central anterior chamber depth and angle wide in all cases.

• F043

Experimental application of high-frequency electric welding of biological tissues for iridoplasty and trabeculectomy

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Purpose To estimate the possibility of using of high-frequency electric welding of biological tissues for iridoplasty and trabeculectomy in the experiment.

Methods In experiment we used devices and instruments made by the original method in the E.O.Paton Electric Welding Institute. Experimental studies in vitro were performed on the isolated porcine eye. After dissection of the iris edges of the cut combined with a bipolar instrument. In the second phase studied the possibility of using the method of high-frequency electric welding (frequency - 66 kHz - 440 kHz) for trabeculectomy with monopolar electrode, which was injected into the anterior chamber through the corneal incision. The second electrode was fixed to the sclera with special clip. For experiment in vivo we used 10 chinchilla rabbits. Morphological studies of the samples were performed.

Results We have observed the formation of solid welded connection of cut edges of the iris. In vitro trabecular tissue of the anterior chamber angle was removed using different settings. In vivo during iridoplasty observed minimal changes in the surrounding tissues in the area of electrical effects. It was also noted the formation of solid welded connection of iris edges. In vivo were removed structures of the anterior chamber angle of the rabbit without bleeding complications.

Conclusion These results indicate the possibility of using the method of high-frequency electric welding of biological tissues for microsurgery of the eye trabecular apparatus and iris. Requires further study of the characteristics of the developed method for working out the optimal parameters of exposure.

• F044

Ultrasonic circular cyclo coagulation in patients with primary open-angle glaucoma: preliminary results of a multicenter clinical trial

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Purpose To evaluate the efficacy and safety of the Ultrasonic Circular Cyclo Coagulation (UC3) procedure in patients with primary open-angle glaucoma (POAG).

Methods Prospective multicenter clinical trial. 39 eyes of 39 patients with POAG, intraocular pressure (IOP) > 21 mmHg, an average of 1.65 failed previous surgeries and an average of 3.2 hypotensive medications were insonified with a probe comprising 6 piezoelectric transducers. 18 patients (group 1) were treated with a 4 seconds exposure time for each shot and 21 patients (group 2) with a 6 seconds exposure time. Follow-up visits were performed at 1 day, 1 week, 1, 2, 3, 6 and 12 months after.

Results IOP was significantly reduced in both groups ($p<0.05$), from a mean preoperative value of 28.9 ± 6.8 mmHg in group 1 and 29.2 ± 6.9 mmHg in group 2 to a mean value of 18.1 ± 4.4 mmHg in group 1 and 16.1 ± 8,5 mmHg in group 2 at last follow-up. Success (IOP reduction >20%) was achieved in 15 of 18 (83%) eyes of the group 1 with an average of IOP decrease of 42% and in 19 of 21 (90%) eyes of the group 2 with an average of IOP decrease of 49%. No major intra- or post-operative complications occurred.

Conclusion UC3 seems to be an effective and well-tolerated method to reduce intraocular pressure in patients with POAG.

Commercial interest

• F045

Efficacy of pneumatic trabeculoplasty in patients with primary open angle glaucoma and ocular hypertension in combination with prostaglandin monotherapy

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Purpose To evaluate the safety and efficacy of pneumatic trabeculoplasty (PNT), a non invasive treatment to lower intraocular pressure (IOP), in patients with primary open angle glaucoma or ocular hypertension under prostaglandin monotherapy.

Methods 38 patients were enrolled from may 2009 to october 2010 to determine the IOP lowering effects of PNT. All the eyes had been diagnosed primary open angle glaucoma (87%) or ocular hypertension. PNT was performed in one or both eyes at day 0, 7, 90 and 180. Assessments were peformed at day 0,7, 45, 90 and 180 including visual acuity, IOP by goldmann tonometer, slit lamp examination and optic disc evaluation. Safety was adressed at all visits. A 15% reduction of IOP defined responder patients.

Results Mean IOP before PNT was 23.21 +/- 2,92 mmHg. 57 eyes were treated and analysed. All patients completed 6 months of follow up. After PNT, a statistically significant reduction of IOP occured at all visits: at days 7, 45, 90, 180, IOP was 19,92+/-5,05, 19,32+/-5,22, 18,89+/-5,00, 17,76+/-4,81 mmHg ($p<0,05$). The IOP decrease was up to 23,4% at day 180. The rate of responder patients was 54,4% after one week and 76,4% at day 180. After 6 months, 76% patients had IOP reduction more than 15%, 69% more than 20%, 51% more than 25% and 46% more than 30%. Side effects such as conjunctival hyperhaemia, subconjunctival hemorrhage and corneal epithelium disorder occured. No significant complications were observed.

Conclusion PNT seems to be a safe technique allowing a significant IOP reduction with prostaglandin monotherapy. It could be helpful especially in patients having troubles in following their local treatment correctly.

• F046

Epidemiology of primary congenital glaucoma: a study lasting 11 years

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Purpose Primary congenital glaucoma is a rare affection, which could lead to blindness. Till now in France, few epidemiological and clinical data are available. This study aims to determine epidemiological factors found in the children affected by severe primitive congenital glaucoma requiring surgery.

Methods This retrospective study including patients diagnosed for primitive congenital glaucoma was led between January, 2000 and November, 2011 in a department of Pediatric Ophthalmology of the South of France. Studied parameters were: age at the time of diagnosis, gender, presenting signs, hereditary and environmental factors, prematurity and medical histories to determine the epidemiological characteristics of these children.

Results 60 children were included in the study, classified in early congenital glaucoma (n = 26 either 44 %), infantile (n = 24 or 40 %) or late (n = 10 or 16 %) according to the age of diagnosis. The average age of diagnosis was respectively of 3.8, 8 and 35 months. The sex ratio was 1,1 times more boys than girls. The most common presenting signs were megalocornea (65 %), stromal scars (30 %), watering eyes (26 %), photophobia (21 %) or the association of some of these criteria (39 %). A family history of congenital glaucoma in the first degree exists for 14 % of the children and the rate of consanguinity recorded between the parents is 14 %. The rate of prematurity is 12 %. Seven children (12 %) presented a polymalformative syndrome and six patients (15 %) neurological disorders with delay of psychomotor development.

Conclusion This French study led over a long-term period and on a large cohort shows results comparable to those found in the international literature for similar populations.

• F047

Megalocornea, iris desinsertion and crystalline luxation in congenital glaucoma

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Purpose To present a case report of a patient with congenital glaucoma and megalocornea, who suffer iris desinsertion and crystalline luxation during adulthood.

Methods We present a 46-year-old male with bilateral congenital glaucoma treated with bilateral goniotomy in pediatric age and right eye (RE) blind after a traumatism. He refered visual acuity (VA) loss in his left eye (LE). The visual acuity was light perception in RE and count fingers at 50 cm in LE. Ophthalmological exams evidenced asymmetric bilateral buphthalmos. The LE shows 21 mm of diameter corneal, transparent cornea, severe iridodonesis, 360º iris desinsertion, afaquia, and 22 mmHg of intraocular pressure by applanation tonometry. This eye was treated with dorzolamide and timolol maleate. Posterior luxation of the crystalline was found in the ophthalmic ultrasound.

Results A +14 diopters lens provided the best corrected visual performance achievable of 0.05 with LE. Non-invasive treatment was selected in order to avoid surgery complications.

Conclusion Ophthalmologists should to monitor intraocular pressure and corneal diameter in patients with congenital glaucoma because increase in corneal diameter is a biomarker of progression of glaucoma. In these patients, interdisciplinary valuation of systemic and ophthalmological findings should be performed.

• F048

Glaucomatous optic neuropathy complicated by pituitary adenoma: case report

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Purpose The authors report on a case of Glaucomatous optic neuropathy complicated by pituitary adenoma

Methods Caucasian 54 year old male patient. At the age of 2 divergent strabismus in both eyes and amblyopia in left eye was present; surgical correction for strabismus of both eyes at the age of 7.Since 2000 primary open angle glaucoma in both eyes treated with medical therapy (initially with beta blockers, and later adding carbonic anhydrase inhibitors): mean intraocular pressure of 16 mmHg. Visual field defects typical of glaucomatous optic neuropathy were present and stable over time. The patient underwent surgical removal of cataract in 2007 and 2009 in each respective eye.

Results During 2009 very fast deterioration of the visual field in both eyes (OD>OS) with well-controlled intra ocular pressure (IOP) with medication. No neurological symptoms associated.Magnetic resonance imaging (MRI) of the brain showed a macro pituitary adenoma compressing the optic chiasm. In 2010 the patient underwent surgical removal of the adenoma.

Conclusion After removal of the pituitary adenoma and decompression of the optic nerve, the visual fields over the past two years have remained stable with the same defects greater in the right eye than in the left eye.However, the visual quality continues to deteriorate possibly due to surgical intrasellar herniation of the optic nerve.

• F049

Experimental glaucoma model using polyurethane microbeads in rats

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Purpose To establish a new experimental glaucoma model using intracameral injection with various microbeads of different sizes and materials.

Methods Chronic elevation of intraocular pressure (IOP) was induced by unilateral microbeads injection into the anterior chamber of Sprague-Dawley (SD) rats. The effectiveness of different materials (polymethylmethacrylate (PMMA, 7 and 15 μm), polyurethane (PU, 7 and 17 μm), Silica (13 μm)) on IOP elevation was compared. Reinjection of the microbeads was performed at post-injection day 7. Difference of IOP between both eyes was observed for 4 weeks. Axonal degeneration was assessed by the analysis of light microscopic and transmission electron microscopic photos.

Results Total 54 SD rats weighing 250~300g initially were included in this study. After a single injection, the ratio of increased IOPs (mean value) at post-injection day 3 were 56.6 %, 24.1 %, 23.8 %, 98.1 %, and 153.0 % in PMMA 7 μm, PMMA 15 μm, PU 7 μm, PU 17 μm, and Silica 13 μm, respectively. Since inter-animal variability of PU 17 μm injected group was smaller than others, so that it was more adequate to produce constant IOP elevation with good repeatability (whereas Silica injected eyes showed severe inflammation). Sustained elevation of IOP by twice of PU 17 μm injection for at least 4 weeks resulted in approximately a 25.5 % loss of axon density (p=0.023, Mann-Whitney U test). No axonal damage was noted in safety study group.

Conclusion These data supports that the polyurethane microbeads injection is an applicable and versatile model for high tension glaucoma in rats. Among several biomaterials, PU showed more stable IOP elevation with safety. Future studies about suitable size and biomaterial of microbeads are more needed to secure this novel model.

• F050 / 4657

Retinal MMP expression is upregulated in an excitotoxic mouse model of glaucoma

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Purpose Multiple studies in glaucoma patients and animal models, have reported differential expression and activity of matrix metalloproteinases (MMPs). These data have led to the hypothesis that MMPs are involved in glaucoma disease onset and/or progression. However, their in vivo functions remain poorly understood and contradictorily results prevent a clear definition of their role. Here, we describe the expression of MMP-2, -3, -9 and -14 in the retina of mice subjected to an acute excitotoxic glaucoma model.

Methods Excitotoxic RGC death was induced via intravitreal injection of 20 mM NMDA. Expression of MMP-2, -3, -9 and -14 was examined via immunohistochemistry, Western blot and quantitative RT-PCR.

Results MMP-2 and -3 are expressed by glia, presumably Müller glia, in the healthy retina and are strongly upregulated at 24h after NMDA injection. MMP-9 expression, which is not detectable in naive retinas, is observed in RGCs at 24h post NMDA injection, which confirms its suggested role in RGC apoptosis. In the naive retina, MMP-14 is expressed by bundles of RGC axons in the nerve fiber layer, from where its expression is extending through the optic nerve to the primary visual areas in the brain. Within the first 48h after NMDA injection, MMP-14 expression increases and is also seen in the inner nuclear layer and both plexiform layers.

Conclusion Our results reveal a strong upregulation of MMP-2, -3, -9 and -14 in the mouse retina after NMDA injection, suggesting that these proteinases might be involved in excitotoxic neurodegeneration and/or glial reactivity. Further analysis of their involvement, including studies in MMP knockout mice, is currently ongoing.

• F051

Experimental glaucoma model in two lines of rats using polystyren microspheres (Bead Model)

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Purpose The purpose of this study is to develop a method to get simple and reproducible rodent glaucoma model in rats of Wistar and Long-Evans line. The intraocular pressure (IOP) and loss of number of retinal ganglion cells (RGCs) were measured to evaluate the success of model.

Methods 20 male rats were used in this study. 7 of them were excluded because of incidence of eye inflammation. Finally 13 rats (6 Wistar rats and 7 of Long-Evans lines with a mass about 200 g) were included. IOP was elevated by injection of polystyrene microbeads into the anterior chamber and measured by Icare TonoLab. For each rat, the right eye was treated with different combinations of polystyrene microspheres with a diameter of 6 and 1 um separately and the left eye was treated as a control. RGCs were labeled retrogradely with a fluorescent marker "FluoroGold" 5 days before euthanasia and after harvested and made slices for a counting of surviving ganglion cells.

Results Mean intraocular pressure (IOP) of examined group was 24 mmHg ± 5,4. The highest IOP appeared after injection on 3rd day, and rose a bit lasting till 21st day. The mean IOP in contralateral eyes during experiment was 10,8 mmHg ± 0,5. Mean number of RGCs in eyes with elevated IOP was 3014±655 cells (semiquantitative method was used). In control group it was 4106±852 cells. In examined group values of IOP were significantly higher and number of RGCs was significantly lower according to control eyes.

Conclusion "Bead model" method could be used to create rat model of glaucoma with stable increasd IOP. The different size microspheres could provide the IOP with the desired values.

• F052

IOP lowering effect of low intensity ultrasound on experimental glaucoma model using microbeads in rats

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Purpose To report the intraocular pressure (IOP) lowering effect of low intensity ultrasound (LIUS) on eyes of ocular hypertensive rats.

Methods Continuous radiation of LIUS on ocular hypertensive eyes induced by unilateral microbeads injection was performed. A round plane ultrasound transducer operating at a frequency of 1MHz was utilized to deliver a sonication of 240mW/cm2 in acoustic intensity. LIUS was treated on both eyes of rats (n=5) simultaneously and the IOP measurements of treated group were compared with those of untreated group (n=5).

Results The mean IOPs of LIUS-treated eyes and un-treated eyes were 9.4 ± 0.55 mmHg and 9.6 ± 0.55 mmHg, respectively at baseline. After an intracameral injection of microbeads, IOPs were reached to 18.6 ± 4.037 mmHg and 22.8 ± 3.493 mmHg (p=0.580) at 3 days after microbeads injection. Then the IOPs were decreased by 39.47 % and 9.68 % at 1 day after a single sonication.

Conclusion These results showed that continuous low intensity ultrasound suppresses the IOP elevation in experimental glaucoma model using microbeads injection into anterior chamber. By the reason of its non-invasiveness and repeatability, LIUS could be an alternative method for glaucoma treatment in near future.

• F053

Controlled pupilar miosis to improve mesopic visual function in drivers over 40 years old

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Purpose To evaluate the influence of a diffuse illumination device located outside the field of vision that provokes a controlled pupillar miosis, on the visual acuity and contrast sensitivity in drivers tested in mesopic conditions

Methods Cross-sectional prospective observational study in which visual Acuity 100% and 20% contrast by ETDRS Test (VA100 and VA20) and Contrast Sensitivity by Pelli-Robson Test (CS) were evaluated in 39 drivers individuals under 40 years old and 30 drivers over 40. The study was carried out in a simulated setting for night driving with and without the interposition of the diffuse illumination device

Results In individuals aged over 40 years, an statistically significant improvement of visual function was exhibit. Baseline visual acuity and contrast sensitivity scores were: VA100=0.02±0.18logMAR, VA20=0.21±0.2logMAR, and CS=0.62±0.32, whereas values for the interposition of diffuse illumination device were: VA100=-0.03±0.14logMAR(p=0.02), VA20=0.19±0.17logMAR(p=0.3), and CS=0.76±0.33(p=0.0003). On the other hand, in drivers aged under 40, statistically significance was not found. In this condition, baseline visual function was: VA100=-0.1±0.11logMAR, VA20=0.13±0.19logMAR, and CS=1.06±0.2, whereas the interposition of the mentioned system showed the following values: VA100=0.01±0.09logMAR(p=0.9), VA20=0.09±0.14logMAR(p=0.3), and CS=1.08±0.16(p=0.6)

Conclusion Using diffuse illumination device in the interior of the vehicle, provides significant improvement in both high contrast visual acuity and contrast sensitivity in the group older than 40 years

• F054

Changes in contrast sensitivity perception due to protector screens for welding tasks: conventional protective optical filter vs novel protective optical filter of selective absorbance

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Purpose To evaluate differences in contrast sensitivity perception in central visual field using protective optic filters for welding tasks. Two interposed filters are compared: a conventional protective optical filter and a new protective optical filter with selective absorption designed by University Complutense of Madrid (UCM).

Methods 36 people of working-age were included in a cross-sectional prospective observational study. Contrast sensitivity threshold in central visual field was evaluated using FDT Perimeter, C-20 procedure (Humphrey systems, USA). Three conditions were set: a) without optical filters; b) with an interposition of conventional protective optical filter for welding (shade 2.5) and c) with an interposition of a novel protective optical filter of selective absorbance that fully blocks the short wavelength light and minimally attenuates the remaining bands of the visible spectrum.

Results Contrast sensitivity in all visual field areas evaluated diminished 91-98% with the conventional protective optical filters. UCM optical filters provoked a low-level decrease in contrast sensitivity (9-19%). Mean contrast sensitivity thresholds were 29.5±5dB, 25.5±4dB, 1.8±2dB in conditions a, b and c respectively

Conclusion Conventional optical filters resulted in drastically diminished contrast sensitivity. UCM optical filter minimally diminish the visual function, allowing a suitable visibility and also maintaining an appropriate level of protection against phototoxic damage.

• F055

Vision quality in population research of children and adolescents in Siemianowice Slaskie (southern Poland)

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Purpose The aim of this study was to determine the quality of vision, refraction, and aberrations in a group of children and adolescens in selected schools of the city Siemianowice Slaskie (Southern Poland).

Methods Visual quality was evaluated as visual acuity measured with two methods: OPTEC® Vision Tester and FrACT computer programme as well as contrast threshold for 30 arc min size optotypes. Refraction was determined with Topcon KR-1W aberrometer which enables its measuring with "refractor" method or its calculation from low-order Zernike aberrations.

Results Totally 556 children aged from 8-to-17 years (average age 13.87, standard deviation 2.29), were investigated. Visual acuity varied within great range, but average value remained almost constant on the level slightly better that V = 5/5 (ca. -0.06 logMAR) in the group whithout vision problems. In the group of children with detected refraction errors (wearing glasses) average visual acuity decreased by 0.1 log units in every 5 years.There was high correlation between contrast threshold and visual acuity. We noticed an increase in the average spherical error in the amount of –0.5 D in the time interval of about 5 years.

Conclusion Both methods testing visual acuity investigated by the authors are comparable and may be used as screening for children. The FrACT test for screening visual acuity and contrast is a method that would be appropriate to be used in children and teenagers in view of its similarity to computer games and its short time duration. The distribution of visual defects is comparable to that found in other screening tests on the Polish and European populations.

• F056

Morphometrical indices in acquired myopia

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Purpose On an etiology myopia can be congenital and acquired (school myopia), and on character of development – stable and progressing. According to experimental works (Ai L, Li J, Guan H, Wildsoet CF,2009, Nickla DL, Wildsoet CF, Troilo D., 2002) it is known, that the thickness of a retina varies at eyeball growth, and also at defocus change. The probability of myopia growth in each patient remains difficult to predict. The purpose was to reveal differences in patients with acquired myopia and divide them on studied indices

Methods A child of 7-15 years old (53) with myopia were observed, a criterion of inclusion in research was acquired myopia. Parameters which were studied: visual acuity, refraction, axis length of an eye, accommodation reserves, intraocular pressure, retina layer thickness and peripapillary fiber layer thickness, optic nerve disk indices by optical coherent tomography under standard protocols by SOCT Copernicus, Optopol Technology Sp.z o.o., Poland

Results Optimum points of division of acquired myopia on stable and progressing were established by ROC analysis. The discriminate analysis with high reliability has shown, that the progressing form of myopia will be observed in children with average thickness in a zone 3mm more than 246,3mk , with a refraction more than 4,5 dptr and axes more than 25,3mm (P=0,0001). Fisher's discriminating functions are defined and the equations for definition of the stable and progressing forms of acquired myopia are offered. Effect of classification is 80,3%.

Conclusion Results have allowed to offer model of classification for the stable and progressing forms of myopia on morfometric indices, axis length and refraction in patients with acquired myopia

• F057

Mesopic pupil amplitude depending on the age and the wavelenght of the stimuli

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Purpose In the present study, values of the phases of pupil light reflex were recorded and analyzed depending on the age, and the spectral content of the incident light, in order to determine changes on the pupil light reflex by means of various types of lights and compare their effects in every sub-sample and between them.

Methods The sample consists in 30 old subjects and 32 young subjects. To evaluate possible dementia in old subjects, the clock drawing test was applied. The pupillometer used was Power Refractor II, a binocular, infrared based instrument and autorefractometer. Four optical filters were interposed on the flash: a neutral density filter 05, and three interferential filters with peaks of transmission in 450 nm, 510 nm and 600 nm. Our team designed a parser programmed in java that calculates all the variables implicated.

Results In the old age group, the average amplitude were 1.23 ±0.3 mm, 1.03 ± 0.3 mm, 1.11 ± 0.4 mm, and 0.85 ± 0.3 mm for white light, blue monochrome light, green monochrome light and red monochrome light, respectively. In the young age group, the average amplitude to white light was 2.29 ± 0.4 mm, and the average amplitude for blue, green and red monochrome lights were, respectively, 1.91 ± 0.3 mm, 2.04 ± 0.5 mm, and 1.60 ± 0.6 mm. Both groups exhibited a similar behaviour when reactions were compared depending on the different wavelength.

Conclusion Age affects considerably to mesopic pupil amplitudes values provoked for luminous stimuli. Likewise, blue and green monochrome lights bias the response in both groups.

• F058

Undercorrection of refractive error and cognitive function. The Beijing Eye Study 2011

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Purpose To assess whether ocular parameters are associated with the level of cognitive function.

Methods The Beijing Eye Study is a population-based study performed in rural and urban regions of Greater Beijing. The study included 3469 individuals (56.6%) women) with a mean age of 64.6+/-9.8 years (range: 50-93 years). A detailed ophthalmic and medical examination was performed. The cognitive function score was measured by the MMSE (mini mental state examination) scale.

Results Cognitive function measurements were available for 3127 (90.1%) study participants (56.5%) women). The mean cognitive function score was 26.3+/-3.7 (median: 27; range: 2-30). In multivariate analysis, after adjustment for older age (P<0.001; standardized coefficient beta:0.14), male gender (P=0.003;beta:0.06), urban region of habitation (P=0.005;beta:0.07), lower body height (P=0.001;beta:0.07), lower level of education (P<0.001;beta:0.56), type of occupation (P=0.004;beta:0.08), higher score of psychic depression (P<0.001;beta:0.06), lower self-reported history of cardiovascular disorder (P=0.02;beta:0.07), decreasing cognitive function score was significantly associated with lower BCVA (P<0.001;beta:0.11), higher amount of undercorrection of refractive error (P=0.004;beta:0.04) and non-wearing of glasses (P<0.001;beta:0.09).

Conclusion After adjustment for systemic parameters and BCVA, the cognitive score was significantly higher in subjects wearing glasses and simultaneously, in subjects with less undercorrection of their refractive error. Although the longitudinal cause-effect relationship could not be addressed in this cross-sectional study, the results are in agreement with that correction of refractive errors may be useful to reduce the risk of cognitive under-functioning.

• F059

Eye refraction: a comparative study between autorefractometer, aberrometer and subjective test

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Purpose To compare the ocular refractions given by three different techniques and to determine which provides better visual comfort.

Methods All subjects underwent a completed optometric examination including clinical history, biomicroscopy of the anterior segment, subjective best corrected visual acuity, autoref/keratometer WAM-5500 and aberrometer iTrace. Monocular measurements were made under natural accommodation and pupil size. The conditions of the tests were vertex distance 12mm, resolution of the refraction 0.12D, distance 7m and 3 measures each time. Subjects were classified as myopic group (20 eyes) if they presented subjective refraction ≥|-0.50|D and low-hyperopic/emmetropic group (22 eyes) if their subjective refraction was <|-0.50|D. The equipments were calibrated with an artificial eye before the tests were done.

Results Subjects chose as the best refractive option the subjective refraction (over 50% in all cases). In hyperopic/emmetropic eyes, subjective refraction showed smaller spheric values (0.22 and 0.18 D comparing to the autorefractor and the aberrometer respectively) and cylinder (0.17 D and 0.21 D, respectively), whereas in the myopic group, the autorefractor gave higher spheric values (0.21 and 0.26D comapring to the aberrometer and the subjective method respectively).

Conclusion Most subjects involved in the present study achieved a better visual comfort with subjective refraction. Significant differences among the three techniques were found, although objective methods represent a good approximation to the refraction.

• F060

Fish-eye disease with retinal involvement associated with mutation in the LCAT gene

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Purpose A 38-year-old Egyptian man was referred to our department due to bilateral loss of vision over a six-year period.Slit lamp examination revealed extensive bilateral corneal opacitiesBlood analysis revealed lipid metabolism abnormalities with a lack of plasma alpha-lecithin:cholesterol acyltransferase (LCAT) (high-density) activity

Methods We used PCR to amplify, to sequence and to determine the genotype of the LCAT gene. Direct sequencing of the six exons of the gene (figure 2) revealed a new homozygous mutation in exon 1 confirming the diagnosis of Fish Eye Disease (FED). This new homozygous mutation caused a C-to-T transition, resulting in a substitution of a leucine by a proline at position 34 of the protein.

Results We performed a penetrating keratoplasty on right eye in december 2004. Despite a clear graft with normal anterior segment and normal fundoscopy, the patient did not recover significant visual acuity from the graft. His visual acuity was 20/100 on right eye .Visual Evoked potential and neuroimaging was normal, but electroretinography revealed a bilateral maculopathy.

Conclusion Similarly to what occurs in cornea ,retinal deposits could explain the macular involvement we have discovered in Fish eye disease. Full-thickness corneal transplantation should be performed in cases of severe corneal opacification with impaired vision, but success of keratoplasty could be limited by visual impairement due to retinal degeneration. The indication for perforating keratoplasty has to be thought very carefully in these multimorbid patients.

• F061

Relationship between visual acuity and other optical parameters in no presbyopic eyes

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Purpose To study the relationship between visual acuity (VA) and fluctuation of accommodation and aberrometric data in a population of no presbyopic eyes.

Methods Forty-two no presbyopic eyes with natural pupil and scotopic lighting conditions were involved in the study. Subjects were studied with an autorefractor to determine the refraction and accommodation fluctuations, a ray tracing aberrometer to measure the refraction as well as aberrometric data, and a system to generate charts and determine the subjective refraction and the AV. The equipments were calibrated with an artificial eye before the tests were done. The subjects were divided in several subgroups of 1) subjective refraction (≥|-0.50|D or <|-0.50|D); 2) fluctuation of accommodation (≤0.1D or >0.1D) and 3) RMS of different high order (HO) aberrations: 3a) RMS of HO total (≤0.25µm or >0.25µm), 3b) RMS of spherical aberration (≤0.15µm or >0.15µm), 3c) RMS of coma (≤0.15µm or >0.15µm) and 2d) RMS of trefoil (≤0.15µm or >0.15µm)

Results The mean value for VA was 1.28 and 0.16 D for fluctuations of accommodation. No significant differences among fluctuations of accommodation and VA were found in any group. We found normal values about RMS of HO (0.34 µm), RMS of coma (0.19 µm), RMS of trefoil (0.17 µm) and spherical aberration (0.11 µm). No differences between RMS and VA were found in any group. A moderate correlation (R2=0.19) between the VA and the spherical aberration was observed.

Conclusion The values of fluctuation of accommodation and aberrometric data were within normal ranges reported in the literature. Differences between VA and other optical parameters were not found.

• F062

The effect of simplified and traditional chinese character on accommodative reponses in myopes and emmtropes

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Purpose This study investigated the effect of simplified and traditional chinese character on accommodative lag, accommodation microfluctuation, near work-induced transient myopia (NITM) during the near task as well as the subsequent decay time. We aimed to analyze if the traditional Chinese character had the trend of inducing the myopia progress.

Methods Young adults were classified into emmetropes and myopes . Two size (12pt,8pt) and two type (simplified and traditional chinese character) were used to give four different reading targets on computer screen. It was presented in random order at 25 cm and was read for 5min. For each target, accommodation response , accommodation microfluctuation NITM and its decay were measured using the free space Grand-Seiko auto-refractor.

Results For myopic subjects, accommodation microfluctuation was greater for traditional chinese character 0.35±0.17 D than for simplified chinese character: 0.29 ±0.11 D, (p=0.017) ,NITM was larger for traditional chinese traditional character 0.61±0.34 D than for simplified chinese character 0.53±0.33 D,p=0.028, however there was no difference in emmetropic subjects. Myopes had larger accommodation microfluctuation 0.35±0.17 D than emmetrope 0.24±0.11 D p=0.02,myopes had greater NITM0.61±0.34 D than emmetropes 0.42±0.25 D P=0.013. For all targets, The accommodative lag of myopes is 0.74±0.32 D while the emmetropes 0.53±0.35 D P=0.000 ;The decay time for myopes was15.88±19.53 seconds while the emmetropes 9.04±12.62 seconds P=0.012.

Conclusion The study showed that compare to the simplified Chinese character, the traditional chinese character had significant effect on myopic subjects, it may be more susceptible of inducing the myopia progress.

• F063

Evaluation of magnitude and phase of sweep-visual evoked potentials

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Purpose Sweep visual evoked potentials (SVEP) are frequently used for the assessment of visual acuity. Several studies have shown the presence in a significant number of subjects of a reduction of the response amplitude ("notch") at intermediate spatial frequencies. The purpose of this study was to evaluate if this reduction of amplitude was related to a change in phase of the response.

Methods SVEP records from 16 subjects presenting a notch were analyzed. The sweeps were performed with a checkerboard pattern reversing at a frequency of 12 Hz. The duration of the sweep was 12 seconds and a Fourier analysis was performed over a sliding time window. A vector average was calculated over the different sweeps recorded from each subject and the resulting magnitude and phase were plotted for the 2nd (12Hz) harmonic.

Results The amplitude notch was found between 1.5 and 3 CPD. It was systematically correlated with a discontinuity of phase, typically constant for spatial frequency below the notch and increasing at a constant rate above that frequency. A numerical simulation pas performed to evaluate the effect of phase changes and demonstrated that a discontinuity of phase can produce a transient reduction in the measurement of magnitude similar to the notch found in the responses of some subjects.

Conclusion This result gives a new possible interpretation for the notch found in SVEP responses of some subjects. It may help understand underlying physiological mechanisms. It also suggests that new algorithms taking into account phase changes may be more appropriate to analyze SVEP responses.

Commercial interest

• F064

Spatial tuning affects diagnostic efficacy of pseudoisochromatic plates

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Purpose To demonstrate that the diagnostic efficacy of pseudoisochromatic plates is reduced by oversized and by undersized angles of observation.

Methods Pseudoisochromatic "C" and "E" plates accounting for equal demands on color vision in repeated exams were presented to 7 daltonian and 10 normal observers. An illuminant D 65 source (Unity Color Light2go) rendered 170 cd/m2 of luminance. The standard viewing time was 3 s, the viewing angles were 33.4°, 7.4° and 1.8°.

Results Daltonians failed to recognize the plates at 7.4° of visual angle which correspondes to the recommended standard viewing distance. At a viewing angle of 33.4° the plates were recognized by 4 of 7 Daltonians. At a viewing angle of 1.8° the plates were recognized by 3 of 7 Daltonians. With 1.8° of viewing angle, normal observers claimed fusion of i) those various pseudoisochromatic picture elements which are on the red side of yellow, and of ii) those various elements which are on the green side.

Conclusion A standardized observation distance (0,7 m) is necessary for pseudoisochromatic plates, as recommended by Ishihara and Velhagen. At small viewing angle, antagonistic processing of colored picture elements is impaired, causing loss of optotype camouflage. At large viewing angle, individual elements may activate weak color opponent mechanisms in a daltonian retina where green cones or red cones are scarce but not entirely lacking. Poster visitors may observe spatial tuning within their own color vision.

Commercial interest

• F065

Visual capacity in albino mice. Are albino mice good for every neuroscience's experiment?

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Purpose To show the visual capacity in two different albino mice (NMRI and CD1).

Methods 66 albino mice from two mice's strains were analyzed: CD1 and NMRI, obtained about from two different organizations. Full field Electroretinogram was used in the functional analysis. The recommendation of the International Society for the Clinical Electrophysiology of Vision (ISCEV) was followed. Furthermore, we recorded ERG responses at chromatic sensitivity. We have compared immunohistoquimical photoreceptor's stain with arrestin, rodopsin, S-opsin and M-opsin. We have used antibodies anti-achromatopsia gens, like GNTA2 and CNGB3.

Results CD1 and NMRI electroretinogram results showed two different visual patrons: a normal responses and coneless vision. An important per cent of CD1 mice (≈ 30%) and NMRI mice (≈ 20%) have visual defects in the photopic responses. The affected mice show a very significant reduction on the cone responses (p<0,01). Because we used chromatic stimulus we can say that the photopic defect occur in every cone, we can appreciate colorblindness. The structural study allows us to say how the photoreceptors are affected when the electroretinogam photopic response is not adequate. The functional and cellular results seem to indicate that these mice suffer an achromatopsia.

Conclusion Our experiments show the significant number of coneless mice in a normal order of the experimental animals. Ignorance of visual problems in experimental animals might compromise the results of conductual experiment or other kinds of studies. Electroretinogram tests are recommended before conductual studies with albino mice or different works, to know if the mice have a correct vision.

• F066

Vision in subjects with hyperawareness of afterimages and "visual snow"

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Purpose Some patients complain of persisting visual noise, often described as "visual snow" (VS) and / or prolonged afterimages, but show no obvious clinical abnormalities. The purpose of this study was to examine the extent to which the processing of different stimulus attributes remains normal in VS patients.

Methods Seven VS patients and nine control subjects were examined. Advanced vision and optometric tests were used to assess visual acuity (VA), red / green (RG) and yellow / blue (YB) colour sensitivity, rapid flicker sensitivity, chromatic afterimage strength and duration and pupil response amplitudes and latencies to chromatic stimuli.

Results The VS patients exhibited normal VA, colour and rapid flicker sensitivity and chromatic afterimage strength. Both controls and four of the VS patients exhibited pupil constrictions to the onset of the coloured stimulus, followed by recovery during the stimulus and a further constriction at stimulus offset, normally attributed to perception of chromatic afterimages (Prog.Brain Res. 144:243-259, 2004). The pupil responses in three of the VS patients lacked the rapid recovery phase following the initial constriction to stimulus onset.

Conclusion The absence of recovery following the initial constriction of the pupil in three of the VS patients deviates from normal responses and suggests the presence of a more sustained retinal afferent signal that drives the pupil response. The latter may be linked to differences in retinal processing of visual signals that cause the perception of visual snow when the coloured stimulus is viewed against a uniform background.

• F067

Comparison of visual evoked potentials between premature and full-term childrens

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Purpose To evaluate the correlation of visual evoked potential(VEP) abnormalities with prematurity, presence of brain lesion, brain lesion localization, especially visual cortex in children under five.

Methods We evaluated VEP responses in children under five, and compare the responses according to prematurity, presence of brain lesion, and brain lesion localization. We divided the subjects into two groups, which the visual pathway involvement (retina, optic nerve, optic chiasm, lateral geniculate body, optic radiation, visual cortex) group, and non-involvement group. The VEP responses were classified into 3 scores, Score 0: normal waveform and normal latency, Score 1: mildly or moderately attenuated waveform or delayed latency, Score 2: severely attenuated waveform or no response.

Results Subjects were 58 children, 16 premature(25 weeks ~ 38 weeks), and 42 full-term children. In premature children, 5 out of 16 had visual pathway involvement, and 12 out of 32 had it in full-term children. In full-term children, higher score was seen in visual pathway involvement group. On the other hand, in premature children, there was no significant difference of score between visual pathway involvement group and non-involvement group.

Conclusion In full-term children, the incidence of VEP abnormality seems to be higher in case of visual pathway involvement. In premature children, the VEP abnormality is vulnerable although there is no visual pathway involvement.

• F068

Functional activity of retinal neurons and Muller cells in idiopathic full-thickness macular holes

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Purpose To determine the changes of neurons and Muller cells functional activity in idiopathic macular holes (MH).

Methods 7 patients (59-70years) with a full-thickness MH (3rd stage by Gass, 6-8 months duration) were examined. Optical coherent tomography (Stratus3000 OCT, Carl Zeiss) used to detect the maximum size of the MH, total macular volume (TMV) and foveal thickness (FT). The central and general macular sensitivity (Sc within 3° from the fixation point, and Sg) were tested with microperimetry (macula 12°, MP1 Nidek). The cone ERG, photopic flicker ERGs (FERG) at 8.3, 10, 12, 30Hz were recorded (RETIport/scan21, Roland Consult), and glial indices were calculated as the ratio of amplitudes of the ERG b-wave and every FERG.

Results The best corrected visual acuity was 0.23±0.09, FT=345±12μ; TMV=7.3±0.1mm3; the maximum hole size 581±62μ. Sc =7.9±1.1dB; Sg=12.2±1.3dB. In MH, a moderate reduction of a- and b-wave amplitudes was noted up to 67% and 88.3% of the norm. The b/a ratio was to 50% higher than in control, reflecting a violations in the outer/post-receptor retina interface. The amplitude of 24Hz-FERG (but not the 8.3-12Hz FERG) showed a sharp reduction (up to 31.4%), indicating to a drastic violation of the bipolar cell activity. The less significant depression in the single-flash ERG b-wave may reflect the compensatory hyperactivity of Muller cells, which masks the true reduction of bipolar cells activity. Glial indices increased more than two times at 24Hz, testifying a violation of cone bipolar and Muller cells interaction.

Conclusion MH is associated with the reduction in the function of photoreceptor and bipolar cells, sharp increase in Muller cell activity and interaction of cone bipolar and Muller cells.

• F069

New clinical measure to assess the visual awareness in peripheral field loss (PFL)

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Purpose Individuals with PFL have problems moving about, and there are some optical aids that are proposed to enhance mobility performance. However, currently the efficacy of these aids cannot be determined without extended wear. This study aims to design a new clinical measure to assess the visual awareness in PFL patients, so that this new test could be used to determine the efficacy of optical aids in a clinical setting

Methods PFL was simulated using goggles in 50 normally-sighted subjects. The simulated field of view (FoV) was varied from 5° to 20°. In the new test, observers were asked to search for a stimulus in a 60° field of view and the detection time (DT) & detection efficiency (DE) (DE is the Inter-quartile range of the DT responses at each eccentricity for every subject) were measured. Head and eye movements were allowed and the presentation time was unlimited. Clinical validity was investigated by correlating the DT and DE scores with the percentage preferred walking speed (PPWS) and the number of collisions on an indoor mobility course

Results The DT and DE scores were inversely correlated with the FoV ($r=-0.60$; $p<0.0001$, for both of them). These scores varied linearly with eccentricity. The DE was inversely correlated with the PPWS ($r=-0.50$; $p<0.0001$) and positively with the collisions score on the indoor mobility course ($r=0.50$; $p<0.0001$)

Conclusion The awareness test was sensitive to FoV and stimulus eccentricity. The test results have good correlation with mobility course scores which indicates that the new test is valid. The test is unique, quick, and simple to deliver. The new visual awareness test could be a valuable tool to test the efficacy of optical aids that are intended to enhance mobility performance in PFL patients.

• F070

Detection of colour signals in objects defined by luminance contrast

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Purpose The aim was to compare chromatic detection thresholds using two methods that are often employed to isolate the use of colour signals:a. Colour thresholds measured in dynamic luminance contrast (LC) noise when a spatially structured object is defined only by colour signalsb. Thresholds for detection of colour changes in objects defined by luminance contrast (i.e., the luminance pedestal (LP) technique that is often used in visual psychophysics to isolate the use of colour signals) Earlier findings in patients with cerebral achromatopsia (Proc.R.Soc.Lond.B. 258 :327-334 (1994)) suggest that different neural mechanisms handle the use of colour signals in the two conditions. It is therefore of interest to establish whether the corresponding colour thresholds in (a) and (b) are also different in normal subjects.

Methods Colour detection thresholds were measured using both LP and LC noise methods for discrete LP contrast levels and background luminances. The same four-alternative, forced-choice staircase procedure was used to measure thresholds for every combination of target and background luminance.

Results The amplitude of dynamic LC noise does not affect colour thresholds. In general, technique (a) yields smaller thresholds when compared to the LP technique (b) for all pedestal LC levels and background luminances. Negative luminance contrast pedestals yield increased colour thresholds for both the red/green and yellow/blue axes.

Conclusion When chromatic signals are added to objects defined by negative luminance contrast, the corresponding colour thresholds are no longer processed independently and increase monotonically with luminance contrast.

• F071

Normal range of Cambridge low contrast grating test: a population based study

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Purpose To determine the normal range of contrast sensitivity in a representative sample of the population of Mashhad, Iran, and its determinants

Methods In this report, Contrast Sensitivity (CS)c data of 2449 out of 3213 selected individuals was analyzed. CS was determined using Cambridge low contrast squarewavegrating and to evaluate its determinants, age, gender, Visual Acuity (VA) and Spherical Equivalent (SE) were analyzed.

Results The mean age of the participants was 29.1±17.3 years (range: 4-89 years) and 66.4% of them were female. The score of CS for the right and the left eye and itsbinocular score were 239.6±233.3, 234.6±228.6 and 310.9±249.0 cps, respectively. Multiple linear regression showed that CS significantly correlated with age ($\beta=-1.1$,$P<0.001$), gender ($\beta=-40.1$, $P<0.001$), LogMAR BCVA ($\beta=-165.4$, $P<0.001$) and SE($\beta=10.2$, $P<0.001$)

Conclusion Since our study was population-based, normal range of Cambridge low contrast grating test can be used as a reference guide in a general population. Our findings can be used in both research and clinic, especially evaluation of the results of refractive surgeries. However, in clinical evaluations, it should be noted that the meanCS is lower in older, myopic individuals who have a lower BCVA.

• F072

Normal aging: capturing changes in contrast acuity at low light levels

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Purpose Visual tasks that require discrimination of fine spatial detail become a challenge to older subjects, particularly when the light level is low. This worsening of vision is increased further when diseases of the eye are also involved, and these effects are difficult to separate. An index to describe the health of the retina (HRindex) by capturing how contrast acuity (CA) worsens as a function of light level is introduced and the statistical limits of variability established in normal eyes.

Methods CA thresholds were measured at five light levels (in the rage 0.12 to 34 cd/m^2) in 80 subjects, aged 18-80 years using the CA assessment test (ASEM, 74, 551-559, 2003). Long wavelength light was used to minimise variability. Stimuli were presented at 0 and ±4 degrees. Pupil size was measured throughout and used to calculate subject-specific retinal illuminances. The measurements were carried out binocularly and monocularly and in addition to clinical examination, a number of filters were also used to screen for normal eyes.

Results The HRindex was calculated for each subject using a method similar to that developed to investigate changes in colour vision (JOSA, 29 (2):27-35, 2012). Limits for CA have been established for normal eyes. The effects of aging were examined as well as differences between binocular and monocular thresholds and retinal location.

Conclusion The results show that when appropriate screening for normal vision is applied the HRindex becomes largely independent of age. The new approach and the limits of normal vision obtained in this study make it possible to screen for early-stage, subclinical retinal disease using CA assessment.

• F073
Colour vision losses in diabetes in the absence of proliferative retinopathy

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Purpose There are over 30 published studies evaluating colour vision in diabetes. The evidence is, however, not consistent – the predictive accuracy of the studies does not support the use of colour vision as a screening test for diabetic retinopathy (Health Technol Assess, 13 (60), 2009). The CAD colour vision test (Expert Rev.Ophthalmol. 6(4):409-420, 2011) addresses some of the major flaws in clinical colour testing. This poster reports the application of the CAD test to 214 diabetic patients.

Methods A consecutive series of diabetics attending a diabetes center in Abu Dhabi were invited to participate in the study. Inclusion criteria were a best corrected visual acuity of 6/18 or better, no more than moderate non-proliferative retinopathy or moderate maculopathy and no co-existing glaucoma. Patients had a full eye examination (including colour photography and macular OCT), a full assessment of their diabetes and the CAD colour test.

Results Age-corrected binocular colour threshold limits were employed to screen for normal colour vision. Abnormal colour vision was noted in 80% of Arab and 67% of non Arabs. This did not correlate with duration of diabetes, age, HBA1C, body mass index, visual acuity or central retinal thickness.

Conclusion Colour vision is abnormal in the large majority of the study population. The severity of colour vision loss is not correlated with age or gender of the patients, duration or severity of diabetes, current diabetic control, or central macular thickness. These findings suggest the existence of early retinal changes in diabetes that affect specifically colour vision and occur independently of factors such as those causing macula edema.

• F074
Evidence of neuroplasticity in the human visual cortex following beneficial anti-VEGF treatment in exudative age-related macular degeneration

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Purpose Anti-vascular endothelial growth factor (VEGF) agents have been shown to improve visual acuity and prevent vision loss in exudative age-related macular degeneration (AMD). As the vision improves relatively quickly in response to intravitreal injections, we wanted to know whether this improvement is reflected in electrophysiolocal markers of visual cortical processing.

Methods Our interventional case series included 6 elderly patients who underwent injection treatment to the affected eye. Their visual acuity, tomographic images of retinal thickness and visual evoked potentials (VEP) were assessed before of the treatment and six weeks after the last injection.

Results All patients showed improved visual acuity and reduced retinal fluid after the treatment. All but one patient showed increased VEP P100 component amplitudes and/or shortened latencies in the treated eye. These VEP changes were consistent with improved vision while the untreated eyes showed no changes.

Conclusion Our results indicate that anti-VEGF injections improved visual function of the treated eyes both in the level of the retina and in level of visual cortical processing.

• F075 / 4286
Adjuvant stem cell-based therapy in acute retinal injury after sodium iodate administration in mice

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Purpose The aim of this study was to determine and optimize a new strategy of SC-based therapy of selectively damaged retina after sodium iodate (NaIO3) administration in C57BL/6J mice.

Methods To address this issue, we investigated the effects of NaIO3 administrated in two different concentrations, i.e. 40 and 20 mg per kg of the body mass. Electrophysiological function of the retina using dark-and light-adapted full field flash ERG as well as morphological characteristics, were determined at several time points after each dose administration. Next, we performed intravitreal transplantation of murine GFP+Lin- cells on the 1st day since NaIO3 administration. We analyzed the retinal functional changes as well as the number, localization and phenotype of intravitreally injected GFP+Lin- cells within recipients' retinas.

Results Our findings revealed that massive destruction of the tissue was associated with irreversible retinal dysfunction, whereas moderate retinal injury triggered regenerative mechanisms that restore bioelectrical function of the damaged retina. By employing SC-based therapy we achieved noticeable improvement of the retinal function, particularly in the short-term observation. We observed the presence and proliferation of the injected cells at the site of RPE injury.

Conclusion Our study provides evidence that NaIO3-induced retinal damage triggers a sequence of pathophysiological events dedicated to supporting the self-regeneration of injured tissue. Our results indicate that if the scope of retinal destruction is profound, endogenous regeneration is ineffective and may ultimately require therapeutic transplantation of specific stem cell subpopulations and other adjuvant therapies.

• F076 / 4287
Fructose diet induced short-term impairment of cone sensitivity and gene expression in rat retina

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Purpose A high fructose diet has been widely used to trigger insulin resistance in rodent; insulin resistance is one of the major risk factor for the development of type 2 diabetes. Thirty to 40% of diabetic patients develop diabetic retinopathy. In this study, we aimed to evaluate the short-term effect, at 1, 3, 5, 8 days, of a 60% fructose diet, on photoreceptor sensitivity and gene expression in the retina of Brown Norway rats.

Methods Flicker electroretinograms (8Hz) were recorded under anesthesia, from both eyes simultaneously in order to study sensitivity of photoreceptors. Then, rats were euthanized and enucleated. Retinae and posterior poles were collected to analyze gene expression by RT-PCR. We specifically focused on 45 genes involved in cholesterol homeostasis, lipid trafficking, vascular changes and inflammation.

Results Our data showed that a short period of fructose feeding induced early changes in retinal functionality and homeostasis. Interestingly, we reported a partial loss of cone sensitivity after 8 days of feeding rats with the high-fructose diet. No effect was found in rod sensitivity.

Conclusion These findings are consistent with the sensibility and susceptibility of cones to dietary changes. These data deserve further investigations on the cross-talk between cones and rods upon metabolic changes associated with aging.

• F077
Adhesion molecules in experimental autoimmune uveitis

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Purpose Non infectious uveitis are characterized by the penetration of immune cells into the eye which depends on adhesion molecules expression on the blood retinal barrier (BRB). In this work, we have studied the expression of the adhesion molecules VCAM-1 and ICAM-1 in experimental autoimmune uveitis (EAU) by adoptive transfer and the expression of their ligands, VLA-4 and LFA-1, on autoreactive T-lymphocyte (TL)

Methods Autoreactive TL, obtained from the lymph node of C57BL6 mice immunized with IRBP 1-20, were purified using CD4+ magnetic cell sorting. Those cells were studied by flow cytometry for their expression of VLA-4 and LFA-1. ELISAs and intracytoplasmic flow cytometry were performed to study the cytokine expression profile. Then, EAU were induced by adoptive transfer of those cells into naive mice. VCAM-1 and ICAM-1 histological and cellular expression was studied by immunofluorescence on eye cryosections

Results Autoreactive TL were found to be from the Th1 and Th17 phenotypes. LFA-1 was expressed on all T and non T cells and VLA-4 mostly on non T cells. Only a minority of TL showed VLA-4 expression. In the eye of naïve mice VCAM-1 was absent and ICAM-1 present only at very low level. VCAM-1 and ICAM-1 expression is correlated to the severity of the disease. Interestingly, VCAM-1 was more expressed on the internal BRB and ICAM-1 on the external BRB

Conclusion This work shows that the adhesion molecules VCAM-1 and ICAM 1 were expressed differently on the internal and external BRB and that their respective ligands VLA-4 and LFA-1 were also expressed differently on lymphocytes. This works complete the understanding of the major role of the adhesion molecules VCAM-1 and ICAM-1 in the induction uveitis in the adoptive transfer model

• F078
Cytokines in patients with HLA-B27 + acute anterior uveitis

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Purpose In this study, we assessed 27 different cytokines in peripheral blood of patients with HLA-B27 + acute anterior uveitis (AAU), the most common form of immune-mediated uveitis. Goal of the study was to determine if cytokine levels in peripheral blood are associated with disease activity in AAU.

Methods Blood samples were collected from 14 consecutive patients with AAU in active and inactive disease phase (2 samples per patient at different time points) and from 14 age and gender matched controls. Patients with systemic treatment were not included. Samples were stored at -20 °C. Subjects were evaluated for cytokines in peripheral blood by Bio-Plex Pro Human Cytokine 27-Plex Panel. Percentages of each cytokine were compared for patients with active vs inactive disease and to age and gender matched group of healthy controls. IRB approval has been obtained.

Results Comparing active to inactive disease status we found signifficantly higher levels in 12 of the 27 accessed cytokines in active disease compared to inactive. In active status, we found significantly higher levels of Il-1b,IL-1ra, IL-5, IL-6, IL-7, IL-9, IL-1o, IL-17 and IFN-g. Interestingly, we did not see a significant difference in levels of IL-2 and TNF alpha. In all but one tested cytokine (IL-6), there was no significant difference between samples of patients in inactive disease and controls.

Conclusion Results show that there are significant differences in serum levels of many different cytokines in patients with active and inactive AAU.

• F079
Polyphenolic compounds reduce inflammation in ARPE-19 cells

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Purpose Age-related macular degeneration (AMD) is a major cause of blindness among the elderly in western countries. Currently, the majority of AMD patients are out of any treatment modalities. In the aging eye, a variety of intrinsic and extrinsic factors contribute to the development of inflammation which plays a major role in the pathogenesis of AMD. Several fruits, berries, and vegetables contain polyphenolic compounds which have shown to possess anti-oxidative and anti-inflammatory properties. In the present study, we have examined the influence of quercetin, fisetin, and luteolin on the inflammatory response in ARPE-19 cells.

Methods In order to induce inflammatory response, the cells were exposed to the lipid peroxidation end product 4-hydroxynonenal (HNE). Polyphenols were added concurrently with HNE, or one hour before or one hour after the exposure of the cells to HNE.

Results Our results show that the addition of polyphenols significantly decreased the production of pro-inflammatory cytokines interleukin (IL)-6 and IL-8. Moreover, the compounds decreased the release of lactate dehydrogenase (LDH) enzyme to the culture medium. This implies that the polyphenols are able to help the cell to maintain the integrity of its cellular membrane under stressful conditions.

Conclusion Our present results indicate that plant-derived polyphenols are effective in reducing the inflammatory response in ARPE-19 cells, and could be useful in the therapy of AMD.

• F080
Oxidative stress activates NLRP3 inflammasomes in ARPE-19 cells

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Purpose Oxidative stress, which refers to cellular damage caused by reactive oxygen species (ROS), contributes to many age-related diseases, including age-related macular degeneration (AMD). Retinal pigment epithelial (RPE) cells must endure a high level of oxidative stress because of their high oxygen consumption, high levels of polyunsaturated lipids, and the long periods of exposure to light. Inflammation plays a major role in the pathogenesis of age-related macular degeneration (AMD). Oxidative stress is known to activate inflammasomes, intracellular protein complexes which assemble to process the precursors of interleukin (IL)-1beta and IL-18 to mature and secreted cytokines by caspase-1. In the present study, we have studied the presence of inflammasome platforms in ARPE-19 cells.

Methods After the cell exposures, ELISA and qPCR methods were used to examine the inflammasomal activity.

Results In order to activate TLR pathway and NF-kappaB signaling for inducing the production of the IL-1beta and IL-18 precursors, the cells were stimulated with LPS. Thereafter, 4-hydroxynonenal (HNE) was used to provide the second signal needed for the inflammasome activation. Using the qPCR method, we showed the inflammasome receptor component to be the NACHT, LRR and PYD domains-containing protein 3 (NLRP3).

Conclusion Our data indicate that oxidative stress is able to activate NLRP3 inflammasomes in human ARPE-19 cells.

• F081

The dynamics of molecular markers expression of blood lymphocytes activating at patients with an uveal melanoma at the different types of treatment

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Purpose To study the dynamics of molecular markers expression of blood lymphocytes activating at patients with the uveal melanoma at the different types of treatment.

Methods Research was conducted in the dynamics at patients (n=67) in age 63,4±5,7 years old with the uveal melanoma at the different types of treatment. The photocoagulation was conducted in the first group (n=42), the enucleation was in the second group (n=19), the combine therapy (photocoagulation + brachytherapy) was in the third group (n=6). The level of molecular markers expression of lymphocytes activating was determined by the gistoimmunocitochemical method through the monoclonal antibodies (CD7, CD25, CD38, CD45, CD54, CD150 and CD95). The estimation of statistical meaningfulness of distinctions was executed by Mann-Whitney and Wilcoxon tests.

Results After the photocoagulation at patients with uveal melanoma was marked the reliable increase of molecular markers of lymphocytes activating (CD7, CD38, CD150 and CD95) as compared to indexes at the beginning of treatment. After the enucleation the level of molecular markers of lymphocytes activating (CD7 and CD95) was for certain increased as compared to the initial level. The combine therapy (photocoagulation + brachytherapy) was accompanied the reliable increase of activating markers (CD7, CD25, CD38, CD45, CD54, CD150 and CD95).

Conclusion The highest level of the immune system activating is marked at the combine treatment. Less expressed activating at the enucleation and photocoagulation.

• F082

An antimicrobial peptide can enhance the activity of a fluoroquinolone in reducing the colony counts of fluoroquinolone-resistant MRSA in the NZW rabbit keratitis model

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Purpose Future therapy of ocular infections may depend on enhancing current drugs if no new drugs are developed. We tested whether an antimicrobial peptide, Nisin (NIS) could enhance the activity of ciprofloxacin (CIP) in a NZW rabbit keratitis model.

Methods A total of 48 rabbits were inoculated intrastromally in both eyes with ~1000 CFU of fluoroquinolone and methicillin-resistant Staphylococcus aureus. After 4 h, the rabbits were divided equally into 4 treatment groups: 1) 0.075% NIS; 2) 0.3% CIP; 3) 0.075% NIS + 0.3% CIP; 4) PBS. Topical treatment was instilled in both eyes every 15 min for 5 hours. One hour after treatment the corneas were harvested, homogenized, and processed for colony counts. Colony counts were Log10 transformed and analyzed using ANOVA. The data is expressed as mean ± sd Log10 CFU/ml.

Results CIP alone (6.76 ± 0.35) demonstrated no difference in colony counts compared to PBS (6.87 ± 0.30) ($p>0.05$). NIS alone (4.90 ± 1.84) significantly decreased colony counts compared to PBS and CIP ($p<0.05$). NIS + CIP (3.84 ± 2.01) significantly decreased colony counts compared to NIS alone, CIP alone, and PBS ($p<0.05$).

Conclusion Combination therapy with 0.075% NIS and 0.3% CIP significantly decreased colony counts compared to PBS and either drug alone. This study provides "proof of principle" that in vivo enhancement of antibiotics can be achieved and may be evaluated using a rabbit model.

Commercial interest

• F083

Diagnosis of Herpetic Uveitis is Aided by Confocal Microscopy with the HRT RCM

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Purpose Herpetic uveitis (HU) is a frequent infectious cause of anterior uveitis. A definite diagnosis can be obtained by anterior chamber puncture and PCR, an invasive procedure not all patients consent to. We hypothesized that patients with HU typically have high amounts of dendritiform inflammatory cells (DCs) in their corneal subepithelial nerve plexus (SNP),which are detectable by in vivo confocal microscopy and distinguish HU from other uveitis types.

Methods Patients with clinical suspicion of HU without keratitis and patients with Fuchs Uveitis Syndrome (FUS) were imaged with the Rostock Cornea Module attachment on the HRT III (HRT-RCM)(Heidelberg Engineering) on both eyes. DCs in the SNP were counted by two observers using a cell counting software. Means of the cell counts were used for analysis. Diagnosis of HU was confirmed by anterior chamber puncture or by clinical improvement due to Acyclovir therapy. Statistical significance was assessed with a Kruskal-Wallis or a Mann Whitney U test,when appropriate.

Results Patients with HU showed significantly higher amounts of DCs in their affected eyes (93.3±10.6 cells/mm2, Mean±SEM, n=10) but also in their unaffected eyes (59±25 cells/mm2, n=7), than patients with FUS, who had an average DC-density of 46.4±10.4 cells/mm2(n=15) in their affected and 21±6 cells/mm2(n=15) in their unaffected eyes.

Conclusion High amounts of DCs in the corneal SNP were a typical finding in herpetic AU. Much lower numbers of DCs were present in FUS, a clinical similar uveitis type presumably also of viral origin. Imaging corneas of patients with clinical suspicion of HU with the HRT-RCM is a non-invasive, low risk technique which can be a useful addition in distinguishing HU from other anterior uveitis aetiologi

• F084

HSV1-specific meganuclease may reduce ocular infection in a mouse model of herpes keratitis

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Purpose Current anti-viral treatments of Herpes simplex virus type 1 (HSV1) inhibit the viral replication but do not impair the latent form of the virus. This could be addressed by rare cutting endonucleases, such as meganucleases. The aim of this study was to demonstrate the antiviral activity of a HSV1-specific meganuclease in a mouse model of herpes keratitis.

Methods Three weeks after bilateral subconjunctival inoculation of recombinant associated-adenovirus (rAAV) encoding either a HSV1-specific meganuclease or a reporter gene (GFP), both cornea of mice were inoculated with a wild-type HSV1 strain. Mice were sacrificed 6 or 28 days later and corneas were analyzed for the presence of HSV1 genome and viral transcripts.

Results At 6 dpi, there was no clinical difference in the rate of acute herpetic keratitis, but the amounts of viral products were lower in mice treated with meganuclease-encoding rAAV. At 28 dpi (stage of HSV1 latency), the rate of clear cornea was more important in the mice treated with meganuclease ($p = 0.03$), and the amounts of viral genome and transcripts were significantly less important ($p<0.01$.

Conclusion The transduction of HSV1-specific meganucleases in the ocular tissues by means of a subconjunctival inoculation of r-AAV is associated with an improvement of corneal recovery, and a reduction in the viral load and replication in the cornea. These results suggest that specific meganucleases could be qualified as a new class of antiviral agent, with the potential to address replicative as well as latent viral DNA.

Commercial interest

• F085

Regulation of immune response in post-operative endophthalmitis

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Purpose Endophthalmitis is the most feared complication of all ophthalmologic surgeries. The aim of our study is to study the immune response in aqueous humor of infected patients.

Methods In a prospective and multicenter study, clinical datas and aqueous humors of patients with endophthalmitis and control (cataract surgery) were collected. Multiplex immunoassay was done in order to define cytokines patterns. Two-way ANOVA test was realized for each inflammatory marker to determine any difference between infected and control patients. Pearson linear regression was done to analyse correlation between clinical datas and cytokines levels.

Results Aqueous humor was sampled in 49 patients with endophthalmitis and 88 controls. Microbial identification was obtained in 67% of cases. Endophthalmitis was leading to high levels of cytokines and chemokines of the Th1, Th17 and Treg ways. Moreover, very high levels of VEGF were noted in aqueous humors of patients with endophthalmitis as compared to the control. Better visual acuity after one year of evolution was correlated with decreased levels of IL-8, MCP-1 and VEGF.

Conclusion Th1 and Th17 cells may play an important anti-infectious role in modulating pathogen proliferation in infected eyes. But this huge inflammatory response may be responsible for retinal destruction as a collateral effect. Moreover, pro-angiogenic factors are secreted in infected eyes. Antagonism of TH17 and anti-angiogenic drugs could be a way to limit ocular lesion and may open new therapeutic approach associated with antibiotics therapy.

• F086 / 2646

Miltefosine and polyhexamethylene biguanide, a new drug combination for the treatment of Acanthamoeba keratitis. Results from in-vivo toxicological and efficacy studies

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Purpose Miltefosine (MLT) and combinations of Miltefosine and polyhexamethylene biguanide (PHMB), chlorhexidine (CHX), and propamidine isethionate (PI), respectively, have been tested in a rat efficacy model for treatment of Acanthamoeba keratitis. In a second step, the most promising treatment regimens from efficacy studies have been tested for local tolerance in a fully GLP-compliant toxicological study in pigmented rabbits.

Methods The cornea of rats were infected with Acanthamoeba hatchetti. Cornea infections were graded microscopically. Nine groups were treated with varous treatment regimens for 28 days (8 times per day during the first week, and 3 times per day for the last three weeks). Efficacy of treatment was examined by determination of the degree of infection and culturing of excised eyes after the end of the treatment period. On day 28 the eyes were inspected under the microscope, re-graded and were then compered with the grades before starting the therapy.

Results Best treatment results were obtained from PHMB-MLT group. The ratio of fully recovered eyes was 28.4%. The highets therapeutic activity was yielded by the combination MLT-PHMB (86%), followed by MLT, CHX, or PI (72%) and the combination MLT–PI (70%. The fully GLP-compliant study in pigmented rabbits (28 days, 8 treatments per day) showed excellent local tolerance.

Conclusion Thus the combination of Miltefosine and PHMB can be seen as a highly effective and save option for treatment of AK.

• F087

Lattice dystrophy complicated by Cryptococcus curvatus infection

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Purpose To present a novel case of Cryptococcus curvatus (CC) keratitis in a patient with Lattice dystrophy (LD).

Methods A 57 year old lady with a family history of LD had a right re-graft for suspected recurrent lattice dystrophy. Her initial penetrating keratoplasty (PK) was in 2004 after which she kept good vision. 5 years later she developed a small ulcer caused by presumable Candida which healed completely following topical miconazole and short course of oral fluconazole. In 6 months she developed gutter, increasing astigmatism, recurrent erosions without inflammation and progressive peripheral opacities leading to a 2nd PK.

Results Histology of the 2nd PK revealed amyloid deposits in both host and graft elements confirming recurrent LD. In addition the graft contained numerous yeasts within epithelium and stroma along scars from previous PK. The capsulated fungi were seen on PAS, grocott and mucicarmine stains. No inflammatory response was associated with the fungi. Microbiology confirmed these as (CC). On review of findings from initial infection, it seemed that Cryptococcus instead of Candida was indeed the causative agent of her previous ulcer. Interestingly, she had no history of local trauma prior to her first corneal ulceration and there was never evidence of infection elsewhere. Unfortunately, 2 years after the 2nd PK the graft developed new opacities that lead to a 3rd PK which revealed recurrent (CC) keratitis again without any inflammatory response. The left eye also had a corneal graft in 2009 given her underlying LD and mercifully has never been infected.

Conclusion To our knowledge Cryptococcus curvatus keratitis was never described in English literature.In fact, it seems that this is the first description of ocular infection by this species.

• F088

Syphilitic uveitis: Vilnius region perspetive: 6 case reports

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Purpose To examine the clinical manifestations of syphilitic uveitis in Vilnius region population over four years and review trends in incidence

Methods A retrospective case series of 6 patients (8 eyes) with syphilitic uveitis who were managed in Vilnius region between 2009 and 2012

Results Between 2009 and 2012 were 6 patients (mean age 42,67 years, range 28 - 66) all of them with positive Treponema Pallidum Chemiluminescent Immunoassay (CLIA) and negative Human Immunodeficiency Virus (HIV) serology. Venereal Disease Research Labarotory (VDRL) and/or Treponema Pallidum Heamaglutination Assay (TPHA) and/or non – reactive Rapid Plasma Reagin (RPR) were obtained in all 6 patients. Posterior uveitis was the commonest presenting finding (5/8 eyes), panuveitis was seen in 3 eyes at presentation. Posterior uveitis manifests as chorioretinitis with or without vitritis, optic neuritis, neuroretinitis. Panuveitis – granulomatous anterior uveitis, neuroretinitis, vitritis. One patient with bilateral involvement, had rare symptom – syphilitic roseola of the iris. Five patients were treated with intravenal benzylpenicilin and one – oral cefriaxone

Conclusion Ocular syphilis presented most frequently as posterior segment inflammation. An increasing trend in the number of cases of ocular syphilis in the past four years was observed in Vilnius region population

• F089 / 2277

Tocilizumab for anterior uveitis and juvenile idopathic arthritis – a case report

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Purpose We report a case of Juvenile Idiopathic Arthritis (JIA) and Anterior Uveitis (AU) responding well to Tocilizumab, a new humanized monoclonal antibody against the IL-6 receptor, after having been refractory to classical immunosuppressive agents as well as to TNF-α inhibitors.

Methods The Patient was treated in our center from 2007-2012. Collected data included: visual acuity (VA), anterior chamber cells and –flare, flaremeter measurements, intraocular pressure (IOP), presence of macular edema (ME) and cataract, topical and systemic medications, number and site of affected joints, laboratory inflammation parameters.

Results Patient was born 1996, diagnosed with JIA 1998 and with AU 2005. Inflammation was initially controlled with methotrexate and corticosteroids, VA fluctuated between 20/40-20/15(OD) and 20/20(OS). In 2007 VA decreased to 20/200(OD) as ME developed. Additional systemic therapy included between 2008 and 2009: Ciclosporin, Adalimumab, Mycophenolate, Leflunomide, and Infliximab. Control of ocular and/or joint inflammation was always insufficient or short lived. Between 2008 and 2010 ME required multiple periocular Triamcinolone injections.IOP first rose in 2008 to 34mmHg(OD), requiring combined topical and systemic therapy and finally trabeculectomy in 2010. Cataract developed on both eyes.Tocilizumab therapy was started in 02/2010. Since then AU and joints are free from inflammation. Cataract-surgery and implantation of an artificial lens in OD was performed successfully in 2011. Systemic steroids could be reduced to 2 mg/d. IOP is <20mmHg; VA is stable at 20/32(OD) and 20/50(OS).

Conclusion Tocilizumab may be another treatment option for JIA-associated uveitis which is refractory to established immunosuppressants.

• F090

Use of tuf PCR for staphylococcal and streptococcal genus detection in endophthalmitis

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Purpose This study reports the contribution of specific conventional PCR of the Staphylococcus and Streptococcus genera followed by sequencing for the microbiological diagnosis of endophthalmitis.

Methods Specific PCR assays targeting the tuf gene of the Staphylococcus and Streptococcus genera were performed in addition to the reference techniques (conventional culture and panbacterial PCR) on samples of aqueous humor and/or vitreous in patients with acute post operative endophthalmitis when Staphylococcus or Streptococcus had been identified using reference methods or no identification had been possible.

Results Out of the 125 samples analyzed (60 aqueous humor and 65 vitreous of 85 patients) , the culture was positive in 61 cases (48.8%) and panbacterial PCR was positive in 78 cases (62.4%). By combining culture and panbacterial PCR bacterial identification was obtained in 94 of the 125 samples (75.2%, 72 Staphylococcus, 22 Streptococcus). Staphylococcus-specific PCR was positive in 72 out of the 103 samples tested and allowed 8 additionnal identifications. The Streptococcus-specific PCR was positive in 13 cases. The Streptococcus-specific PCR provided no additional diagnosis to the pan-bacterial PCR. By adding Staphylococcus and Streptococcus tuf specific PCR to the reference methods, bacterial identification was obtained in 102 of the 125 samples (81.6%, 80 Staphylococcus, 22 Streptococcus).

Conclusion The Staphylococcus- and Streptococcus-specific techniques used in this study were complementary to the panbacterial PCR techniques and improved sensitivity in the identification of Staphylococcus and better identification of the species with sequencing.

• F091

Baseline predictive factors of visual prognosis in acute bacterial postcataract endophthalmitis

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Purpose To identify baseline clinical factors of visual prognosis in patients with acute endophthalmitis following cataract surgery.

Methods 99 patients of four academic hospitals (FRIENDS group). Factors were analyzed based on the final visual outcome, defined as poor (<20/100) or good (≥20/40) using univariate and multivariate analysis

Results Multiple logistic regression analysis showed that high bacterial virulence was the only independent factor (odds ratio [OR]= 14, 95% confidence interval [CI]: 2.7–71, p=0.001) for poor visual outcome. On the other hand, low bacterial virulence (OR=0.1 95%CI: 0.03–0.6, p=0.01) and the absence of complications (OR=0.07, 95%CI: 0.01–0.4, p=0.003) during cataract surgery were independent factors for good VA.

Conclusion Visual outcome factors in acute postcataract endophthalmitis identified in this prospective study (2004–2007) were similar to those reported by the EVS 10 years ago. The bacterial virulence level was the main predictive factor of final visual prognosis. This emphasizes the need for rapid bacterial identification and characterization using new biomolecular tools.

• F092 / 2647

Time profile of viral DNA in aqueous humor of patients treated for VZV acute retinal necrosis using quantitative real-time PCR

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Purpose To evaluate the kinetics of varicella zoster virus (VZV) load using quantitative PCR (qPCR) in patients treated for acute retinal necrosis (ARN). Design: Cohort study, evaluation of diagnostic test or technology.

Methods Six patients (52±13 years) with ARN syndrome were consecutively studied. Aqueous humor (AH) was sampled from all eyes for qPCR evaluation. The patients were treated with intravenous aciclovir and intravitreal injections of antiviral drugs. The mean follow-up was 17.6±16.4 months.

Results Two main portions of the viral load curves were observed for each patient: a plateau phase (27.8±24.9 days) followed by a decrease in the number of viral genome copies. The mean baseline viral load was 3.4×107±4.45×107copies/ml (6×106 to 1.2×108). The viral load decreased following a logarithmic model, with a 50% reduction obtained in 3±0.7 days. There was a significant viral load (> 102 copies/ml) at 50 days after the onset of treatment, despite antiviral drugs.

Conclusion qPCR use demonstrated reproducible VZV DNA kinetics with a two-phase evolution: plateau followed by logarithmic decrease. These data suggest that high-dosage antiviral therapy during the conventional 10 days duration is insufficient in most patients. This patient's series responded with a similar decrease in viral load once initiated, this may be used to predict the progression of future patients. The correlation of the viral load threshold with clinical improvement needs to be more clearly defined.

• F093

Evaluation of the early diagnosis of uveitis toxoplasma using only western blot

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Purpose The aim of this study is to evaluate which methods, between the Goldmann-Witmer coefficient (GWC) and immunoblotting (IB), in aqueous humor samples, can be sufficient, associated with clinical findings, to diagnosis ocular toxoplasmosis, in running practice, especially in the first three weeks.

Methods Ocular Toxoplasmosis (OT) is one of the most frequent causes of posterior uveitis.The diagnosis of toxoplasmic retinochoroiditis is based upon ophthalmoscopic findings and can often allow the clinician to start specific treatment when needed. But in most cases, laboratory tests are required to confirm the etiology, especially when other diseases are suspected and cannot be ruled out by the lonely clinical findings.Thirty patients with ocular toxoplasmosis and 36 patients with other ocular inflammatory diseases were analyzed by these two methods.

Results The GWC was significant (GWC > 3) in 57.9% patients presenting OT. IB was positive in 85.3% of samples. The combination of these two methods increases the sensitivity to 89.2%. Based upon the interval between symptom onset and paracentesis, IB has a greater sensitivity than GWC when sample of aqueous humor (AH) was taken in the first three weeks (78.6% verus 35.7%).

Conclusion IB seems to be more useful than the GWC if only one of these methods can be perform and especially in the first three weeks. On top of that, IB is easier to perform and require a smaller sample.

• F094

Serratamolide as a novel hemolytic factor produced by Serratia marcescens

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Purpose The Serratia marcescens bacterium causes vision-threatening keratitis, life-threatening hospital acquired infections and contaminates contact lens cases. The goal of this study was to identify a hemolytic factor produced by keratitis isolates and laboratory strains of S. marcescens.

Methods Hemolysis was measured using sheep and mouse erythrocytes. S. marcescens was mutated with a mariner transposon. Hemolysin defective mutants were isolated on blood agar plates. Transposon insertion sites were mapped by marker rescue and sequencing. Complementation analysis was performed with plasmids. Serratamolide was extracted with ethyl acetate and purified by preparative HPLC and verified as pure with high-resolution mass spectroscopy (HR-MS) and 1H NMR analysis. Cytotoxicity to human airway and ocular epithelial cells was performed using Alamar Blue viability dye. The presence of swrW in ocular isolates was determined using PCR.

Results Mutation of the swrW gene conferred a hemolysis defect that was complemented by the wild-type swrW gene on a plasmid. The SwrW protein catalyzes production of the cyclic lipopeptide serratamolide. Purified serratamolide was hemolytic to mammalian erythrocytes, and cytotoxic to human airway and ocular cells in vitro. The swrW gene was found in the majority of contact-lens associated keratitis isolates.

Conclusion Serratamolide is a novel hemolysin produced by S. marcescens ocular isolates and may contribute to the ability of contact lens associated bacteria to cause infections.

• F095

Successful management of recurrent Acanthamoeba keratitis using topical and systemic miltefosine

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Purpose Acanthamoebae are ubiquitous free-living amoebae. As facultative pathogens, they are the causative agents of Acanthamoeba keratitis (AK), a sight-threatening ocular surface infection. AK can have a favorable prognosis when diagnosed and treated early in the disease course but available treatment options can remain ineffective even when started early.

Methods Case presentation

Results AK can have a favorable prognosis when diagnosed and treated early in the disease course but available treatment options can remain ineffective even when started early. We present a case of AK that was successfully treated with topical and systemic miltefosine after showing sight-threatening recurrences under recommended therapy including a combination of propamidine 0.1%, miconazole nitrate 1%, neomycin, diamide and cationic antiseptics over a 12 months period.

Conclusion In previous studies, miltefosine (hexadecylphosphocholine), an alkylphosphocholine, approved for the oral and topical treatment of leishmaniasis, proved to be highly active against Acanthamoeba in vitro [Walochnik et al. 2002]. This has been confirmed by several other studies [e.g. Schuster et al. 2006, McBride et al. 2007, Walochnik et al. 2009, Polat et al.2012].

• F096 / 2847

Atypical panuveitis parasitic and Herpes virus co-infection in immunocompetent adults: real co-infection or false positive?

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Purpose Acute panuveitis with retinitis diagnosis may sometimes be difficult. Contribution of microbiological analyzes of intraocular samples currently allows a rapid diagnosis to guide therapeutic management when visual function is severely threatened.

Methods We report three original cases of panuveitis with retinitis for which analyzes showed concomitant infection with Toxoplasma and Herpes viruses.

Results PCR techniques have increased the sensitivity and specificity of diagnostic tests for ocular pathogens, including Toxoplasmosis and Herpes viruses. For Toxoplasmosis, Western blot and Desmonts coefficient remain standards tests in immunocompetent adults. As for central nervous system infections, Herpes viruses PCR is the gold standard test for intraocular samples. The clinical cases described here are atypical and the clinical examination failed to set the diagnosis. The detection of two infectious agents has led to the establishment of a double etiologic treatment, due to the severity of the ocular involvement. However, we may suppose that certain viruses in dormant states can be liberated in an inflammed eye, causing DNA to be detected on PCR testing, making more than one true positive result both possible and clinically relevant.

Conclusion In actual clinical use, false-positive results are possible from contamination, and false-negative results are possible from polymorphism, specimen degradation, or failure to sample in the acute stages of disease. It remains difficult to determine the responsibility of both infectious agents revealed. Is it a real co-infection, or false positive?

• F097

Effect of tocilizumab for uveitis accompanied with Castleman disease

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Purpose Although multicentric Castleman disease is a rare but life-threatening disease, eye complications are extremely uncommon. We present a case of refractory uveitis accompanied with Castleman disease successfully treated with tocilizmab.

Methods A 58-year-old man with Castleman disease was introduced for refractory uveitis to Chiba University Hospital. Large cells were detected in the anterior chamber and increased vascular permeability of retinal vessels has been found in both eyes. Although the patient was treated with oral and eye drop steroid treatment, the uveitis symptoms had not decreased. The serum levels of CRP and IL-6 were increased. The level of IL-6 concentration in the anterior chamber was the same as the serum level of IL-6. The humanized anti-IL-6 receptor-antibody (tocilizumab: 8 mg/kg per two weeks) was administrated for the patient because of poor general condition. The effect of tocilizumab was evaluated with routine ophthalmological examinations, fluorescein angiography (FA), Glodmann perimetry, and OCT.

Results After tocilizmab treatment, large cells in the anterior chamber were undetectable and vascular permeability was improved in FA. The serum levels of CRP and IL-6 decreased and the general condition improved. The side effect of tocilizumab was not observed during the treatment.

Conclusion Tocilizumab treatment was significantly effective for uveitis accompanied with Castleman disease. Although it is extremely rare, uveitis accompanied with Castleman disease may reflect poor general condition in patients with Castleman disease, and it may be one of the hallmarks to consider tocilizumab treatment.

• F098

Efficacity and safety of TNF alpha blockers in patients with Behçet's disease uveitis

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Purpose To determine the efficacy and safety of infliximab, an anti-TNF alpha antibody, in patients with severe and sight-threatening uveitis associated with Behçet's disease.

Methods Retrospective, single center study on 11 cases of panuveitis due to Behçet's disease managed between July 2001 and November 2011. Patients were treated with infliximab at a dose of 5 mg/kg intravenously. Efficacy was monitored by complete clinical examination, fluorescein angiography and OCT. The general tolerance was evaluated by a regular clinical and biological analysis.

Results Infliximab was used in 11 patients with a mean age of 32.7 years [20.9-45.7]. Nine patients with panuveitis and retinal vasculitis were resistant or intolerant to immunosuppressors [average 2.1; 0-4]. Mean duration of uveitis before the use of infliximab was 6.4 years [0.03-10.8]. Infliximab has been used as long-term treatment in 6 patients. The mean duration of treatment was 25.59 months [1.96-82.96] with a mean follow up of 42.32 months [1.38-114.2] and a mean of 17 infusions administered [2-52]. Infliximab was efficient in all cases, with rapid regression (after 1-2 injection) of intraocular inflammation. The average dose of corticosteroids was reduced from 40mg/d to 23.6mg/d (p=0.019). Pneumonitis and optic neuropathy occurred respectively in one case.

Conclusion Infliximab has a rapid and powerful but suspensive effect in severe ocular Behçet's disease. It can be used either as first-line before the switch to other immunosuppressors or as a new strategy in severe cases resisting to other drugs, such as azathioprine or interferon alpha.

• F099

Ocular granuloma, uveitis and X-linked chronic granulomatous disease

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Purpose To report 2 cases of ocular inflammation in patients with chronic granulomatous disease (CGD).

Methods A 2-year old boy was referred for red right eye and fever lasting for one month. A granuloma developed in the anterior chamber of his right eye. A CGD was suspected and the X-chromosom analysis confirmed a mutation in the gp 91 phox (the b subunit of cytochrome b558). Steroids were associated with antifungals and antibiotics and the granuloma disappeared rapidly. The other caseis about a 22-year-old womanknown to be a carrier for X-linked cytochrome b558-negative CGD. She presented with a red painful right eye. Slit-lamp examination revealed a nodular scleritisand, funduscopy disclosed chorioretinal granuloma in nasal periphery (RE). A white active but asymptomatic chorioretinal lesion on the temporal part of posterior pole and perivascular retinal scars were found (LE).She was successfully treated with oral prednisone.

Results CGD is a rare inherited disorder of phagocytic cells leading to recurrent life-threatening bacterial and fungal infections, caused by a defect in the nicotinamide adenine dinucleotide phosphate. The most common molecular defect is a mutation in the cytochrome B, b subunit gene located on the X chromosome encoding for gp91. The most frequent ocular manifestations are juxta vascular chorioretinal lesions, keratitis and conjunctivitis. Current therapy for CGD is based on antimicrobial prophylaxis, early and aggressive treatment of infections.

Conclusion Ophthalmologists must be aware of the different ocular localisations in CDG that may be the presenting symptoms.

• F100

Iritis and angle closure glaucoma caused by caterpillar hairs

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Purpose To report on a child presenting with iritis and angle closure glaucoma caused by caterpillar hairs.

Methods A 12-year-old girl complained of sudden pain and visual loss in her left eye while she was playing in a pinewood. Two hours later, she developed maculo-papular rash on her limbs. On examination, left visual acuity was 1/10. The affected eye showed conjunctival hyperemia, corneal edema, anterior chamber flare (4+ cells). Corneal staining with fluorescein disclosed diffuse superficial punctate keratopathy. Left IOP was 55 mm Hg. Visante OCT of the affected eye showed a thin, translucent, linear foreign body into the cornea and anterior chamber up to the irido-corneal angle. Topical steroids, antibiotics, cycloplegics, hypotensive eyedrops, and intravenous mannitol were given.

Results Inspection of the place where the girl was playing revealed the presence of numerous processionary pine caterpillars. On the basis of this finding and the clinical data, a diagnosis of iritis and angle closure glaucoma caused by caterpillar hairs was made. After 3 days' treatment, corneal edema and anterior chamber inflammation resolved, IOP returned to normal, and visual acuity was 10/10 again. However, a small iris cyst was still visible on OCT scans.

Conclusion Ocular lesions caused by caterpillar hairs are uncommon. Ophthalmologists should be aware that intense iritis with angle closure glaucoma may be the result of the penetration of caterpillar hairs into the eye. OCT scans may be important to confirm the diagnosis.

• F101 / 2273
Paediatric rheumatology clinic outcome at Leeds Teaching Hospitals, UK

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Purpose Present 1-year data of the combined ophthalmology and rheumatology pediatric uveitis clinic at Leeds Teaching Hospitals.

Methods Retrospective data collection

Results An estimated 230 patients with JIA were screened by ophthalmology in this time period.21 different paediatric patients with iritis were managed from June 2011 to May 2012 in the joint clinic.8(38%) patients were male and 13(62%) female with age at diagnosis ranged from 0.5 – 12 years. 11 patients (52%) were diagnosed with oligoarticular and 5(23%) with polyarticular JIA,3 patients were ANA +, 3(14%) did not have any joint involvement.9 patients(43%) presented with vision of 0.2logMar or worse, and 4 continued to have vision worse than 0.2 logMar while 17 patients (81%) improved or maintained stable vision of 0.1 or better.3 patients had intermediate uveitis,1 had panuveitis and 1 had papillitis with iritis.2 had eye complications of lens opacities and 1 patient had retinal detachment.17(81%) patients received systemic treatment, with 12 receiving methotrexate +/- mycophenolate mofetil and 5(29%) receiving anti-TNF α therapy (infliximab or adalimumab) in addition to methotrexate +/- mycophenolate mofetil. 13/16 patients with JIA (81%) had iritis associated with their joint flare-ups. 9 patients (50%) out of 18 with joint pathology received intra-articular steroid injections during this period and 6 received (28%) periocular steroid injection. A survey of the joint clinic by the patient and medical staff showed significantly high satisfaction rate.

Conclusion The joint clinic has numerous benefits and is the right approach to manage a condition where communication is crucial between team monitoring (ophthalmology) and managing (rheumatology) the condition

• F102
Uveitis and ocular wall granulomas associated with brimonidine treatment

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Purpose Anterior granulomatous uveitis has been recently reported as a side effect of chronic topical use of brimonidine tartrate. Clinical features of eight patients with brimonidine induced uveitis and ocular wall granulomas are here described.

Methods Medical history, ocular features, progress of events, pathological aspect, and clinical evolution of all patients were analyzed. For each patient, the search of systemic sarcoidosis was performed including angiotensin converting enzyme dosage, chest computed tomography and accessory salivary gland biopsy.

Results Three women and five men with a mean age of 68 years (varying from 50 to 83 year-old). All patients presented with glaucoma and two patients had a previous history of unilateral uveitis before treatment with brimonidine. Two patients receiving unilateral treatment had unilateral disease whereas patients receiving bilateral treatment had bilateral disease. At the time of diagnosis, the mean duration of treatment with brimonidine was 18.5 months. Epithelioid granulomatous lesions infiltrated conjunctiva and/or episclera. Remission was obtained after a 4 to 6 weeks of withdrawal. Uveitis and ocular surface inflammation flared up when treatment was tapered.Unfortunately, brimonidine was later reintroduced in one patient and diffuse granulomatous lesions recurred

Conclusion Brimonidine associated uveitis arises after sustained treatment in susceptible patients.Coexisting granulomatous anterior uveitis and ocular wall granulomas in patient treated by brimonidine eyedrops should evoke a drug induced disease.Treatment withdrawal leads to resolution of added inflammation with return to the basal state. Reexposure to brimonidine induce recurrence of uveitis after several months of exposure.

• F103
Protective effects of Crepidiastrum denticulatum on oxidative stress-induced retinal degeneration

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Purpose This study was to determine whether Crepidiastrum denticulatum, is effective at blunting the negative influence of 1-buthionine-(S,R)-sulfoximine (BSO, 0.5 mM) plus glutamate (10 mM) in transformed retinal ganglion cells (RGC-5) and of N-methyl-D-aspartate (NMDA) to the rat retina.

Methods RGC-5 cells in culture were given negative insult such as BSO plus glutamate for 24 hours, after which cell survival were tested. Reactive oxygen species (ROS) quantification was performed by 2′,7′-dichlorodihydrofluorescein diacetate and dihydroethidium. Apoptotic cell death was measured by propidium iodide (PI)/Hoechst 33342 double staining and western blot analysis. NMDA-induced retinal damage in vivo was tested by hematoxylin-eosin staining and terminal deoxynucleotidyl transferase-mediated dUTP nick-end labelling (TUNEL) staining. The lipid peroxidation was tested by amount of formation for thiobarbituric acid reactive species.

Results The ethanol extract of C. denticulatum (EECD) significantly attenuated RGC-5 cells death caused by BSO plus glutamate. Treatment of the RGC-5 cells with EECD reduced the ROS caused by various radical species such as H2O2, OH• or O2•-. The up (cleaved PARP and cleaved caspase-3) and down (Bcl-2) regulations of apoptotic proteins caused by BSO plus glutamate were significantly blunted by EECD. EECD protected the negative influence of NMDA on the retinas of rats of the thinning of the inner plexiform layer (IPL) and of the increased TUNEL in positive ganglion cells in the ganglion cell layer. Chlorogenic acid and 3,5-dicaffeoylquinic acid were found to be major components of EECD.

Conclusion EECD could be promoted as a potential neuroprotective agent for glaucoma against oxidative stress.

• F104
Supplement enriched in antioxidants protects the retina from light-induced damage

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Purpose To evaluate the effect of the dietary supplement Nutrof-Total, enriched in antioxidants and fish oil, on retinal fatty acid composition and its potential neuroprotective effect.

Methods Six-7 weeks old Sprague Dawley rats were not treated or administrated orally daily with 0,2 ml of water or Nutrof-Total for a period of 10 days. Then, they were sacrificed for fatty acid analysis on plasmas and retinas or they were exposed to bright cyclic light for one week. At the end of light exposure, electroretinograms are recorded and animal are sacrificed for histologic analysis and apoptotic cells detection.

Results One week of Nutrof-Total treatment induced a significant increase of EPA, DPA and DHA in the plasma to respectively 163%, 133% and 19%. In the retina, there is also a significant increase of EPA and DPA but not of DHA and LNA is significantly decreased. In parallel, there is a reduced level of omega-6 fatty acid in plasma and retina. In untreated animal, bright-cyclic light induced a reduction of the ONL thickness, an increased in apoptotic cells leading to a reduction of retinal function. Animals treated with Nutrof-total for 10 days before and during the bright cyclic light have a preserved retinal structure, a reduced number of apoptotic cells and a preserved retinal function.

Conclusion Nutrof-Total can protect the retina from light-induced retinal damage. Nutrof-Total may be beneficial in preventing the toxic effect of light on the retina.

Commercial interest

• F105

Effects of low intensity ultrasound (LIUS) on the macular degeneration model in vitro

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Purpose The retinal pigment epithelium (RPE) is compose of monolayer of tightly connected pigmented cells and supports the function of the normal vision function. Structural deformation and/or inflammation in RPE are commonly accompanied with and in many cases severely aggravate macular degeneration. We have reported previously low-intensity ultrasound (LIUS) of less than 1 mW/cm^2 shows cyto-protective and anti-inflammatory effects on chondrocytes and cartilage tissue under pathologic environments. The aim of this study is to investigate the effects of LIUS on RPE cells in macular degeneration models in vitro.

Methods ARPE-19 cells were grown on a plastic dish or permeable transwell inserts and were treated with various damaging agents such as PlGF (an agonist of VEGF receptor), NaCN and H2O2. Then, cells were untreated or treated with varying intensities of LIUS with a maximum of 200 mW/cm^2 once for 20 min a day. Viability of cells was examined with Wst-1 and TUNEL assays. Permeability of the cell monolayer on transwell membrane was tested by trans-epithelial electrical resistance (TEER) system. JC-1 staining was also performed to measure mitochondrial activity in cells.

Results Cell damaging agents increased cell death and permeability of cell monolayer in a dose-dependent dose manner. LIUS treatment significantly reduced both of the cell death and permeability. Changes in the mitochondrial membrane potential were also decreased by LIUS.

Conclusion This study demonstrated that LIUS inhibits cell death of ARPE-19 by various pathologic stresses, thereby might be a promising treatment for RPE under macular degeneration.

• F106

Hypoxia stimulates the synthesis and release of Brain Natriuretic Peptide (BNP) in RPE cells

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Purpose Blood flow and oxygen availability of the retina are modulated by locally produced peptides that also can change the function of neurons. The natriuretic peptide system has been isolated and characterized in human retina and these peptides localize in retinal pigment epithelium (RPE) cells. A high concentration of natriuretic peptides has been previously measured from the vitreous of patients suffering of proliferative diabetic retinopathy (PDR). However, the stimulus to which the natriuretic peptide system responds in PDR has remained unknown. We hypothesized that hypoxic conditions will increase the synthesis and release of Brain Natriutretic peptide (BNP) from human RPE cell culture.

Methods Human RPE cell were exposed to hypoxia for several hours. Samples were collected at time intervals and analyzed for BNP peptide and for BNP mRNA. A simultaneous measurement of VEGF served as a positive control.

Results In hypoxic conditions RPE cells secreted statistically significant amounts of BNP.

Conclusion These findings characterize for the first time a stimulus for the natriuretic peptide system in the retina and explain previous clinical findings. Thus, the measurement of natriuretic peptides from the vitreous may guide the treatment of the intraocular diseases in which the retina is suffering from hypoxia.

• F107

Augmentation of the ocular penetration of dexamethasone with β-blocker and α-agonist co-administration

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Purpose This study evaluated the ocular penetration of the radiolabelled corticosteroid 3H-dexamethasone after topical administrations of the β-blocker Ophtim®(0.5% timolol) and the α-agonist Iopidine®(1% apraclonidine) alone or in combination in pigmented rabbits.

Methods Animals were randomized in 4 treatment groups : Ophtim® or Iopidine®, or both of them, or NaCl 0.9%, first in 3 3-min apart topical administrations of 30 µL, followed by a single 30 µL instillation of 3H-dexamethasone (5 µCi), in both eyes and then in a single instillation every 2 hours, each also followed by a single instillation of 3H-dexamethasone. At 1, 2 and 8 hours after the first instillation, animals were euthanized and the aqueous humor, vitreous, retina and choroid were taken to determine 3H-dexamethasone concentrations with a liquid scintillation counter.

Results 3H-dexamethasone was detected in all tested ocular matrices, regardless of the pre-treatment. The 3H-dexamethasone concentrations tended to moderately increase in ocular tissues from animals pre-treated with either Ophtim® or Iopidine®. However, the preliminary topical administration of Ophtim® associated to Iopidine® resulted in a significant increase in the 3H-dexamethasone concentrations in sampled ocular tissues, including a nearly 3-fold increase in aqueous humor, compared with NaCl 0.9%.

Conclusion In conclusion, the association of the β-blocker Ophtim® with the α-agonist Iopidine® in multiples instillations prior to 3H-dexamethasone instillation increased the ocular penetration of the radiolabelled corticosteroid.

Commercial interest

• F108

Effects of intravitreal injection of anti-TNFα and anti-VEGF in experimental branch retinal vein occlusion in rats

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Purpose To investigate the effect of intravitreal injection of anti-TNFα and anti-VEGF antibodies on the inner blood retinal barrier (iBRB) in a rat model of experimental branch retinal vein occlusion (BRVO). Claudin-5, a tight junction protein seen in the retinal vascular wall was examined in order to evaluate the iBRB integrity.

Methods BRVO was induced in the right eye of Long Evans rats, using laser photocoagulation. The left eye served as control. The intravitreal injection with either anti-TNFα or anti-VEGF was performed in the right eye of each animal, 6 hours after BRVO. Two days after laser application, animals were sacrificed and retinas were harvested. The expression and distribution of claudin-5 were examined by immunofluorescent staining of flat-mounts under confocal microscopy.

Results Confocal micrographs showed that claudin-5 is specifically expressed on the cell boundaries of retinal vessels. Two days after laser induced BRVO, the distribution of claudin-5 in retinal veins of non-treated rats was weaker, rougher and less linear compared to the images seen in control animals. The staining of claudin-5 in retinal veins of rats treated with anti-VEGF or anti-TNFα was stronger, more linear and uniform.

Conclusion The anti-TNFα and anti-VEGF drugs seem to partially restore the integrity of the iBRB which may contribute to the reduction of macular edema. Ongoing experiments using RT-PCR will determine the effect of those drugs in the expression of genes that influence the development of macular edema after BRVO.

• F109

Examination of between eye retinal oxygenation saturation in the peri-papillary region

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Purpose To measure the inter-ocular agreement of retinal vessel oxygen saturation in the peripapillary retina of healthy individuals.

Methods Twelve otherwise healthy individuals (mean age 36.5 (SD 10.5)) underwent dual wavelength retinal oximetry (ImedosSystems, Germany), non-contact tonometry (Keeler Pulsair, UK) and manual shygomanometry in both eyes on the same day. For analyses purposes the major branches of the central retinal artery and vein crossing through a circular segment located one half disc diameter (DD) away from the optic nerve head (ONH) and 1DD in width were selected from 3 consecutively taken images. Arterial and venular oxygen saturation was then used to calculate the arterio-venous oxygen saturation difference.

Results Arterio-venous difference of peri-papillary retinal vessel oxygen saturation showed good inter-ocular agreement and no dependence on age, blood pressure or intraocular pressure (Right eye 37 (7)% and left eye 38 (5) %, r=0.71).

Conclusion There is good inter-ocular agreement of peri-papillary retinal oxygenation parameters in healthy individuals.

• F110

Flicker-induced retinal vasodilatation is not dependent on complement factor H polymorphism in healthy young subjects

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Purpose We have previously shown that choroidal blood flow regulation in healthy subjects is abnormal in carriers of the CC allele at rs1061170, a complement factor H polymorphism that is closely related to the risk of age-related macular degeneration. This is compatible with data in complement factor H deficient mice showing abnormal choroidal and retinal vasculature associated with endothelial damage. In the present study we hypothesized that the carriers of CC at rs1061170, which have an increased risk of AMD, already show abnormal retinal blood flow regulation at ages below 35 years.

Methods A total of 99 healthy subjects (aged between 19 and 35 years) were included in this study. Flicker-induced retinal vasodilatation was investigated in arteries and veins using the dynamic vessel analyzer (DVA) and genotyping at rs1061170 was performed.

Results Out of the 99 subjects 18 were homocygous for the CC allele, 50 were homocygous for the TT allele and 31 subjects were heterocygous. The response in retinal arteries (p=0.376) and retinal veins (p=0.617) to flicker stimulation was similar between the three studied groups. In addition, the baseline diameters of retinal arteries (p=0.619) and veins (p=0.471) was also comparable between the groups.

Conclusion Our data indicate that healthy young carriers of the CC allele at rs1061170 do not show abnormal flicker-induced vasodilatation in the retina. This is in contrast to our previous results in the choroid, where these individuals have abnormal blood flow regulation. Whether this is due to the differences in vasculature or the difference in the stimulus is unclear.

• F111

How much flicker is enough?

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Purpose To assess the impact of flicker length on retinal vessel dilation.

Methods Seven healthy individuals underwent manual shygmomanometry, non-contact tonometry (Keeler Pulsair, UK) and dynamic retinal diameter measurements using the retinal vessel analyser (ImedosSystems, Germnay). In order to evaluate the influence of flicker length on vessel dilation each subject was measured with 5 protocols of varying flicker length. Protocols consisted all of 50 second baseline measurements followed by 3 cycles of either 5 sec, 7 sec, 10 sec or 20 sec flicker provocation and 80 second recovery, whereas the fifth protocol consisted of 50 sec baseline, 50 sec flicker provocation and 120 sec recovery (single cycle). All protocols were administered on the same day but in random order with a minimum of 5-10 minutes recovery between protocols.

Results Most of the flicker induced dilation (~85%) is reached within the first 7 to 10sec post provocation start independent of flicker length. Any additional flicker provocation does not significantly increase arterial dilation (ANOVA p>0.05). However, venous dilation does increase with increasing flicker lengths but at a slower rate compared to the initial ten seconds.

Conclusion Through administering the different protocols it becomes apparent that the vessel dilation due to flicker light provocation is a two stage process: the first being the immediate reaction to accommodate increased metabolic demand and the second being the maintenance reaction to address prolonged demand. This two stage process could be useful in assessing patients with various ocular and systemic vascular insufficiencies and potentially be a more useful marker than the absolute dilatory response.

• F112

The influence of age on retinal vessel oxygenation

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Purpose To validate weather regional differences in retinal vessel oxygenation depend on age.

Methods Fifty three healthy individuals (age range 19-61 years; mean age 35 (SD 11) years) underwent manual sphygmomanometry, non-contact tonometry (Keeler Pulsair, UK) and retinal vessel oxygen saturation measurements using dual wavelength oximetry (ImedosSystems, Germany). In order to analyse regional saturation differences, all vessels were grouped according to their location into major superior and inferior artery and vein as well as into macula and peripheral feeders (MF and PF respectively for arteries) and macula and peripheral drainers (MD and MF respectively for veins).

Results Multiple regression analysis revealed no influence of age, blood pressure (SBP: 116 (13)mmHg, DBP:73 (11)mmHg) and intraocular pressure (12 (3)mmHg) upon arterial and venous oxygen saturation measurements (p>0.05). Superior and inferior MF, PF, MD and PD were comparable (MF: 97 (9)% and 97 (8)%, p=0.955; PF: 92 (11)% and 91 (9)%, p=0.607; MD: 87 (14)% and 85 (13)%, p=0.594; PD: 61 (14)% and 58 (16)%, p=0.381). MF and PF were significantly different in the superior and inferior retina (p=0.006 and p=0.0002) as were MD compared to PD (p<0.0001 and p<0.0001).

Conclusion Regional variations in oxygen saturation of retinal arterioles and venules are independent of age, blood pressure and intraocular pressure.

• F113

Retinal vessel reactivity after cigarette smoking

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Purpose To evaluate the acute impact of cigarette smoking on retinal vessel reactivity during flicker light provocation.

Methods 12 otherwise healthy smokers (mean age 28 (SD 5) years) underwent non-contact tonometry (Keeler Pulsair, UK), manual shygomanometry and continuous retinal vessel diameter measurements using flicker light provocation (RVA, ImedosSystems, Germany) at baseline and after smoking one cigarette. Smokers had regularly smoked for at least 6 months. For retinal vessel diameter measurements we used a standard protocol with 50 sec baseline diameter recording followed by 3 cycles of 20 sec flicker and 80 sec recovery.

Results Immediately after smoking systolic, diastolic blood pressure and heart rate increased significantly (SBP: 112 (13)mmHg to 124 (11)mmHg, p=0.0001; DBP: 69 (10) mmHg to 78 (8)mmHg, p<0.0001; HR: 73 (11)bpm to 83 (10)bpm, p=0.009). However, intra ocular pressure as well as arteriolar and venular diameter were unchanged (IOP: 15 (3)mmHg to 15 (3)mmHg, p=0.633, arteriolar diameter: 126 (15)au to 125 (15)au, p=0.416; venular diameter: 163 (16)au to 167 (15)au, p=0.329). Area under the curve results revealed no effect of acute smoking (arterial: AUC(FL) at baseline 61 (57) and post-smoking 60 (34), p=0.923; AUC(Cess) at baseline -22 (38) and post-smoking -11 (49), p=0,309; venous: AUC(FL) at baseline 54 (56) and post-smoking 65 (29), p=0.322; AUC(Cess) at baseline 51 (36) and post-smoking 50 (26), p=0.976).

Conclusion The acute effect of a single cigarette did not have an effect on dynamic retinal vessel dilation to flicker light stimulation in cigarette smokers arterioles and veins

• F114

Correcting influence of arsenic mineral water on structural characteristic of the retina of rat eyes in model chronic immobilization-emotional stress

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Purpose To study influence arsenic mineral water (AMW) on possible structural variations in retina to rat eyes with model of chronic immobilization-emotional stress (CIES), strengthened by situational factors.

Methods Experience has realized on 30 white rat-males which were divided into three groups: I – control group (10 rats). II group — comparison group — 10 rats with model of CIES. III group — experimental group — 10 rats with model of CIES which had an easy access to drinking AMW.

Results Model of CIES at rats is accompanied with change of a retina of an eye which appear in stretching and non-uniformity of cells in ganglionary layer; the centers of merge internal and external mesh layers. Vessels a part spasmed, are expanded by a part. The described variations appear for 15 day of supervision, become expressed and diffusive for 30 day.

Conclusion At rats with model of CIES had an easy access to drinking AMW, the picture of change in eye retina conforms to the above-stated description of results of experience of 15 day.

• F115

Blindness due to mistake of antituberculosis treatment

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Purpose Antituberculosis drugs such as Ethambutol and Isoniazid may induce toxic optic neuropathy, that has lead to recommendations on the follow-up of patients under antituberculosis treatment. In Central African Republic, as in many countries where tuberculosis is endemic, this affection may also develop as an opportunist illness of AIDS. Treatment with antituberculosis drugs is often long, and the incidence of ocular toxicity increase.

Methods Since 1998, we noticed an increasing number of bilateral blindness in the population of patients treated by Ethambutol in our outpatient practice. We report here 10 from 23 clinical cases of visual impairment, observed in ophthalmological service of Bangui Teaching National Hospital Center.

Results Two patients received the recommended dose (25mg/Kg/day) throughout the treatment. The others have found themselves in overdose because of a loss of weight. Visual symptoms begin on the average during the 3rd month of treatment. Three patients had a visual improvement, 3 others a stabilization of vision, and the remaining 4 a worsening of vision.

Conclusion We raise from this series a necessary awareness for patients, prescribers and the practitioners in charge of the National program for Tuberculosis Control, on importance of the ocular toxicity of antituberculosis drugs. Yet efficient and extensively used, these drugs require special clinical and biologic balance before every prescription, and close ophthalmologic survey throughout the treatment.

• F116

Galenic and analytic development of Tacrolimus 0.06% eye drops

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Purpose The administration of topical tacrolimus (FK506) eye drops or ointment is used in treating corneal immune pathologies and in the prevention of the high-risk corneal graft rejection. The purpose of this study is to develop a new well-tolerated formulation of tacrolimus 0,06% eye drops. Procedure and the preparation are presented and discussed.

Methods Tacrolimus monohydrate powder and virgin castor oil are used in this new formulation. The manufacturing process guarantees the product sterility. Analytical validation of the assay by high-performance liquid chromatography allows precise control of the concentration of tacrolimus.

Results The manufacturing and packaging of these eye drops provide good product stability. The concentration of tacrolimus 0.06% was maintained for 28 days, and no mycological or bacteriological contamination was found. Eye drop can be conserved close and exposed to the light during three months after production.

Conclusion Tolerance studies are currently being carried out.

• F117

Damage of tolerance to glucose (TG) is the predecessor of insular diabetes (ID) and is accompanied by different metabolic changes, which need all-round research

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Purpose To research changes of water-electrolytic exchange (WEE) in lens and liquid of anterior chamber of eye of rats with latent changes of carbohydrate metabolism.

Methods White rats Wistar were taken once subcutaneous introduction of alloxan solution in dose 0,075 g/kg.

Results After 14 days in lens and liquid of anterior chamber of eye rats was discovered increase concentration of K+ and decrease concentration of Na+. At the same time content of total tissue water in lens was reduced. Basal level of glucose in blood on an empty stomach was normal. At testing TG was revealed increase of glucose level during 3 hours.

Conclusion It was determined in initial stage of ID genesis have occurred changes of water-electrolytic exchange (WEE). The received results expand concept about pathogenetic mechanisms of ID genesis and may be used in researching of correct influence of natural medical factors (mineral waters, for example).

• F118

Effects of Irifrin 2,5% on the disturbances pupillary-accommodative system in patients

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Purpose The disturbances of pupillary-accommodative system in patients include astenopia, decreasing of visual acuity, headache.The aim of the study was to conduct investigation of direct and consensual pupillary reactions on the flashlight, accommodative-convergence reaction on a fixed object with the help of elaborated pupillography device before and after instillation of Irifrin 2,5% in both eyes

Methods Irifrin 2,5% was applied for diagnoses and treatment of pupillary-accommodative system disturbances in 34 patients aged 7–13 with myopia and hypermetropia. Vision acuity, reserves of accommodation, autorefractometry, pupillography of direct, consensual, pupillary- accommodative reactions before and after instillation of Irifrin 2,5% in both eyes were studied. Balance of autonomic nervous system was appreciated by Cerdo index: positive (+) means the prevalence of simpatic; negative (-) means the prevalence of parasimpatic. It was estimated by following formula: Cerdo index = (1-D/P) x 100

D – diastolic blood pressure;

P – number of heart systoles per min;

For treatment one drop of Irifrin 2,5% was used once before sleeping in the both eyes during one month.

Results Irifrin 2,5% was effective for treatment in all patients with disturbances of accommodation, who had sympathycotonic autonomic balance. During one month after treatment visual acuity increased and normal pupillary- accommodative reactions normalized, astenopia and headache disappeared.

Conclusion Irifrin 2,5% was effective for diagnoses and treatment of pupillary-accommodative system disturbances in patients. Irifrin 2,5% instillations is recommended for treatment 3-4 times a year.

• F119

Sunglasses with wide temples and thick frame severely constrict temporal visual field extent

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Purpose To compare the impact of two types of sunglasses on visual field and glare: one ("thick sunglasses") with a thick plastic frame and wide temples, and one ("thin sunglasses") with a thin metal frame and thin temples.

Methods Using the Goldmann perimeter, visual field surfaces (cm2) were calculated as projections on a 30 cm virtual cupola. A V4 test object was used, from seen to unseen, in 15 healthy volunteers in the primary position of gaze ("base visual field"), then allowing eye motion ("eye motion visual field") without glasses, then with "thin sunglasses", followed by "thick sunglasses". Visual field surface area differences superior to the 14% reproducibility error of the method and having a p-value inferior to 5% were considered significant. A glare test was done using a surgical lighting system pointed at the eye(s) at different incidence angles.

Results No significant "base visual field" nor "eye motion visual field" surface area variation were noted comparing tests done without glasses and with the "thin sunglasses". In contrast, a 22% "eye motion visual field" surface area decrease (p-value = 2.7.10-13) was noted comparing tests done without glasses and with "thick sunglasses". This decrease was most severe in the temporal quadrant (-33%; p-value = 6.3.10-20). All subjects reported less lateral glare with the "thick sunglasses" than with the "thin sunglasses" (p-value = 6.10-5).

Conclusion The better protection from lateral glare offered by "thick sunglasses" is offset by a severe temporal "eye motion visual field" surface area constriction.

• F120 / 4744

Role of nitric oxide in optic nerve head blood flow regulation during experimental increase of intraocular pressure in healthy humans

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Purpose Several studies have indicated that the choroid shows some regulatory potential during changes in ocular perfusion pressure (OPP). For the optic nerve head (ONH) only few data are available. The present study set out to investigate the behavior of ONH blood flow (ONHBF) during an experimental decrease in OPP and to explore whether inhibition of Nitric Oxide Synthase (NOS) alters this response.

Methods Twelve healthy subjects participated in this randomized, double-masked, placebo-controlled three-way crossover study. For each subject, three study days were scheduled, on which they either received intravenous infusions of NG-monomethyl-L-arginine (L-NMMA), phenylephrine, or placebo. OPP was increased stepwise by the suction cup method. ONHBF was assessed continuously with laser Doppler flowmetry and OPP was calculated as 2/3*mean arterial pressure-intraocular pressure.

Results Administration of L-NMMA and phenylephrine significantly increased resting OPP compared to placebo ($p<0.001$ and $p=0.016$, respectively). As expected, L-NMMA decreased resting ONHBF compared to phenylephrine ($p=0.04$). The relative decrease in OPP during suction cup application was comparable with all drugs administered (between -69% and -72%, $p=0.19$). In all three groups, the decrease in ONHBF was less pronounced than the decrease in OPP, but not significantly different between groups.

Conclusion The present data indicate that NO plays an important role in the regulation of basal ONHBF, but not in ONHBF autoregulation.

• F121 / 4746
Eye motion increases temporal visual field extent

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Purpose To study the impact of eye motion on visual field extent.

Methods Visual fields were tested in 15 healthy volunteers with the Goldmann perimeter using a V4 test-object, from seen to unseen, first in primary position of gaze, then allowing eye motion. Temporal points falling out of the cupola were tested again after a controlled nasal head rotation using a headband prototype fitted with a line-laser level having two orthogonal vial levels. Visual field surface areas (cm2) were calculated as projections on a 30 cm virtual Goldmann cupola whose extent would have been large enough to include all points. Reproducibility error of the method assessed by calculation of the relative difference between surface areas of 12 visual field tests and 12 visual field retests was estimated at 14%. Hertel exophthalmometry was recorded to study the influence of globe position on visual field extent.

Results Binocular visual field surface area increased by 37% with eye motion (p-value = 1.20.10-9). This increase was highest (46%; p-value = 1.2.10-24) in the temporal quadrant. Median maximal visual field temporal excentration with eye motion was 128.3° (minimum: 109.5°; maximum: 137.7°) and more than 135° in 4 eyes of three subjects. Hertel exophthalmometry was positively linked to visual field temporal surface area with eye motion (p-value = 0.013).

Conclusion Eye motion greatly expands the temporal visual field. This peculiarity is likely an adaptation to terrestrial life with upright bipedal locomotion, and may save head movements through horizontal eyeball scanning.

• F122 / 4266
Oxidative stress in retinal pigment epithelial cells: protective effect of wood-derived phenolic compounds

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Purpose Oxidative stress is related to chronic diseases including age-related macular degeneration (AMD), which is the leading cause of blindness in the elderly worldwide. Functional roles of wood-derived phenolic compounds such as flavonoids, phenolic acids, tannins and stilbenes are not well known, but some of them are effective antioxidants capable of providing defence against oxidative stress. Besides reducing ROS production by their antioxidant activity, phenolics can also activate the expression of phase II genes via the activation of transcription factors, such as Nfr2.

Methods In this work, the protective effect of wood phenolics against oxidative stress were determined by pre-incubating ARPE-19 cells in medium containing wood compounds (pinosylvin, piceatannol, trans-resveratrol or pinosylvin monomethyl ether) at different concentrations. After pre-incubation with phenolics, cells were treated with oxidative stress causing agent, hydroquinone, for 24 hours. The viability of cells was determined by using MTT assay. To elucidate the mechanisms behind the phenolics-mediated protection against oxidative stress and inflammation, the activity of genes such as Nrf2, IL-6 and p62 was determined.

Results Wood-derived phenols were well tolerated by the cells and some of the compounds such as pinosylvin were able to increase the viability of cells in response to induced oxidative stress.

Conclusion These results suggest that wood-derived phenolic compounds can provide additional protection against oxidative stress in retinal cells.

• F123
Aqueous erythropoietin level in retinal vein occlusion

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Purpose To investigate the aqueous level of erythropoietin (EPO) and associated factors in patients with retinal vein occlusion (RVO).

Methods The aqueous EPO level was measured prospectively with chemiluminescent immunoassay in consecutive patients with macular edema (ME) secondary to branched retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO). Aqueous fluid of cataract patients served as control. Patients taking anti-hypertensive medication with angiotensin converting enzyme inhibitor or angiotensin II receptor blocker, prior intraocular surgery or injection of steroid or antiangiogenic factors, or longstanding (3> months) BRVO or CRVO were excluded. We also evaluated whether aqueous EPO was associated with factors such as serum EPO concentration, non-perfusion area, and arterio-venous (AV) transit time, and central macular thickness (CMT).

Results Aqueous level of EPO was higher in RVO (27 eyes; BRVO 16 eyes/CRVO 11 eyes) than in control subjects (RVO, 68.1 [19.8-190] mU/ml vs. control, 12.9 [5.4-24.4] mU/ml, P<0.001). More specifically, aqueous EPO was higher in CRVO than in BRVO (CRVO, 118.9 [31.8-190] mU/ml vs. 33.3 [19.8-62.5] mU/ml, P<0.001). However, no differences were found in serum levels of EPO among controls, BRVO, and CRVO groups (CRVO, 11.1mU/ml[5.4-16.4] vs. BRVO, 10.0mU/ml[6.7-16] vs. control, 9.2mU/ml[5.7-11.2], P=0.091). CMT in RVO patients had positive correlation with the aqueous level of EPO in RVO (P=0.003). Also, in terms of non-perfusion area, there was a significant difference in the aqueous level of EPO between ischemic and non-ischemic subtypes of CRVO (ischemic, 172 [156-190] mU/ml vs. non-ischemic, 83.6 [56.3-142.5] mU/ml, P=0.0027).

Conclusion In RVO, aqueous levels of EPO are elevated and could be associated with retinal ischemia and ME

• S001

Structural changes of the cornea in a patient with mucopolysaccharidosis (Hurler- Scheie) in confocal microscopy images

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Purpose To determine the characteristic structural corneal changes in a 22 years old patient with Hurler Scheie syndrome using confocal microscopy in vivo.

Methods The study was conducted in 22 year old man with Hurler syndrome. The patient presents typical phenotype of this syndrome. Additionally the symptoms reduced by enzymatic treatment confirms the diagnosis of disease. Slit lamp examination, corneal scans using the Scheimpflug camera (Pentacam, OCULUS) and corneal confocal microscopy in vivo (Rostock Cornea Module, Heidelberg Engineering Retina Tomograph III) were performed.

Results In all performed examinations the edema and loss of transparency of the cornea have been documented, but the characteristic structural changes were only demonstrated in in vivo confocal microscopy images. Abnormalities in microscopic images were described in all layers of the cornea. The tear film was found containing numerous non-characteristic inclusions, as well as in the epithelial layer. The most common change was found in front part of corneal stroma - a system of highly hyperreflected, stimulated, vacuolisated keratocytes of "honeycomb-like" structure and a very sparse amount of stromal matrix. Posterior stroma appeared non-characteristic hazes, presence of scarring and corrugations up to Descemet's membrane. Due to the thickness of the cornea more than 1000 microns, it was impossible to image the endothelium.

Conclusion Corneal confocal microscopy in vivo, is a useful tool in the diagnosis of corneal opacities in the course of MPS Hurler. By characteristic structural features, it can be used for confirming the diagnosis.

• S002

Digital analysis of the changes in carcinomatous conjunctiva using Aperio nuclear v9 algorithm

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Purpose To analyze and evaluate biological and morphometrical changes and differences of healthy and carcinomatous conjunctiva using Aperio nuclear v9 algorithm.

Methods A pilot study for the objective evaluation of carcinomatous conjunctiva in 6 cases. There were analyzed 6 excised conjunctival tumors specimens from 6 patients (6 eyes). Medium age of the patients was 68 years. There were two males and four females. In 3 patients (3 eyes) conjunctival tumor was excised, cryoaplication and amniotic membrane transplantation was performed. In 3 patients excisional biopsy was performed without additional surgical manipulations. Conjunctival specimens were stained with hematoxilin and eosin. Immunohistochemical (IHC) staining with a proliferation marker of cells Ki-67 was performed for all specimens. Digital slides of the IHC of Ki-67 from these biopsies were obtained by Aperio ScanScope GL. Aperio Nuclear V9 algorithm was applied to assay proliferation indices (PI) of nuclei stained with Ki-67 and size of all nuclei in both abnormal and normal conjunctiva.

Results There were analyzed from 1585 till 5020 malignant and 242-714 normal cells. PI of Ki-67 ≥19% (range 19.3-62.1%) was found in carcinomatous conjunctiva comparing with normal conjunctiva PI ≤13.5% (range 1.9-21.6%) in the same patients. No significant difference was found between nucleus size in pathological (mean 41 μm2, range 33-64 μm2) and normal conjunctiva (mean 35.5 μm2, range 34-36 μm2).

Conclusion Aperio nuclear algorithm can be used for carcinomatous and healthy conjunctiva analysis. Further studies of the malignant and healthy eye tissues using larger cohort are required.

• S003

Sebaceous carcinoma : diagnosis and therapeutic difficulties

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Purpose Sebaceous carcinoma is a malignant neoplasm that usually arises in the sebaceous glands of the eyelids (Meibomian and Zeiss glands). It can invasive the eyelid and the cunjunctiva and can metastasize to regional lymph nodes and distant organs.This tumor affects most frequently women after fifty years.The clinical diagnosis is difficult due to atypical presentations simulating benign lesions or other malignant tumors. Furthermore, its surgery is complicated because as we must perform large tumor excision with often difficult eyelid reconstruction. Through our small case series, we describe the clinical describe the clinical features and our management of this tumours.

Methods We report six patients presenting with eyelid sebaceous carcinomas: three nodular sebaceous carcinoma, one spreading sebaceous carcinoma and two cases with no safety margin after the initial surgery.

Results In all the cases , we completely removed the tumour with safety margin of at least five millimeters and then we reconstructed the eyelid.The diagnosis of sebaceous carcinoma was confirmed by the histological study .Afterward, all our patients benefited from an adjuvant radiotherapy.

Conclusion Due to its difficult diagnosis and the delay in treatment, the overall survival rate of sebaceous carcinoma is about 5 to 10 % and can reach 30% for infiltrative forms. The presence of yellowish material within tumour, which can simulate a chalazion, is highly suggestive of sebaceous carcinoma.The best management is the large tumoral excision.In our opinion, the adjuvant radiotherapy must be systematic due to the high grade of malignity.Moreover,the biological behavior of this kind of tumour requires long-term oncologic following.

• S004

Amelanotic conjunctival melanoma: diagnosis and therapeutic management

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Purpose To present a case report of a patient with atypical presentation of a conjunctival melanoma as an amelanotic tumor.

Methods A 82-year-old female presenting a large amelanotic tumor in inferior tarsal conjunctiva of the right eye was referred to our hospital. Previous histological analysis diagnosed intraepithelial carcinoma. Imaging digital analysis techniques showed infiltration of the extrinsic ocular muscles but not the scleral tissue. Excisional biopsy was obtained by removing the tumor with free margins and preserving as many unaffected tissue as possible. Amniotic membrane graft was used to cover the surgical injury.

Results Histopathological diagnosis confirmed amelanotic conjunctival melanoma. Systemic evaluation with imaging techniques (MRI, TC scan, Ecography...) revealed liver and kidney masses suggestive of metastasis and chemotherapy was prescribed to control the disease. Ophthalmological controls showed remission of tumor for 4 months, but new conjunctival masses appeared. At the present the patient is treated with palliative chemotherapy. Age and systemic status do not allow aggressive therapies in this patient.

Conclusion Amelanotic melanoma is an atypical subtype of melanoma lacking of pigmentation. Its macroscopic aspect makes it almost impossible to clinically distinguish this tumor from less aggressive tumors, such as intraepithelial carcinomas. The diagnosis delay makes early treatment difficult in this malignant tumors.

• S005 / 3682
Valproic acid (VPA), a class I and II histone deacetylase (HDAC) inhibitor and conjunctival melanoma

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Purpose To investigate the expression of histone deacetylases (HDACs) in human conjunctival melanoma (CM) cell lines and primary melanocytes, and assess the effects of VPA, a broad Class I and II HDAC inhibitor, on cell viability and growth.

Methods CM cell lines (CRMM1 & 2; CM2005.1) and primary melanocytes were immunolabelled with antibodies to HDACs: Class I (HDAC1, 2 and 3), Class IIA and IIB (HDAC4 and HDAC6), and Class III (SIRT2). Antibody localisation was visualised with immunofluorescence and confocal microscopy. Dose-response and proliferative potential following treatment with VPA was assessed for up to 72hrs using MTT and colony assays, respectively Cell cycle dynamics were also assessed.

Results Differential HDAC expression was observed in CM cells and melanocytes, for both immunolocalisation (nuclear vs cytoplasmic) and cell type. CM2005.1 cells displayed lower level expression of HDACs compared to CRMM1 and 2 cells. VPA IC50 (72hrs) was 3.75mM, 5.42mM and 8.33mM for CRMM1, 2 and CM2005.1 cells, respectively. Colony assays showed similar patterns of response, with surviving fractions 0.2 and 0.5 for CRMM1 (VPA 0.3125mM) and CRMM2 (VPA 2.5mM) respectively. Cell cycle analysis showed dose-related G1 block for CRMM1 and G2 block for CRMM2 cells at 24hrs (0mM to 1.25mM VPA).

Conclusion Overall, CM2005.1 cells are more resistant to VPA compared to CRMM1 and 2 cells. VPA inhibition of CM cell growth and proliferation may be related to the observed differential expression of HDACs between cell lines. Combination therapies using VPA and other HDAC inhibitors may be potentially useful in managing the growth of primary CM. Supported by Sydney Foundation for Medical Research.

• S006
Iris tuberculous granuloma simulating medulloepithelioma

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Purpose Pediatric ocular granuloma is a rare condition which may result from several causes including trauma, inflammatory diseases, or infectious agents such as fungi, viruses, or mycobacteria. The purpose of this case report is to increase the knowledge about the ophthalmic clinical picture, magnetic resonance imaging findings, histological pattern of a rare case of iris tubercular granuloma occurring in a 4-year-old boy.

Methods Case report

Results Inflammatory granulomas are usually the expression of systemic inflammatory diseases. Clinical picture may be that of an anterior or posterior uveitis and it may occur with uveal granulomas or episcleral nodules. Our case at diagnosis simulated a medulloepithelioma, both for ophthalmogic and neuroradiologic findings. Pathology following biopsy revealed a tuberculous granulomatous lesion.

Conclusion A complete systemic investigation confirmed tuberculous aetiology of this granulomatous lesion.

• S007 / 4668
Pink pseudohypopyon as a presenting feature of large B-cell lymphoma

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Purpose To describe the clinicopathologic features of a patient who developed an anterior chamber (AC) infiltrate mimickina pink pseudohypopyon as a presenting feature of large B-cell lymphoma.

Methods The clinical and pathologic findings in a patient with AC infiltrates secondary to systemic B-cell lymphoma are reviewed. Main outcome measurements were clinical observation and cytologic/flow cytometric examination of the infiltrate after AC aspiration.

Results A 51-year-old woman was evaluated for decreased vision in her right eye.On examination, her visual acuity was 20/30 in the right eye (RE) and counting fingers in the left eye. Abnormalities were confined to the RE. Slit lamp examination revealed +1 AC cells with a pink pseudohypopyion occupying 40% of the AC. The iris was corrugated and had small new vessels in the stroma. An anterior chamber aspirate was performed, and 0.8 ml of fluid was obtained. The sample was formed by 32% of lymphocytes and 54% of neutrophils. B-lymphocytes were predominant over T-lymphocytes (91% and 8%, respectively). Cytologic examination showed scattered atypical mononuclear cells. Immunohistochemical stains were positive for CD19 in the atypical cells. Flow cytometric immunophenotyping revealed a clonal, kappa restricted population of B-lymphocytes comprising 97% of the viable cells in the sample. These results were consistent with a large B-cell extranodal lymphoma.

Conclusion Anterior chamber/iris infiltration from systemic lymphoma is exceedingly rare, present in less than 10% of patients. Herein, we describe a patient with systemic lymphoma in whom the first manifestation was a pink pseudohypopyon.

• S008
Never miss uveal lymphoma

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Purpose Primary intraocular lymphomas can mimic many other diseases. The purpose of this presentation is to underline the crucial importance of biopsy.

Methods We described two cases of atypical primary uveal lymphomas.

Results The first case concerned a 35 year-old man who presented a painful intraocular tumor with ciliary body infiltration. Enucleation was performed because of high suspicion of melanoma. Pathological findings revealed MALT lymphoma. No other localization was found and no further treatment was done. The second case concerned a 49 year-old woman who presented blurred vision secondary to a choroidal mass associated with choroidal yellow infiltrates in right eye. An internal chorioretinal biopsy was performed, leading to the diagnosis of diffuse large B cell lymphoma. This high-grade lymphoma was treated with chemotherapy associated with radiotherapy.

Conclusion These two cases illustrate the variety of clinical features of uveal lymphomas, which can mimic choroidal melanoma as in our first case. In our second case, histological findings were not typical and required an aggressive treatment. Biopsy and histological analysis remains the only way to diagnose a primary uveal lymphoma especially in cases of atypical presentation.

• S009

A new and standardised method to sample and analyse vitreous biopsies

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Purpose To investigate and prepare a universal protocol for sampling and analysing vitreous material. Vitreous biopsies are difficult to handle because of the paucity of cells, the gelatinous formation and structure of the vitreous, the low frequency of biopsies and the burden of long-during, delicate handwork by the technician.

Methods After a standardised 23gauge vitrectomy, 50 consecutive vitreous samples were analysed with the Cellient® tissue processor (Hologic). This machine is a fully automatic processor from a specified container with PreservCyt® (fixative fluid) with cells to paraffin. Cytology was compared with fixatives Cytolyt® (contains a mucolyticum) and Preservcyt®.

Results In 96% (48 of 50 cases) sufficient material was found for diagnosis. Cytolyt® wash was necessary in 15% of cases to prevent clotting of the delicate tubes in the Cellient®, this procedure causes a loss of cellular material. Immuno-histovhemical stainings were equal in quality with both preservatives. Labour hours of processing by technician was diminished by 4, compared with former, not-standardised techniques.

Conclusion A standardised protocol for sampling and handling viteous biopsies by a 23G vitrectomy, fixing in PreservCyt® and processing by the Cellient® gives a superior result in morphology, number of cells, possibility of immuno-histochemical stainings and technician labour hours.

• S010

A case of spontaneously regressed uveal melanoma

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Purpose To present a case report of spontaneously regressed uveal melanoma.

Methods Complex clinical and instrumental diagnostics was done.

Results A patient, 62 y.o. complained of right eye vision absence during last 10 years. Several months ago appeared pain in the eye and this was the cause to visit to the ophthalmologist. The investigation revealed the eye subatrophy, deviation about 20°, moderate conjunctiva injection, corneal edema and dystrophy. Anterior chamber was deep. The iris was infiltrated with heterogeneous pigmented mass. Pupil had irregular form and complicated cataract was present. Eye fundus was not able to visualize. Vision OD=0, OS=1,0. The right eye pressure was decreased. CT-scanning demonstrated the intraocular mass with calcification spreading into the orbit along the optic nerve sheets. Enucleation with orbitotomy was performed. During the operation the defect of sclera with black mass infiltration around the optic nerve was revealed. The pathomorphologic examination confirmed the spindle cell uveal melanoma with massive zones of calcification in intraocular lesion forming extraocular extension.

Conclusion All subatrophy eyes must be examined in details to exclude the intraocular tumors.

• S011

The mitotic index in secondary enucleated eyes of previously treated uveal melanoma patients

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Purpose The aim of this study is to evaluate the difference of mitotic activity in secondary enucleated uveal melanoma cases in two different groups of patients who have been treated previously with conservative therapy.

Methods We evaluated two groups of patients. The first group consisted from treated uveal melanoma patients who developed a blind painful eye due to end stage of vascular glaucoma, while the second group consisted from uveal melanoma patients who developed a recurrence of uveal melanoma in the same eye after several years. Moreover, we assessed the relationship of the mitotic activity with the other clinicopathological features of the enucleated eyes of the two groups of uveal melanoma patients. We also, recorded and analysed the data including the age of the patients, the size of the tumor, the location, the cell type, and the treatment modality and correlated with the survival rate.

Results Our results showed that there was a significant difference in the mitotic activity between the two groups of patients. The mitotic index was higher in the enucleated eyes of uveal melanoma patients who developed a recurrence at the same eye as opposed to the enucleated eyes of uveal melanoma patients due to other reasons such as vascular glaucoma and blind painful eye. The mitotic activity was almost absent in the majority of enucleated uveal melanoma cases due to vascular glaucoma.

Conclusion To the best of our knowledge this is the first report that evaluates the mitotic index in secondary enucleated eyes of uveal melanoma patients.

• S012

Treatment of macular oedema following proton beam therapy for choroidal melanoma with dexamethasone 700µg intravitreal implant

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Purpose To report the treatment of radiation macular edema following proton beam therapy for choroidal melanoma with dexamethasone 700µg intravitreal implant.

Methods Retrospective cases report

Results Five patients were treated with a single injection of intravitreal dexamethasone 700 µg. These patients presented with an uveal melanoma (mean thickness: 4.44 mm, mean highest diameter: 11.14mm) located at 2.58mm (range 0 to 3.5mm) from the macula. Patients were treated with proton beam irradiation (60 Gy cobalt relative biological effectiveness in 4 fractions) 26.75 months (range 16-43 months) before the occurrence of radiation macular edema. The intravitreal injection of dexamethasone700 µg was performed 5.5 months (1-14) after the diagnosis of macular edema. Best corrected visual acuity improved for 4 patients (5; 7; 9 and 10 letters), and remained unchanged for 1 patient, over a 5 months follow-up period. Central retinal thickness decreased for 3 patients (231; 151 and 97 µm) and remained unchanged for 2 patients. Intraocular pressure increased for 1 patient (IOP>25 mmHg at month 3). No other ocular or systemic side effects were noted.

Conclusion Radiation macular edema is a common vision threatening complication following proton beam therapy. The available therapeutic options are limited. Intravitreal injections of dexamethasone implant can be of benefit in selected cases.

• S013

Identification of mRNAs and proteins specifically associated with transformation in ocular malignant melanoma cells

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Purpose Ocular malignant melanoma has several morphological specificity when compared to melanoma tissues from other body regions. To assess and evaluate specific molecular factors of ocular melanoma we decided to screen clinical specimens from patients with melanoma from different tissue and organs, including eye.

Methods To identify a number of factors to be analyzed in clinical samples, we selected mRNAs specifically associated with the transformation state of cultured human melanoma cell line A375 This cell line was used as typical reference status of melanoma cells. These cells were then compared to similar cells in which Bag3 mRNA was silenced by transfection with specific siRNA (small interfering for Bag3). This mRNA encodes a protein which has a potent anti-apoptotic effect and is generally expressed in melanoma cells, being part of the molecular mechanism of their transformation status.

Results Microarray techniques took advantage to compare the whole pattern of cellular mRNAs in the two conditions of A375 cells: untreated neoplastic and Bag3 silenced cells. Several mRNA species resulted differentially expressed between the two conditions both as induced or as decreased when comparing the more transformed condition vs. Bag3 silenced cells. We then tested the expression of some of these mRNA and of their encoded proteins within the clinical samples of ocular and non-ocular melanoma tissues.

Conclusion Preliminary results indicated the expression of nephroblastoma overexpressed gene (NOV) as typical of melanoma transformation and of a small pattern of proteins as selectively modulated in ocular melanoma.

• S014

Antitumor evaluation of the new Bcl-2/Bcl-xl inhibitor S44563 in primary human uveal melanoma xenografts

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Purpose Nearly half of primary Uveal melanoma (UM) metastasizes in liver, but there are currently no effective therapies. Human UM are characterized by a high expression of Bcl-2, ranging between 50% and 100%. This observation has been confirmed in our panel of 16 human UM xenografts obtained from patient's tumors (Némati et al, CCR 2010). We have investigated the efficacy of the new Bcl-2/Bcl-XL inhibitor S44563 on 4 primary human UM xenografts.

Methods Four well characterized primary human UM xenografts were used. S44563 (50 or 100 mg/kg, days 1-5/8-12/22-26/29-33) was administered IP alone or combined with fotemustine, concomitantly (15 or 30 mg/kg days 1 and 22), or after chemotherapy (100 mg/kg, days 43-47/50-54/64-68/71-75). Tumor Growth Inhibition (TGI) was calculated to measure the efficiency of drugs. Bcl-2, Bcl-XL, and Mcl-1 expressions were determined by immunohistochemistry (IHC).

Results S44563 administered alone induced a moderate TGI of about 50% in 1 model (MP41). When combined S44563 to fotemustine, we observed a synergistic activity in 2 models (MP77 and MM66), without impact on the proportion of complete remission. Finally, when S44563 was concomitantly and/or administered after fotemustine, we found a delay of tumor growth in 2 among the 3 tested xenografts (MP77, and MM26). IHC analyses showed that Bcl-2, Bcl-XL, and Mcl-1 expressions were not modified after S44563 administration.

Conclusion We have shown that S44563 increased the efficacy of chemotherapy in concomitant combination or after fotemustine. Such preliminary results underline the therapeutic potential of this new Bcl-2/Bcl-xl inhibitor in human UM.

• S015

Bilateral choroidal metastases as presentation of dissemination of cutaneous malignant melanoma

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Purpose To report the case of a patient with bilateral choroidal mestastases as the first sign of dissemination of cutaneous malignant melanoma.

Methods A 47-year-old Caucasian male presented to our emergency department with rapid-onset blurred vision in his right eye (RE).Ophthalmoscopic examination revealed multiple pigmented placoid lesions located in the posterior pole and half periphery of the retina of both eyes and a serous macular detachment in RE. Optical coherence tomography confirmed the macular neurosensory detachment in the RESince clinical suspicion of choroidal metastases, we referred the patient to the Oncology Department for systematic study. After an exhaustive study, they concluded that it was a dissemination of a cutaneous malignant melanoma with bilateral choroidal metastases, liver and spleen metastases.

Results The patient underwent palliative treatment with chemotherapy with improvement of the visual acuity and reduction of the macular neurosensory detachment in the RE. Nevertheless the patient died months later of the diagnosis of cutaneous melanoma dissemination.

Conclusion Dissemination of cutaneous melanoma to the choroid is rare and is a major prognostic factor. In general the treatment of ocular metastases is palliative, because the presence of metastases indicates hematogenous spread of tumor. The objectives are therefore to maximize the quality of life and restore or preserve vision.

• S016

Retinoblastoma – risk factors and quality of life

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Purpose Evaluation of influence of medium factors in children with retinoblastoma and quality of life after treatment.

Methods Retrospective study for 84 eyes treated for retinoblastoma (Rb) in Ophthalmological Department, Hospital "Prof. Dr. Nicolae Oblu" Iasi. Clinical parameters studied: age of diagnosis, adjuvant factors (hypoxia, pregnancy hemorrhages, congenital rubella, ionizing radiation, endocrinological disease of mother) and hereditary factors. Statistical evaluation: program SPSS 16.0, test Mann-Whitney, Kruskal-Wallis were used.

Results Between 1953 and 2010 in Ophthalmological Clinic were treated 702 eyes tumors and 77 were diagnosticated with Rb. Unilateral cases were 70 cases and 7 cases bilateral Rb. Hypoxia were at 24,7% Rb versus 4,8% children without Rb (cwRb) – risk factor 2,609. Hemorrhages during pregnancy were 27% in mother with children with Rb versus mothers with cwRb – risk factor 1,735. Mother inflammations were registrated at 39% children with Rb versus 17% cwRb – risk factor 2,025. Congenital rubella was at 15,6% children with Rb versus 5,5% cwRb – risk factor 1,943. Endocrinological diseases of mothers were 26% versus 7,9% - risk factor 2,222. Ionizing radiations were found in 81,8% children with Rb versus cwRb – risk factor 8,312. All cases were treated with radical surgery – enucleation associated with chemotherapy.

Conclusion Ionizing radiation is the highest risk factor (Iasi is 500 km near Chernobyl) especially during 1986- 1991. The majority of cases were very late diagnosticated and treatment was for all cases enucleation. Quality of life is poor because of radical treatment and esthetic reasons.

• S017

Massive anterior chamber involvement in advanced retinoblastoma following intra-arterial chemotherapy

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Purpose to describe retinoblastoma massive anterior chamber involvement after treatment with intra-arterial chemotherapy. This condition represents an extremely poor prognostic sign for ocular preservation in patients with retinoblastoma. Therefore, anterior chamber retinoblastoma should be considered an absolute indication for enucleation.

Methods Ultrasound biomicroscopy (UBM) was used to document tumour pseudohypopion, cells in the aqueous humor, implanted clusters of cells on the corneal endothelium, iris nodules and lens capsule deposits.

Results The UBM data were compared with the histopathologic analysis after enucleation and revealed a significant concordance.

Conclusion UBM may represent an important diagnostic tool in retinoblastoma, particularly when the decision about enucleation of the eye, must be made in the absence of histopathologic data.

• S018

Acute dacryoadenitis as atypical presentation in Sjögren Syndrome

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Purpose To present a case report of a patient with acute dacryoadenitis as an atypical clinical presentation of Sjögren Syndrome.

Methods A 37-year-old female developed acute left dacryoadenitis with poor response to oral corticosteroids. She had no history of any other clinical symptoms. During the following weeks she developed cervical lymphadenopathies, arthralgia and mild asthenia. Complete blood analysis, imaging diagnostic techniques, C-reactive protein (CRP) and autoimmunity tests showed normal results, but high levels of anti-Ro antibodies were found, suggesting Sjögren Syndrome (SS) as the etiopathological cause.

Results All symptoms and clinical findings improved after successive treatment with intravenous corticosteroids, hydroxychloroquine and azathioprine. At the present moment the patient remains stable using maintenance treatment with immunosuppressive drugs.

Conclusion Chronic destruction of the lacrimal gland is the most common cause of dry eye and ocular symptoms in SS. Acute dacryoadinitis is considered an atypical manifestation of this syndrome. Classical systemic corticosteroids treatment for SS usually needs association of immunosuppressive drugs, including biological treatments as a recent new option to control the disease progression and inflammatory activity. Topic cyclosporine and pilocarpine have reported benefits for severe xerophthalmia in recent medical trials.

• S019

Posttraumatic periorbital necrotizing fasciitis

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Purpose To present the case report of a patient who developed periorbital necrotizing fasciitis following trauma with favorable response.

Methods 73 year-old-female came to the emergency department after downfall with a trauma in facial region. At the initial examination the patient had a large eyelid swelling in both eyes and a wound that required stitches on the left superciliary region. 5 days later the patient presented to our clinic with general discomfort, fever of 39°C and with slurring, crusty necrotic in the right eyelid, redness and heat in both upper eyelids and in frontal area.

Results Because of clinical suspicion of periorbital necrotizing fasciitis, we performed a debridement of the wound in the right upper eyelid, draining the purulent in frontal area, sampling for culture and intravenous treatment with amoxicillin-clavulanate. In the culture Steptococcus pyogenes isolates. After 15 days of intravenous antibiotic treatment and local cures, the patient was discharged from hospital. One month later, the patient had complete resolution of the lesions with a mild ptosis in the right eye.

Conclusion Although this is a disease with a low incidence, it has a high morbidity and mortality if appropriate treatment is not performed. Treatment consists in an immediate and extensive debridement of the affected area with broad-spectrum antibiotic.

• S020 / 3685

Idiopathic orbital inflammation: a report of 18 cases

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Purpose Idiopathic orbital inflammation is a rare clinical entity which has protean clinical manifestations. It's a diagnosis of exclusion which imposes a biopsy, and which can be made only after a screening to rule out a systemic etiology of inflammation.

Methods Retrospective series of 18 histologically-proven orbital inflammation cases seen in our service between 2006 and 2011.

Results The study encompassed 7 men and 11 women, with a mean age of 47 years old (4-83). Patients complained of a pain (44%), a diplopia (33%), a decreased visual acuity (17%). A swollen eyelid or a palpable mass were presents in 78% of the cases. Less often, we noted proptosis, or a diminished ocular motility. The radiologic analysis (CT-scan, NMR, doppler ultrasound examination) found an inflammation localized to the orbital fat, to the lacrymal gland, and to one or several oculomotor muscle(s) in respectively 89%, 67%, and 39% of the cases. Excisional biopsy was curative for 33% of the cases. 61% of the patients received a corticotherapy, with a relapse or a recurrence in 60% of the cases, making necessary to have recourse to immunosuppressive agents (methotrexate), with a good control rate on the inflammation (75%). Finally, 76% of the patients obtained a complete resolution of their symptoms at the end of the follow-up (mean : 20 months).

Conclusion Treatment lies on surgical exeresis if it is safely. Corticotherapy is frequently not sufficient. Methotrexate seems to be an interesting alternative. Recent works concentrate on Systemic IgG4 Disease, who could be a frequent cause of orbital inflammation, calling the term "idiopathic" into question, and letting us think about targeting treatments.

• S021 / 3686
A patient with eyelid and anterior orbital myeloproliferative hypereosinophilic syndrome

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Purpose the aim of the study is to evaluate the clinical- and histopathological discrepancy of the inflamed eyelid/anterior orbital mass features

Methods case report and literature review

Results the clinical picture revealed an erythemaous eyelid-skin inflamed mass without effect on local and general antibiotic treatments . The histopathological "diagnoses was made as "chalazion material". However the mass was superior located from the tarsus pre- and intraseptal with a lot of eosinophilic cell in the pathological material; where the patient already was known with a pulmonal myoblastic hypereosinophilic disease and treated with hydrea with the extra feature of a red face

Conclusion knowledge of the systemic disease of a patient and the precise location of a pathologic ophthalmic process is important to made the definitive diagnosis. In difficult processes it is always necessary that pathologist and ophthalmologist consulted each other and made together the end conclusion

• S022 / 3687
Congenital orbital teratoma

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Purpose Congenital orbital teratoma is a rare tumor, composed of all three germ cell layers. The purpose is to present a case with congenital orbital teratoma, and discuss the clinical and histological characteristics of the tumor.

Methods Case report of a newborn girl that had a protrusion of the right globe. Imaging disclosed a big intraorbital lesion and capillary hemangioma was suspected, but treatment with propranolol had no effect during 4 months. At the age of 5 months acute progression of the proptosis developed with enlargement of the orbital mass as seen on MRI, pressing on the optic nerve. She underwent surgery and the lesion was removed completely using a cryo-probe.

Results The pathologic diagnosis was orbital teratoma including cysts filled with keratin, hair follicles, glands, bone, cartilage, epithelium and neuronal-brain tissue. On follow-up examination there was no proptosis but some limitation of ocular movements was seen one month after surgery.

Conclusion In order to diagnose clinically orbital teratoma, a high index of suspicion is needed. Surgical excision is the treatment of choice. Early detection and treatment is important in order to prevent mechanical destruction of adjacent tissues.

• S023
Ophthalmological symptoms in carotid-cavernous sinus fistulas

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Purpose This study was designed to compare ophthalmological symptoms of dural fistulas (DF) and carotid-cavernous direct fistulas (CCF), before and after endovascular treatment, and to find out risk factors for ophthalmological sequelae.

Methods We retrospectively studied 44 patients suffering from cavernous sinus fistulas with ophthalmologic symptoms, held in Lariboisière Hospital in Paris and Dupuytren Hospital in Limoges over 8 years. 24 patients had DF, 20 patients had CCF. 2 patients had spontaneous disappearance of the fistula, and 4 patients after non-invasive treatment. The remaining 40 patients underwent endovascular treatment, until complete exclusion of the fistula (33 had a single treatment, and 5 had to be retreated)

Results The main pre-treatment symptoms were proptosis (n=38), episcleral venous congestion (n=31), oculomotor palsy (n=28), visual loss (n=20), glaucoma (n=17) and controlateral ocular symptoms (n=11). Thrill and murmur were more frequent in CCF (6 and 12) than in DF (0 and 5) ($p<0,05$). In patients with DF, the average age was greater ($p<0,005$) and glaucoma was more frequent ($p=0,005$). 14 patients had ophthalmological sequelae, oculomotor palsies in most cases (n=8). Ophthalmological sequelae were more frequent in patients with pre-treatment visual impairement ($p<0,05$).

Conclusion The risk of ophthalmological sequelae was higher in patients with pre-treatment visual impairment, and lower in patients with complete anatomical cure of the fistula. 68% of patients had no ophthalmological sequelae after endovascular treatment, and 93,2% had no ophthlmological sequelae after specific additional medical treatment.

• S024
Topography of the human Henle Fiber Layer (HFL) as revealed by imaging and histology

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Purpose To create a model of the topography of the Henle Fibers (HF) connecting photoreceptor cell bodies of the human fovea to the inner retina based on information available in recent imaging and histological studies. Detailed knowledge of the HF is of importance for analysis of connectivity between the outer and inner retina and for evaluation of radial displacement of retinal neurons from their synaptically connected photoreceptors.

Methods Reported data of the Henle Fiber Layer (HFL) thickness (HFLt) at different eccentricities along the horizontal meridian of the human fovea from studies with optical coherence tomography (OCT) and histology was used.The radial displacement caused by HF was calculated from data of total displacement within the retina, corrected by data of other displacements obtained from Sjöstrand et al(unpublished).

Results A comparison of OCT and histology data showed a similar profile of HFLt vs eccentricity and similar HF topography. The angle of the Henle fibers vs. the external limiting membrane (ELM) was low centrally ranging from a few degrees (deg) to approximately 6 deg at a cone eccentricity of 0.9 mm.Thereafter the angle slowly increased with increasing eccentricity to an angle of 9-10 deg at cone eccentricity of 1.8 mm .The locations of the maxima of HFLt and projected HF length were at a cone eccentricity of approximately 0.5 mm.A model was constructed displaying the characteristics of the topography of HFL.

Conclusion Published data of the topography of HFL fits with a model where the the maximal HFLt is attained at a cone eccentricity where the fiber angle vs ELM still is of low degree and the HF length reaches a maximum.

• S025

The human fovea revisited-a proposed new strategy based on neural connectivity for analysis of retinal images

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Purpose To present a model useful for analysis of images of central retina based on functional connectivity between outer retina with its photoreceptors and retinal ganglion cells (RGC) of the inner retina.In addition, to evaluate the nomenclature and to propose clinically relevant definitions of the fovea and surrounding zones based on neural connectivity, function and development.

Methods Published measurements of radial displacement of inner retina relative to outer retina were used to determine the area of RGC corresponding to central photoreceptors. A model of central retina with displaced outer and inner retinal zones was constructed based on data from histological reports and data from recent studies with non-invasive imaging studies, the convention of the ETDRS study, and psychophysical studies.

Results A model is presented where functional relationships within the retina are based on neural connectivity, i.e the radial displacement of RGC and synaptically connected cones. The statement by S. Polyak (1941) that "the entire inner foveal excavation corresponds to a small central region" of photoreceptors is confirmed.The model indicates that the template for analysis should be separate for outer and inner retina in order to mirror corresponding areas and functional relationships.Based on the model we propose a template relevant for clinical analysis of images of the outer retina mainly based on anatomical nomenclature and partly adapted according to the ETDRS convention.

Conclusion A model of the central retina based on neural connectivity is recommended as a frame for analysis of corresponding but displaced zones of the central retina.Templates for analysis of zones of cones and RGC are proposed.

• S026

Peripapillary changes detected by SD OCT in eyes with high myopia

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Purpose To investigate the morphologic alterations around the optic disc by SD-OCT with high myopia

Methods One hundred eyes (54 patients) with high myopia (>-6.00 diopters) were included. The participants had ophthalmologic examinations including stereoscopic fundus observations, OCT examinations. For OCT, multiple horizontal and vertical and cercle scans were obtained around the optic disc and fovea in each patient.

Results Patients were mean age 43.2+/-9.4 years, with a spherical-equivalent refractive error of -11.26+/-4.85 D and mean axial length of 27.65+/-1.82 mm. A peripapillary detachment was detected by OCT in 8 eyes (8%) as a hyporeflective space intrachoroidally and subretinally. It was also observed within the tissue posterior to the conus in eyes without the typical ophthalmoscopic yellow-orange lesions. Microfolds in the retinal vessels were detected at the conus edge in 40 of the highly myopic eyes (40%), and 10 of these eyes had paravascular cysts (10%). A retinoschisis was present at the site of the retinal vessels in 10 eyes (10%).

Conclusion The SD OCT examinations demonstrated different types of peripapillary changes in highly myopic eyes. It is important to detect these peripapillary changes especially peripapillary detachment by OCT to be able to predict the later development of visually disabling conditions.

• S027

Stage 1 macular holes of Gass classification illustrated by Optical Coherence Tomography scans: a review of 4 cases

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Purpose Gaudric classification, stage 1 corresponds to intraretinal pseudocyst in the inner part of the foveola. The prolongation of the cyst laterally results in a split between the inner retina and the photoreceptor layer and a disruption of the outer retinal layers.

Methods Four patients presented with a history of blurred vision and metamorphopsia. OCT examination showed a foveolar serous detachment between pigment epithelium and photoreceptor layer. Six months later, two patients presented lamellar holes and two patients evolved into stage 3 macular holes. In all cases we reported a complete resolution of the foveolar serous detachment . A surgical treatment was performed for three patients.

Results OCT scans performed one month after surgery showed a total closure of the macular holes, an increase of visual acuity and a disappearance of the metamorphopsia. The main physiopathological theory formulated about macular holes formation concerns vitreo retinal tractions. As the posterior hyaloid remained attached to the center of the foveola and to the optic disc, displaying a convexity that may indicate the exertion of anteroposterior traction on its vitreous side, Gaudric admits that stage 1a macular hole is the result of antero posterior vitreo retinal tractions.Stage 1 as described by Gass is characterized by a serous foveolar detachment and is a consequence of tangential tractions of the pre foveolar vitreous cortex.

Conclusion Our cases seem to be the tomographic illustration of the anatomic description of the stage 1 macular hole proposed by Gass and not mentioned in the tomographic classification proposed by Gaudric suggesting the implicationof tangential traction in macular holes formation.

• S028

Repeatability of retinal thickness and volume metrics in neovascular age-related macular degeneration using the Heidelberg spectralis optical coherence tomography

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Purpose To estimate the intra-session repeatability of retinal thickness and volume measurements from consecutive raster Heidelberg Spectralis spectral-domain optical coherence tomography (OCT) scans in patients with neovascular age-related macular degeneration (nAMD).

Methods Retrospective analysis of Spectralis OCT scans taken from 27 patients with a diagnosis of nAMD. Three OCT raster scans were performed by the same observer in the same sitting in consecutive patients attending for nAMD treatment, one of which being taken as a follow-up after setting a reference point on the baseline scan and one being taken as an independent scan from the baseline one. Retinal thickness and volume measurements were automatically calculated by the onboard software. Bland-Altman methods of analysis were used to assess repeatability.

Results Data from the 27 patients were analyzed with a mean (SD) age of 78 years (7). Mean visual acuity was 20/63 (range 20/200-20/32) The 95% coefficient of repeatability (CR) was 44 µm and 0.038 mm3 for retinal thickness and volume respectively in the central 1 mm macular subfield for the two independent scans, and it was 32 µm and 0.027 mm3 for the two scans taken with the follow-up reference.

Conclusion We report estimates of the intra-session repeatability of Spectralis OCT retinal thickness and volume metrics in patients with nAMD. There were comparable repeatability estimates for scans taken with or without setting a reference scan with the onboard software. The results are helpful in distinguishing clinical change from measurement variability in clinical practice.

• S029

Diabetic macular oedema and choroidal thickness measured by EDI SD-OCT

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Purpose Present study compared the choroidal thickness in patients with diabetic macular edema (DME) with that in healthy controls to know the true role of choroids in DME.

Methods Twelve eyes of 9 patients with DME (65.5±8.4 years), 9 contralateral eyes without DME (60.2±13.7 years), and 186 eyes of 96 age-matched healthy volunteers (62.1±19.4 years) underwent enhanced depth imaging (EDI) spectral-domain optical coherence tomography with a Heidelberg Spectralis HRA+OCT.

Results Reliable measurements of choroidal thickness were obtained in 72.3% of eyes examined. In the DME group the mean choroidal thicknesses were 232.4±74.7 µm at the fovea, 223.3±70.0 µm nasally, and 234.0±72.9 µm temporally. In the contralateral eyes these measurements were 279.9±103.6 µm, 252.8±86.4 µm, and 283.9±101.4 µm, respectively. Finally, the control group showed slightly higher values: 288.6±114.5 µm, 279.1±112.7 µm, and 283.8±104.3 µm, respectively. However, choroidal thickness did not show any statistically significant differences among the three groups of eyes (p>0.05, ANOVA test).

Conclusion Although a decreased choroidal thickness has been reported in eyes with DME, no differences were found in present study when age was counted as a confounding variable. Age has a strong inverse relationship with choroidal thickness.

• S030

Ratio of foveal thickness to choroidal thickness in caucasians

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Purpose To examine the potential dependence of foveal thickness on subfoveal choroidal thickness and associated factors.

Methods Patients without any macular or optic nerve disease and attending the clinic for cataract surgery underwent biometry and enhanced depth imaging of the deep retinal and choroidal layers by spectral domain optical coherence tomography (SD-OCT, Spectralis).

Results The study included 47 patients (24 women) with a mean age of 73.4 ± 7.3 years (range: 57.1 – 87.4 years) and mean axial length of 23.56 ± 0.88 mm (range: 21.65 – 25.47mm). The ratio of foveal thickness to subfoveal choroidal thickness (RFTCT) was 1.11 ± 0.48 (median: 1.06; range: 0.41-2.60). In multivariate analysis, RFTCT increased significantly with longer axial length (non-standardized regression coefficient B: 0.21; standardized correlation coefficient ß= 0.39; P =0.006) and older age (B:0.02; ß= 0.35; P=0.01).

Conclusion In elderly Caucasians, mean foveal thickness was about 11% higher than subfoveal choroidal thickness. For each mm increase in axial length, and for each increase in year of age, the ratio of foveal thickness to subfoveal choroidal thickness increased by 20 percentage points and by 2 percentage points, respectively. With increasing axial length, and with higher age, the choroidal thickness changes more marked than the foveal thickness changes.

• S031

Subfoveal choroidal thickness in Caucasians

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Purpose Purpose: To examine the normal thickness of the subfoveal choroid and associated factors.

Methods Methods: Patients without any macular or optic nerve disease and attending the clinic for cataract surgery underwent biometry and enhanced depth imaging of the deep retinal and choroidal layers by spectral domain optical coherence tomography (SD-OCT, Spectralis).

Results Results: The study included 47 patients (24 women) with a mean age of 73.4 ± 7.3 years (range: 57.1 – 87.4 years) and mean axial length of 23.56 ± 0.88 mm (range: 21.65 – 25.47mm). In multivariate analysis, mean choroidal thickness (253 ± 103µm; mean: 241µm; range: 94-573µm) decreased significantly with longer axial length (non-standardized correlation coefficient B: -0.46; standardized correlation coefficient ß= -0.39; P =0.006) and older age (B: -4.4; ß= -0.31; P=0.03).

Conclusion Conclusions: Mean subfoveal choroidal thickness in elderly Caucasians was 253 ± 103µm. For each mm increase in axial length, and for each increase in year of age, subfoveal choroidal thickness decreased by 46µm and 4.4µm, respectively. These data are almost identical with those measured for Chinese in the Beijing Eye Study (mean thickness: 254±107µm; decrease in choroidal thickness by 45µm and 4.1µm for each mm increase in axial length and each year increase in year of age, resp.)

• S032

Dexamethasone intravitreal implant in patients with macular oedema related to branch or central retinal vein occlusion, a retrospective study

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Purpose To evaluate the anatomic and visual outcomes of one treatment with dexamethasone intravitreal implant (Ozurdex®) in eyes with macular edema secondary to branch or central vein occlusion (BRVO or CRVO) during the first six months.

Methods The safety and efficacy of the dexamethasone intravitreal implant (Dex. implant) were evaluated retrospectively from January 2011 to May 2012 in a tertiary referral hospital. CRVO or BRVO diagnosis was confirmed with fluorescein angiography. At baseline, patients received a 0.7 mg dex. implant. They were evaluated at one, three and six months. Best corrected visual acuity (BCVA), optical coherence tomography (OCT) and intraocular pressure (IOP) were collected.

Results We included twenty one eyes: 28.5% had a CRVO and 71.5% a BRVO. At baseline, the mean BCVA was 47 letters (ETDRS) (52 in the BRVO group, 22 in the CRVO group). All patients had a macular edema involving the fovea. The mean central retinal thickness (CRT) was 513 micrometer [255-780]. At one month, 47.5% of eyes had more than three line gains and the mean CRT was 286 µm. Only two eyes had an IOP increase (>25 mmHg). However, at six months, only 17% of eyes had more than three line gains and the mean CRT was 380 µm. IOP remained uncontrolled with medication in one eye.

Conclusion The dexamethasone intravitreal implant reduces macular edema and improves visual acuity in patients with either branch retinal vein occlusions or central retinal vein occlusions. However, this efficacy remains transient. A retreament with a dex. implant is necessary for most of the patients.

• S033
Subfoveal choroidal thickness. The Beijing eye study

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Purpose To study the subfoveal choroidal thickness(SFCT) in adult Chinese and its correlation with ocular biometric parameters, ref. error, and age

Methods A detailed ophthalmic examination was performed including SD-OCT with enhanced depth imaging for measurement of SFCT

Results SFCT measurements were available for 3233 (93.2%) subjects.Mean SFCT was 253.8 ± 107.4µm (range: 8µm to 854µm).In multivariate analysis, SFCT was associated with younger age(P<0.001; correlation coefficient r:4.12; beta coefficient: 0.37),shorter axial length (P<0.001;r:44.7;ß:0.46), male gender (P<0.001;r:28.5;ß:-0.13), deeper anterior chamber depth (P<0.001;r:39.3;ß:0.13),thicker lens (P<0.001;r:26.8;ß:0.08),flatter cornea (P<0.001;r:46.0;ß:0.11) and better best corrected visual acuity(logMAR;P=0.001;r:48 .4;ß:0.06). In multivariate analysis, SFCT was not significantly associated with blood pressure, ocular perfusion pressure, intraocular pressure, cigarette smoking, alcohol consumption, serum concentrations of lipids and glucose, diabetes mellitus and arterial hypertension. In the myopic refractive error range of more than -1 diopters, SFCT decreased by 15µm(95% CI): 11.9, 18.5) for every increase in myopic refractive error of one diopter,or by 32µm (95%CI: 37.1, 26.0) for every increase in axial length of one millimeter. For each year increase in age, the SFCT decreased by 4.1µm (95%CI: 4.6, 3.7) (multivariate analysis).

Conclusion SFCT with a mean of 254±107µm in elderly subjects with a mean age of 65 years decreased with age(4µm per year of age) and myopia(15 µm per diopter of myopia). It was additionally associated with male gender and the ocular biometric parameters of a deeper anterior chamber and thicker lens. The association between SFCT and BVCA strongly points towards a functional aspect of SFCT

• S034
Changes in macular thickness measurements repeatability with age using Cirrus Fourier-domain optical coherence

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Purpose To test the intrassession reproducibility of retinal thickness measurements using Cirrus Fourier-domain optical coherence tomography (OCT). To evaluate if there is any relation between macular measurements repeatability and age of the studied subject.

Methods Two hundred and nine of 209 healthy subjects underwent three macular 512x128 volume cube centered on the fovea done by the same experienced examiner using Cirrus HD OCT (Carl Zeiss, USA). Descriptive statistics, analysis of variance, intraclass correlation coefficients (ICC), and coefficients of variation (COV) were calculated for the 9 macular areas described by the Early Treatment Diabetic Retinopathy Study (ETDRS) in the macular protocol. Values were analysed related to other subject factors like age and VA.

Results All measurements were highly reproducible. The ICCs ranged from 0.823 to 0.992 using macular volume cube. Mean COV was 1.4 ±1.09% (ranged from 0.7 to 1.9%) for the nine ETDRS areas. COV values increased with age; a significant correlation was found between them (r=0.300, p≤0.001). COVs were also related to VA.

Conclusion Retinal thickness measurements obtained using Cirrus Fourier-domain OCT show good reproducibility for healthy eyes. Repeatability is related to the subject age.

• S035
Improving diabetic retinal clinics in a district general hospital to conform to UK national screening committee guidelines

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Purpose To determine if new diabetic retinopathy patients, with either 'urgent' (R3M0, R3M1) or 'routine' (R2M1, R1M1) grading, are lasered within the appropriate national guidelines timeframe for:Time between listing (clinic) and first laser treatment following screening (OBJECTIVE 11)- Urgent: Minimum standard 90% of patients<2 wks- Routine: Minimum standard 70% of patients<10 wksTime between screening encounter and first laser treatment (OBJECTIVE 12)- Urgent: Minimum standard 70% of patients<6 wks- Routine: Minimum standard 70% of patients<15 wks

Methods A retrospective audit of new patients (n=121) whom have undergone diabetic retinal laser for either R3 (proliferative retinopathy) or M1 (maculopathy), over a 6 month period (from 1st feb 2011 to 31st July 2011).Data collection method:- Laser logbook- Patient computer archives system - Systematic review of patient's notesPatients were excluded if:- CRVO diagnosis- already under Hospital eye services- repeat laser attenders- no data- ungradeable

Results - No. eyes lasered in time /No. eyes seen (%)OBJECTIVE 11 (clinic to laser):Urgent - 17/31 (55%)Routine - 117/135 (87%)OBJECTIVE 12 (screening to laser):Urgent - 12/32 (38%)Routine - 90/135 (70%)

Conclusion Standards achieved for routine but not urgent referrals for Objective 11 (clinic to laser time) and Objective 12 (screening to laser time).The appointment of a diabetic co-ordinator helps to greatly improve flow of diabetic patient care pathway. Implementing the use of a medisoft connector would aid stream-lining data transfer directly to the screening service, thus improving the quality of patient care.

• S036
Visual acuity and central macular thickness comparison between posterior sub-Tenon's capsule triamcinolone injection and vitrectomy for diffuse diabetic macular oedema

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Purpose To compare the effect of posterior sub-Tenon's capsule triamcinolone acetonide injection (STTA) with the surgical outcomes of pars plana vitrectomy (PPV) for diffuse diabetic macular edema (DME).

Methods The medical records of 52 patients (52 eyes) with diffuse DME were reviewed. 26 eyes underwent STTA (20mg) and other 26 eyes – vitrectomy combined with cataract surgery. The central macular thickness (CMT) measured by OCT and best-corrected visual acuity (BCVA) were examined before and 1, 3, and 6 months after treatment. Statistical analysis was performed with student t-test, Mann-Whitney U-test and repeated measured ANOVA.

Results Preop BCVA was 0.65±0.4 logMAR units in the STTA group and 0.77±0.3 logMAR units in the PPV group. One, 3 and 6 months postop BCVA were 0.59±0.4, 0.53±0.5 and 0.47±0.4 in the STTA group and 0.77±0.3, 0.59±0.4, and 0.59±0.4 in the PPV group. Preop CMT were 608.1±220µm in the STTA group and 534.4±157µm in the PPV group. One, 3 and 6 months postop CMT were 392.1±193µm, 284.4±101.7µm and 331.4±121µm in the STTA group and 386.8±175µm, 354.2±101.7µm and 354.2±156.4µm in the PPV group. The differences in the BCVA and the CMT between two groups were not significant at any periods before and after treatment.

Conclusion Although STTA and PPV can significantly improve the BCVA and reduce the CMT in patients with diffuse DME, the differences in the BCVA and the CMT were not significant. Considering the minor invasion, STTA can be the first choice for the treatment of diffuse DME.

• S037
Multimarkers for diabetic retinopathy screening

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Purpose The aim of the project was to develop a methodology for diabetic retinopathy (DR) screening based on the examination of tear fluid biomarker changes. To evaluate the usability of protein biomarkers for pre-screening purposes different approaches and machine learning algorithms were used.

Methods All persons involved in the study had diabetes. DR was diagnosed by capturing 7-field fundus images. 165 eyes were examined, 55 were diagnosed healthy and 110 images showed signs of DR. Tears were taken from all eyes and state-of-the-art nano-HPLC coupled ESI-MS/MS mass spectrometry protein identification was performed on them. Applicability of protein biomarkers was evaluated by six different optimal parameterized machine learning algorithms.

Results Out of the six identified machine learning algorithms, result of the Recursive Partitioning proved to be the most accurate. The performance indicators of the system applying the above algorithm indicated 74 % sensitivity and 48% specificity.

Conclusion Neither protein biomarkers nor machine learning algorithms are recommended alone for screening purposes because of low specificity and sensitivity values. This tool can be preferably used to improve the results of image processing methods as a complementary tool in automatic or semiautomatic systems.

• S038
Automated measurement of retinal vascular caliber and arteriovenous ratio in type 2 diabetic patients without retinopathy

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Purpose To determine the retinal vascular caliber and arteriovenous ratio (AVR) in type 2 diabetic patients without retinopathy.

Methods We retrospectively reviewed the medical records of 70 patients diagnosed as type 2 diabetes without retinopathy. Digital fundus photographs of the right eye were selected for measurement. The caliber of all retinal vessels passing through an area 0.5 to 1 disc diameter around the optic disc was measured using automated computer software (Zeiss AV ratio). Seventy seven age- and sex-matched healthy subjects were included in the study as a control.

Results The mean AVR was 0.801 ± 0.068 in the diabetic patients compared to 0.762 ± 0.054 in the control group ($P < 0.001$). Higher AVR was significantly associated with increasing blood HbA1c levels ($r2 = 0.106$, $P = 0.006$). However, there was no significant correlation between AVR and body mass index ($P = 0.478$).

Conclusion The rise in AVR seems to be an early feature of retinal vascular caliber in type 2 diabetes and correlates with an elevated blood HbA1c level.

• S039
Preoperative vitrectomy treatment preventing vitreous haemorrhage

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Purpose To compare the results of preoperative intravitreal bevacizumab (IVB) and triamcinolone (IVT) treatment as prevention of early postvitrectomy haemorrhage in proliferative diabetic retinopathy (PDR).

Methods 27 eyes with PDR were distributed in 3 groups (9 patients each): the IVB group received 1.25 mg bevacizumab, the IVT group received 4,0mg triamcinolone and the control group underwent a sham procedure. The incidence of early postvitrectomy hemorrhage, best corrected visual acuity (BCVA) and adverse events were considered.

Results The lowest incidence of vitreous hemorrhage was in IVB group but not statistically significant. The rate of bleeding immediately after surgery was higher in IVT group. Considering VA, in the IVT group the improvement was statistically significant ($p \leq 0.001$).

Conclusion Intravitreal injection of bevacizumab 1 week before vitrectomy seems to reduce the incidence of early postvitrectomy haemorrhage in diabetic patients. There was a better VA outcome in the triamcinolone group.

• S040
Role of Sp1 transcription factor in the pathogenesis of diabetic retinopathy

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Purpose Proangiogenic factors, VEGF and Cyr61, drive aberrant retinal neovascularization in diabetic retinopathy (DR). Their expression is regulated by the transcription factor Sp1. Several layers of the retina participate in the secretion of these factors; however, the contribution of the retinal pigment epithelium (RPE) to the pathogenesis of diabetic retinopathy has remained largely overlooked. Our objective was to characterize the Sp1-dependent production of VEGF and Cyr61 in models of the diabetic retina, specifically focusing on the RPE, with the ultimate goal of identifying potential novel therapeutic targets for the treatment of DR.

Methods Glucose-treated ARPE-19 (human retinal pigment epithelial cells) and TR-iBRB (rat retinal microendothelial cells) were assayed for levels of VEGF and Cyr61 by qPCR, Western blot, and tubule formation assays. RNAi was used to deplete cells of Sp1. Binding of Sp1 to VEGF and Cyr61 promoters was monitored by chromatin immunoprecipitation (ChIP). Immunohistochemistry for VEGF and Cyr61 was done in diabetic mouse retinas.

Results Glucose treatment caused increased VEGF and Cyr61 transcript and protein, and Sp1 depletion abrogated these changes in both cell types. ChIP analysis showed glucose-induced increase in the Sp1 binding to VEGF and Cyr61 promoters. Additionally, expression of both factors was increased in the RPE of diabetic mice.

Conclusion VEGF and Cyr61 are upregulated in ARPE-19 and TR-iBRB in hyperglycemia, which coincides with elevated Sp1 binding at their promoters. Depletion of Sp1 significantly reduced their aberrant expression. Sp1 may participate in the pathogenesis of diabetic retinopathy via upregulation of these proangiogenic genes in the RPE as well as in the vascular retina.

• S041

Intravitreal bevacizumab injection with grid laser photocoagulation for macular oedema in branch retinal vein occlusion

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Purpose To evaluate the effects of intravitreal bevacizumab (IVB) with grid laser photocoagulation for macular edema in branch retinal vein occlusion (BRVO).

Methods This was a retrospective case series. Ten eyes in 10 patients with macular edema secondary to BRVO with at least 3 months of symptom duration were included. The mean follow-up term was 70.2 ± 8.4 weeks. Patients underwent IVB at baseline and macular grid laser photocoagulation 1 week later. Best corrected visual acuity (BCVA) and central macular thickness (CMT) were examined during the monthly follow-up. If persistent or recurrent fluid collection appeared in optical coherence tomography (OCT) , additional IVB were performed. To evaluate differences between baseline and post-treatment BCVA and CMT, Fisher exact test was performed.

Results The mean baseline BCVA was 0.31±0.17 (mean±SD), and the mean CMT was 530±109 μm. The mean BCVA at 4, 12 and 24 weeks were 0.49±0.21 (p=0.030), 0.47±0.60 (p=0.038), and 0.41±0.85 (p=0.041), respectively. The mean CMT were 285±75 μm (p<0.01), 304±120 μm (p<0.01), and 325±145 μm (p=0.015). A mean 1.85 injections were administered and the second injection was done at a mean 3.52 months after baseline.

Conclusion IVB and additional grid photocoagulation were effective for macular edema in BRVO, and the improvement maintained for 6 months.

• S042

RE-MI-DO Study: resultats of a multicenter study of dexamethasone implantation in eyes with macular oedema in retinal vein occlusion

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Purpose Retrospective Multicentric Study of the dexamethasone drug delivery system (OZURDEX) in the treatment of macular edema following retinal vein occlusionTo evaluate the safety and efficacy of the dexamethasone drug delivery system (OZURDEX) in eyes with macular edema following branch (BRVO) or central retinal vein occlusion (CRVO).

Methods Retrospective, noncomparative, multicentric Study with a minimum of 6 months follow-up220 patients with retinal vein occlusion (55.9% BRVO, 44.1% CRVO) have been included in the study with a minimum follow-up of 6 months (mean follow-up = 10.2 months). The patients received one or more OZURDEX in the study eye during the follow-up. 8 French ophthalmic centers have participated to the study.Best-corrected visual acuity (BCVA), central retinal thickness (CRT) intraocular pressure (IOP) variation and cataract progression were evaluated monthly from baseline to 6 months.

Results The initial CRT was 657.2 microns and decrease by 49.8% at M1, 55.2% at M3 and 28.1% at M6.The initial BCVA was 48 letters. AV> 20/40 was observed in 41% of patients at M1, 47.8% at M3 and 19.9% at M6.50.8% of patients at M1, 55.9% at M3, and 35.1% at M6 had an improvement ≥ 15-letters in BCVA from baseline.An IOP > 25mmHg was observed in 15.8% of patients. 6% of had an increase ≥ 10-mmHg from baseline during the first month after the first injection. These IOP increase were transientsAt 6 months, one third of the patients required a second injection.The mean time for reinjection was 5,3 months.

Conclusion Ozurdex provides an efficient and risk-benefit ratio acceptable to the treatment of RVO patients with macular edema.

• S043

Cataract surgery and the dexamethasone drug delivery system for the treatment of retinal venous occlusion

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Purpose To report our case report with sustained-release dexamethasone 0.7 mg intravitreal implant (Ozurdex®; Allergan, Inc., Irvine, CA) in retinal vein occlusion with macular edema

Methods A 81-years old male patient with recent retinal vein occlusion with macular edema treated with sustained-release dexamethasone 0.7 mg intravitreal implant and cataract surgery was performed. On initial examination, the right best-corrected visual acuity (BCVA) was 0,1. Right fundoscopy revealed retinal hemorrhage in the superior quadrant of the retina. The fluorescein retinal angiography showed a delay of filling time and spectral domain optical coherence tomography (Spectralis SD-OCT; Heidelberg Engineering, Heidelberg, Germany) showed macular edema 485 μm

Results The patient was treated with two dexamethasone 0.7 mg intravitreal implant and cataract surgery in one year. During the first six months after implant the right BCVA was 0,4 and OCT: 294 μm. At six months the macular edema increased 335 μm and we treated with the second implant, the macular edema improved 280μm but not the BCVA and we realized cataract surgery and BCVA was improved to 0.5.

Conclusion The dexamethasone drug delivery system is one of the most recent additions to the armamentarium against macular edema, and is intriguing for its potency, dose consistency, potential for extended duration of action, and favorable safety profile but can accelerate cataract surgery.In patients with macular edema in retinal vein occlusion, sustained-release dexamethasone 0.7 mg intravitreal implant may be an effective treatment option to control macular edema

• S044

The effects of exercise on peripapillary retinal oxygenation

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Purpose Blood flow to the retina is maintained by central retinal vessels that exhibit autoregulatory capacity. Physical activity has been demonstrated to have acute, transitory, effects on ocular haemodynamic factors including intraocular pressure and blood pressure. What remains unclear is how the oxygen saturation of retinal blood vessels is affected by prior levels of physical activity. The aim of the study is to assess the impact of physical activity on peripapillary retinal vessel oxygenation.

Methods Eight eyes from eight healthy volunteers were assessed in the study. Peripapillary retinal vessel oxygenation (dual-wavelength fundus images; 548nm and 610nm), blood pressure (automated sphygmamometer) and intraocular pressure (non-contact tonometer) was assessed before, immediately after, and 15 minutes following a period of aerobic exercise (Master's two-step stress test).

Results Average peripapillary arterial oxygenation increased from 95.01% ± 9.62% (mean ± standard deviation) before exercise to 97.57% ± 9.90% (paired t-test, p=0.028) immediately following exercise, and 96.67% ± 10.54% (p=0.163) at 15 minutes following exercise. Average peripapillary venous oxygenation increased from 57.95% ± 17.29% before exercise to 64.06% ± 21.13% (p=0.006) following exercise, and 61.40% ± 17.03% (p=0.055) at 15 minutes.

Conclusion This pilot study demonstrates that modest levels of physical activity can induce significant changes in blood oxygenation across arteries, veins, and the arteriovenous difference. Our results appear to suggest that subjects should be physically rested for at least fifteen minutes before resting retinal oxygenation is assessed.

• S045

Effects of arteriolar constriction on retinal gene expression and müller cells in an experimental retinal vein occlusion

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Purpose To investigate the effect of the laser-induced arteriolar constriction (AC) on branch retinal vein occlusion (BRVO) induced Müller cell responses and alterations in gene expression of factors implicated in the development of edema.

Methods In Brown-Norway rats the BRVO was induced by laser photocoagulation of the veins in one half of the retina. AC of the afferent arterioles was performed 30 minutes later. The expression of Vegfa, Vegfb, Pedf, Kir4.1, Aqp4, Aqp1, Il1ß, and Il6 was determined with RT-PCR in the retina and retinal pigment epithelium (RPE) after 1, 3 and 7 days. Potassium currents were recorded in Müller cells 3 days after BRVO. Immunostaining against GFAP, Aqp4 and Kir4.1 was performed on day 1 and 3.

Results BRVO resulted in the neuroretinal transient upregulation of Vegfa on day 1. The expression of the Kir4.1, Aqp4, and Aqp1 channels were downregulated, and Il1ß and Il6 strongly upregulated, on day 1 and 3. The retinal distribution of GFAP and Aqp4 proteins remained unaltered, while the Kir4.1 protein displayed redistribution from a polarized to a uniform retinal distribution. Müller cells showed cellular hypertrophy and a decrease in potassium currents. AC accelerated the restoration of downregulated Kir4.1, Aqp4, and Aqp1 in the RPE, of Kir4.1 in the neuroretina and of upregulated Il6 in the neuroretina. AC did not influence the gliotic alterations of Müller cells and the redistribution of Kir4.1 protein.

Conclusion The constriction of the afferent artery in the BRVO region had only marginal effect on the BRVO-evoked alterations in retinal gene expression.

• S046

SD-OCT study of vitreoretinal traction at the obstruction site in patients diagnosed with branch retinal vein occlusion

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Purpose Branch retinal vein occlusion (BRVO) typically occurs at an arteriovenous (AV) crossing site. Vitreoretinal traction migh thave a significant role in some cases. The aim of this study was to determine the prevalence of vitreoretinal traction at the obstruction site in patients diagnosed with BRVO.

Methods Prospective observational case-control study. 14 consecutive patients with BRVO were studied and the fellow eyes were taken as a control group. Spectral-domain optical coherence tomography (SD-OCT) was used to detect vitreous adherence or vitreoretinal traction at the obstruction site.

Results SD-OCT directed to the obstruction site revealed an adherence of posterior hyaloids without signs of retinal traction in six eyes (42.9%). Five eyes (35.7%) were associated with vitreoretinal traction at this point, and three eyes (21.4%) had neither vitreoretinal adherence nor vitreoretinal traction.Regarding the same vessel segment of the control eyes, only 2 cases (14.3%) presented a vitreoretinal adherence, whereas none of the cases showed a true vitreoretinal traction in the correspondent AV crossing site. There was a statistically significant difference ($p<0.05$) between both groups of eyes in relation to the prevalence of a vitreoretinal traction.

Conclusion The existence of a common vitreoretinal adhesion at the obstruction site in BRVO patients is reported herein, pointing out the role of vitreoretinal traction in the etiology of some cases of BRVO and the important diagnostic capabilities of SD-OCT and its 3-D image reconstruction in the detection of this vitreous traction and its association with perivascular edema.

• S047

Ozurdex implant in retinal vein occlusions. 3-months clinical outcomes in the first 17 patients

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Purpose To present the our initial clinical outcomes of dexamethasone 0.7mg intravitreal implant (Ozurdex®) in the first three months after the injection.

Methods Seventeen patients (12 male and 5 female, mean age 64.9y) diagnosed with retinal vein occlusions (RVO) and cystoid macular oedema (CMO) received an Ozurdex injection after baseline best corrected visual acuity (BCVA) and central retinal thickness (CRT) was documented. The patients had monthly clinical visits following the injection.

Results Seven patients suffered from central RVO, nine from branch RVO and one patient from hemiretinal RVO. Following the injection of Ozurdex CRT appeared to reduce significantly from a mean of 496.4μm (SD 204.2μm) pre-injection to a mean of 316.4μm (SD 131.3μm) at 1/12 post-injection and further to 293.4μm (SD 95.6μm) at 3/12 post-injection. BCVA was also significantly improved at 1/12 post-injection and further at 3/12 post-injection in nine of the patients especially in the nonischemic sub-groups. Complication rate was relatively low with only four patients having a moderate raise in intraocular pressure managed with topical therapy and one patient suffering a large subconjuctival haemorrhage.

Conclusion Our initial results demonstrate that Ozurdex appears to be a safe and efficient treatment option for RVO related CMO. It provides significant decrease in CRT and anatomical improvement on OCT scans in all types of RVO. Improvement of BCVA is possible but it seems that ischemic damage and chronic CMO have an adverse effect on visual restoration despite anatomical improvement.

• S048

Plasma taurine levels in age-related macular degeneration

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Purpose Taurine is one of the most abundant free amino acids in many tissues, including the retina. It is a scavenger of hypochlorite and carbonyl radicals and also inhibits lipid peroxidation. Little is know about the role of taurine in the pathogenesis of AMD. The purpose of this study was to determine the plasma levels of taurine in AMD patients and in age-matched subjects without AMD.

Methods Plasma taurine levels were measured by capillary electrophoresis in 74 AMD patients (mean age: 78±6.7 years) and in 148 controls (mean age: 77±5.3 years), all accrued in September 2011-March 2012. Statistical analysis was performed using the Mann-Whitney Rank Sum Test.

Results Median taurine was 64.7 (range 28.6-127.2) μmol/L in AMD patients and 65.8 (range 28.1-132.3) μmol/L in controls. Statistical analysis showed no significant difference between the two groups.

Conclusion Results suggest that AMD patients may have similar plasma levels of taurine as matched controls without AMD. Should these results be confirmed by larger studies, this would imply that taurine may play a marginal or no role in the pathogenesis of AMD.

• S049

Prognostic implication of choroidal thickness in ranibizumab-treated eyes with neovascular age-related macular degeneration (nvAMD)

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Purpose To evaluate prognostic factors in newly diagnosed nvAMD.

Methods Forty eyes of 37 patients with nvAMD received 0.5mg of intravitreal ranibizumab (IVR) monthly. One month after the third IVR, responders were defined as patients having improved visual acuity without retinal fluid.

Results 22 eyes (55%) were responders. Multivariate logistic regression identified thicker subfoveal choroidal thickness (SFCT) (p=0.049) and smaller choroidal neovascularization (p=0.043) as predictive factor for responder. SFCT were significantly thicker in responders (257 vs. 167 μm) even after adjusting for age and spherical equivalent. (p=0.024)

Conclusion Thinner choroidal thickness is negative prognostic factor for response to IVR in nvAMD.

• S050

The ring like distribution profile of macular pigment appears highly heritable: a twin study

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Purpose Macular pigment (MP) protects the retina from damage due to blue light and other oxidative stress. Genetic factors determine the distribution profile of MP, which may also be important in protection from oxidative stress. In addition it has been suggested that the ring pattern (with a "shoulder" in the profile at ~0.5 degrees from the fovea) may be protective of AMD .

Methods 300 healthy white female twin volunteers, aged 16-50 years (mean age 40+/-8.7 years) had macular pigment optical density (MPOD) measured by 2-wave-length fundus autofluorescence (AF), figure 1. The sample consisted of 76 monozygotic twin pairs, and 74 dizygotic twin pairs. Case-wise concordance was calculated by the formula 2C/(2C+D) where C is the number of twin pairs concordant for a ring structure, D the number of pairs discordant

Results At baseline, mean MPOD by AF was 0.41 density units (SD 0.21; range 0.04 to 1.25) in the central half-degree field, and exhibited a near- normal distribution. The ring like MP distribution profile was observed in 93 subjects (pre-valence 0.31, 95% CI 0.26-0.36). Concordance in monozygotic twins was 0.85 (95% CI 0.75-0.95) compared to 0.43 in dizygotic twins (95% CI 0.23-0.63), (p for diff<0.001).

Conclusion The finding that the monozygotic twin concordance is approximately double the dizygotic concordance, suggests that genetic factors are important in determining the MP distribution profile in the macula. This agrees with our previous findings of significant MP optical density heritability.

• S051

AMD atrophic areas. Characteristics, evolution study, and its interest. 3 years follow-up

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Purpose To evaluate the characteristics of AMD atrophic areas, their change, evolution and incidence or no of neovascular complication.

Methods 134 eyes of 108 patients, 32 men, 76 women, with AMD Atrophic areas. Atrophic areas were evaluated by autofluorescence imaging Spectralis HRA +OCT (in particular with region finder software), OCT (notably choriocapillary depth), FA, ICG. We evaluate the size, characteristics, topography of the lesions, their growth way. The areas themselves, their edge and rim were considered and evaluated. Each element was studied, compared cut to cut and time to time to itself and to each other data, every 4 months. The impact of AMD and /or Neovascular complication on the evolution of atrophic areas is also valuate.

Results VA impaired in 24% cases, stabilized in 76%. AF imaging and their region finder analyze were the main elements of the atrophic lesions' study. The surface of the atrophic area grows by 14%, the edge changes in 20%, the rim increases 15% in 30% cases, with ZAC spared in 87%. Atrophy extension preferred nasal side, confluence in 65% when multiple areas. At OCT,thickness of photoreceptor, pigment epithelium layer diminished at area and edge. Choriocapillary depth values, FA and ICG data were mainly significative in the large atrophic areas and less than AF indications. Neovascular complication has few effects on atrophic areas evolution.

Conclusion The study of atrophic process and its progression is a main question in AMD, its follow –up, its evolution, its increase. It also allows the evaluation of Neovascular complication impact. Atrophic areas are of main importance to AMD, either no or neovascular.

• S052

Five-year follow-up results of photodynamic therapy for polypoidal choroidal vasculopathy

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Purpose To evaluate the 5-year efficacy of photodynamic therapy (PDT) in patients with polypoidal choroidal vasculopathy (PCV).

Methods Forty-two eyes of 36 patients with PCV followed up for at least 60 months after PDT were retrospectively reviewed. The diagnosis of PCV was based on indocyanine green angiography (ICGA), showing branching vascular network with polypoidal components. All eyes were primarily treated with PDT, and retreated with PDT and anti-vascular endothelial growth factor (VEGF) injection or with only anti-VEGF injection. The recurrence of PCV was defined as the emergence of active polypoidal lesions observed with fluorescein angiography (FA) and ICGA. Retreatment was performed when leakage of fluorescein or subretinal fluid/intraretinal cyst on optical coherence tomography was noted during follow-up examiinations.

Results During the mean follow-up duration, 73.64±13.47 months, the mean number of PDT was 2.21±1.62 times, and the mean number of anti-VEGF injection was 5.05±5.55 times. Recurrence was noted in 33 eyes (78.6%) during follow-up. The mean baseline BCVA was 0.78±0.48 logarithm of the minimum angle of resolution (logMAR), and the final BCVA at 60-month follow-up was 0.68±0.54 logMAR. On the final evaluation at 60 months, the mean BCVA was improved in 14 eyes (33.3%) by at least 0.3 logMAR, stable (mean BCVA change within 0.2 logMAR from baseline) in 23 eyes (54.7%), and decreased in 5 eyes (11.9%) by at least 0.3 logMAR.

Conclusion After 5 years, 88.1% of patients showed stable or improved BCVA after PDT. Despite of high recurrence rate up to 78.6%, PDT was effective for 5 years, and seems to be a good option of treatment in PCV patients.

• S053

Two year follow-up of low-level laser therapy (LLLT) in patients with age-related macular degeneration (AMD)

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Purpose The objective of this study is to examine long-term effects of low-level laser therapy (LLLT) in patients with age-related macular degeneration (AMD).

Methods The research was implemented for a period of two years. For LLLT, a He-Ne Laser with continuous emission at 633 nm (01 mW/cm2) was used in patients with AMD of all stages (dry to wet exudative forms were included). In total, 54 patients (25 men and 29 women - 108 eyes) with AMD of various stages and a mean age of 67.5 ±5.2 years were included in the study. Progressive, exudative AMD was diagnosed in 33 eyes. 75 eyes had drusen or were depigmented. Laser radiation was applied transpupillary 6 times for 3 min once in two days to the macula. 20 patients with AMD (40 eyes) were randomly selected to receive mock treatment (control group 9 men and 11 women with a mean age of 68.5± 4.2 years). Visual acuity was followed for a 2-year period. The perimetry and Amsler test was used to screen central scotomas. Fluorescein angiogram of AMD and control groups was examined.

Results Visual acuity remained unchanged in all patients in the control group. There was a statistically significant increase in visual acuity ($p<0.001$, end of study versus baseline) for AMD patients for the period of 2 years after the treatment. The edema and hemorrhage in the patients with progressive, exudative AMD significantly decreased. No side effects were observed during the therapy.The prevalence of metamorphopsia, scotoma in AMD group was reduced.

Conclusion In conclusion, this study shows that LLLT may be a novel long-lasting therapeutic option for both forms of AMD. This is highly effective treatment that improves visual acuity for a long tme.

• S054

The in vitro anti-inflammatory and anti-angiogenic potential of a new resveratrol-based formula (Resvega)

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Purpose Age-related Macular Degeneration (AMD) is a pathology driven by inflammatory and angiogenic processes.The aim of this work was to study the in vitro anti-inflammatory and anti-angiogenic potential of a new resveratrol-based formula (Resvega, Laboratoires THEA, France) on Human retinal pigment epithelium cell line ARPE-19 after an inflammation induced by the bacterial lipopolysaccharide (LPS).

Methods Human ARPE-19 cells were subjected to inflammation by LPS (0128:B12) and co-treated during 24 hours with Resveratrol (50,30,10 or 1µM) or the Resvega formula (50,30,10 or 1 µM expressed in Resveratrol equivalent). Cell media were collected and the levels of 6 cytokines were measured by the multiplex Cytometric Bead Array Kit (BD Bioscience) : IL-8, IL-1 beta, IL-6, IL-10, TNF alpha and IL-12p70. Finally the level of the major angiogenic factor VEGF-A was measured in these media by ELISA (eBioscience)

Results The results showed that among the 6 cytokines only IL-6 and IL-8 were over-expressed during the inflammation triggered by the LPS treatment. These two pro-inflammatory cytokines were down-regulated by Resveratrol and Resvega treatments by at least 50-60% in all conditions even at the very low concetrations (1 µM). Concerning VEGF-A levels, Resveratrol and Resvega showed a dose-dependent inhibition. The maximum inhibition was observed for the highest concentration of Resvega (50 µM resveratrol equivalent)with a decrease by 74%.

Conclusion In conclusion, we demonstrated that Resvega had an anti-inflammatory and anti-angiogenic effect in vitro, on the human retinal pigment epithelial cells.

• S055

Docosahexaenoic acid protects human RPE cells against oxidative stress via PI3K/Akt m-TOR/p70-p85S6K pathways

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Purpose Oxidative Stress (OS) plays a critical role in the pathogenesis of age-related macular degeneration (AMD), especially by targeting the retinal pigment epithelium (RPE). Dietary habits with high consumption of docosahexaenoic acid (DHA) have been shown to prevent the development and evolution of AMD. Nevertheless, it is still unclear how DHA affects AMD. Our study aimed to investigate the involvement of the PI3K/Akt and m-TOR/p70-p85S6K pathways in human RPE cells after induction of OS, and then to assess the effect of DHA in the signaling pathways and in the protection against RPE cell death.

Methods For this purpose, we used ARPE-19 cells exposed to the prooxidant agent, tert-butyl hydroperoxide (t-BHP).

Results We found that exposing cells to t-BHP (400µM) showed complete inhibition of Akt and p70/p85S6K active forms. However in cells enriched with DHA (20µM) and then exposed to t-BHP (400µM), we demonstrated that Akt and p85S6K, but not p70S6K, remained phosphorylated for a longer time after stress. In addition there was a 2.6-fold decrease in the number of necrotic cells after 48hours of t-BHP treatment, as assessed by flow cytometry.

Conclusion Our study suggests that 1/ PI3K/Akt and m-TOR/P70-p85S6K pathways play an important role in OS, 2/DHA protects RPE cells from apoptosis and necrosis triggered by OS by enhancing the phosphorylation of Akt and p85S6K.

• S056

Incidence of retinal pigment epithelial tears after intravitreal bevacizumab injection for neovascular age-related macular degeneration

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Purpose To determine the incidence of and the risk factors for the development of retinal pigment epithelial (RPE) tears after intravitreal bevacizumab injection (IVB) for the treatment of exudative AMD.

Methods A retrospective, consecutive case series of all patients with subfoveal exudative AMD treated with IVB between September 2006 and April 2012. The main outcome measures were pre- and post-RPE tear visual acuity and choroidal neovascular membrane lesion types, incidence of tears and time from first injection until development of the tear.

Results A total of 369 patients (643 eyes) with exudative AMD were treated with IVB. 9 eyes from 7 patients developed a RPE tear for an incidence of 1.4%. The average patient age was 62.4+/-3.9 years. A vascularized PED was present in 7 of 9 eyes that developed an RPE tear. 44.44 per cent of the RPE tears occurred within the first 6 weeks of treatment, and all tears occurred within the first 24 weeks of treatment initiation. The mean pre-injection visual acuity was +0.6 logMAR with a mean post-tear visual acuity of +1 logMAR. 4 of the 9 eyes continued with bevacizumab injections after tear development, and 2 of these 4 eyes continued to have visual improvement.

Conclusion RPE tears occur after intravitreal bevacizumab injections for exudative AMD in approximately 1.4% of eyes and can cause severe vision loss. Maintenance of therapy may help preserve quality of vision after RPE tear development.

• S057

Prognostic factors for visual outcome after intravitreal bevacizumab injection for pigment epithelial detachment in AMD

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Purpose To evaluate the prognostic factors for visual outcome after intravitreal bevacizumab injection in patients with pigment epithelial detachment (PED) in AMD

Methods Thirty eyes in 30 patients with CNV and PED in AMD who had received intravitreal bevacizumab injections were retrospectively reviewed. Initial visual acuity, pigment epithelial detachment size, retinal or subretinal fluid resolution and CNV location were evaluated at 12 months.

Results Initial visual acuity was not correlated with BCVA at 12 months (p=0.063). CNV at the edge of PED appears to respond more favorably at 12 months (p=0.033) than CNV within PED. Sub and intraretinal fluid initially resolved faster than the sub-PED fluid (P = 0.041).The subretinal pigment epithelial fluid was highly resistant. Sub and intraretinal fluid response did not appear to be related to PED size. Visual acuity improvement was similar in both groups: large and minimal PED component.

Conclusion The location of CNV and the retinal or subretinal fluid resolution were the main prognostic factors for visual outcome. Bevacizumab was very effective in reducing more of the sub- and intraretinal fluid than the PED fluid in AMD with CNV.

• S058

Subfoveal perfluorocarbon liquid (SFCL) extraction: a report of three cases

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Purpose To analyze the outcomes after subfoveal perfluorocarbon liquid (SFCL) extraction.

Methods Three eyes of three patients (all males and aged between 43 and 63 years old), with presence of subfoveal SFCL after retinal detachment (RD) with macular involvement surgery. After a variable period of time, which ranged from 1 to 12 months after vitreoretinal surgery, it was performed extraction of the SFCL by a retinotomy in the extrafoveal rim of the SFCL bubble and aspiration with a 38-gauge cannula in one patient and with a 29-gauge cannula in the other two.Full clinical ophthalmological examination, including determination of Best Corrected Visual Acuity (BCVA), funduscopy and Optical Coherence Tomography (OCT)examination was performed in all patients prior and after surgery.

Results BCVA prior surgery was 10/100 in the three patients. Funduscopy and OCT examination showed one SFCL bubble localizated under the fovea. Four months after surgery, it was achieved anatomic restoration, without rests of SFCL, but a severe defect in photoreceptors (PR) was appreciated by funduscopy and confirmed by OCT in all eyes. Visual acuity remained unchanged during the follow-up period, being of 10/100 in the three eyes.

Conclusion Subfoveal SFCL extraction in patients with previous RD with macular involvement surgery may imply bad functional outcomes, probably due to a previous damage of pigment retinal epithelium and PR, aggravated by SFCL toxicity.

• S059

Age related macular degeneration in the algerian population and comparison with the italian one

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Purpose To identify the risk factors for Age Related Macula changes (ARM and ARMD) in the Algerian population. The results will be compared, in a second time, to the results of a similar previous survey performed in Italy on Maghreb population. Finally, a predictive algorithm in order to detect the individual risk for developing AMD will be defined

Methods Multicenter epidemiological study has been carried out in Algeria by 23 ophthalmologists who aimed to include all the patients aged of 55 years or more. Data were collected by questionnaire: age, gender, BMI, ethnical origin, personal and family history, smoking, alcohol consumption, sun exposure, food habits (fruits, vegetables, fat fish), food supplements, iris color, cataract surgery, refraction, fundus

Results 1183 subjects included, 68 presented ARMD, 288 ARM and 82. People less than 65 years old were 37% and 40% were between 65 and 75 years old and most of them were Caucasian (90%) and 10% black. Factors significantly correlated to ARM and ARMD are: black-African (OR: 9.25 and 19.04 for ARM and ARMD respectively), arthrosclerosis (OR: 3.28 and 1.94), family history of ARMD (OR: 4.48, significant for ARMD only), beer consumption (OR: 9.93 and 14.36), cataract surgery (OR: 1.71 and 2.71), myopia (OR: 3.74 and 5.61), hypermetropia (OR: 1.91)

Conclusion This study is in line with risk factors already described, including the most rfactors already described, including the most recently pointed out -refraction troubles- and shows relevant variations between North-African Caucasian living in their country and those living in Italy. Nevertheless, these preliminary results must be validated by further studies in order to find why there is a difference.

• S060

Effects of bevacizumab on newborn rat retinal proteoglycans gene expression and on cell proliferation, death and differentiation, in vitro

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Purpose VEGF is an important in nervous development, promoting neurogenesis and glial cell growth. Bevacizumab (BVZ), an anti-VEGF agent, has been extensively used for controlling pathological retinal neovascularization in adult and newborn patients, although its effect on the developing retina remains largely unknown. In this study we investigate BVZ effect on proteoglycans and on cell death, proliferation and differentiation in newborn rat retina.

Methods Retinal explants of sixty 2-day-old Lister hooded rats were maintained in culture media with or without BVZ for 2 days. Immunohistochemical staining was assessed against proliferating cell nuclear antigen (PCNA), caspase-3 and beclin-1 and vimentin and glial fibrillary acidic protein (GFAP). Gene expressions for PCNA, caspase-3, beclin-1, vimentin, GFAP and for proteoglycans were quantified by real-time reverse-transcription polymerase chain reaction. Results from treatment and control groups were compared

Results No significant difference in staining intensity of PCNA, caspase-3, beclin-1 and GFAP or in the mRNA levels of PCNA, caspase-3, beclin-1, vimentin, neurocan and phosphacan was observed. However, a significant increase in vimentin levels, decrease in GFAP and in syndecan-3 mRNA expression were observed in BVZ-treated retinas compared to controls.

Conclusion Bevacizumab did not affect cell death or proliferation in early developing rat retina but appeared to interfere with glial cell maturation (by interfering with vimentin and GFAP). It can also alter syndecan-3 gene expression. Thus, we suggest anti-VEGF agents be used with caution in developing retinal tissue.

• S061
Isolated juxtapapillary haemangioma

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Purpose To report a case of a juxtapapillary retinal capillary haemangioma

Methods A 21-year-old lady was referred from her optician with a six month history of blurred vision in her right eye. She was otherwise fit and well and did not take any regular medication. She had experienced occasional migraines in the last few years. She had no significant family history of note. On presentation, her visual acuity was 6/6 in both eyes. She had evidence of right optic disc swelling with some telangiectatic changes in a peripapillary distribution. In addition there were significant hard exudates temporal to the macula. A fundus fluorescein angiogram and OCT were undertaken which were consistent with a juxtapapillary capillary haemangioma. Although she had no systemic symptoms suggestive of Von Hippel-Lindau (VHL) syndrome, we referred her to a clinical geneticist to initiate investigations to evaluate this, as retinal haemangiomas are a frequent presenting feature of VHL; although they can be an isolated disorder. She underwent an abdominal and pelvic USS which was reported as normal, MRI of the head was reported as revealing no features suggestive of VHL disease, FBC, U&Es were also normal, 24 hr urine collection was normal for adrenaline, nor-adrenaline and dopamine.

Results Sixteen months after her first visit, her vision dropped to 6/12. OCT imaging demonstrated increasing macular oedema and exudation over the fovea. It was decided that the best option for treatment was intravitreal avastin, in combination with photodynamic therapy.

Conclusion Combined anti-VEGF therapy and PDT are a treatment option for juxtapapillary capillary haemangioma; although prognosis is often poor.

• S062
Intraocular pressure response to acetazolamide in patients with retinal detachment

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Purpose Besides the responsibility of vitreous traction, deficient photoreceptors adherence due to lower fluid transport of the retinal pigment epithelium (RPE) has been hypothesized to be involved in the occurrence of retinal detachment(RD). However this adherence remains difficult to evaluate in patients. Acetazolamide reduces aqueous secretion of the ciliairy body and stimulates fluid absorption by the RPE. Recording the intraocular pressure response to systemic acetazolamide could enable to indirectly evaluate the carbonic anhydrase activity of the RPE.

Methods The response to intraveineous acetazolamide was evaluated on the first postoperative day in 30 patients undergoing either RD surgery (n=15) or epiretinal membrane peeling (n=15). Intraocular pressure was measured with a handheld Perkins tonometer in suppine position before (t-2 min) and after the administration of acetazolamide (t+2 min,t+6min ,t+10 min and t+30 min). The mean variation of the intraocular pressure was compared between the two groups.

Results Consecutively to the intraveineous injection of acetazolamide, a reduction of the intraocular pressure was observed in both groups (both n=15). This reduction was significantly lower in the group of patients who underwent RD surgery. The observed difference remained significant until 10 minutes ($p<0,01$ at t= 2, 6 and 10 min). At t=30 min, the intraocular pressure reduction was comparable in both groups.

Conclusion The response to acetazolamide is significantly lower in patients undergoing RD surgery. Further research should aim to confirm the value of the intraocular pressure response to acetazolamide for characterizing photoreceptor adherence.

• S063
Protection of blue light induced retinal degeneration by the free radical scavenger Phenyl-N-tert-butylnitrone and a serotonin receptor 5-HT1a agonist in rats

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Purpose Blue light exposition of rat retina induces retinal damages that mimic age-related macular degeneration (AMD), showing severe photoreceptor cell death, apoptosis of RPE cells, and progressive outer nuclear layer destruction due to reactive oxygen species, and therefore providing an useful model to test potential AMD treatments. Here we proposed to compare the protective effects of two compounds, the antioxidant free radical scavenger, Phenyl-N-tert-butylnitrone (PBN) and the serotonin receptor 5-HT1a agonist 8-Hydroxy-2-(di-n-propylamino)tetralin, 8-OH-DPAT, on photo-oxidative stress in rat retina.

Methods After a period of dark adaptation, Sprague-Dawley rats were exposed to blue light during 6 hours. Animals were divided in three groups: 50 mg/kg PBN injected intraperitoneally on the day of induction, 500µg/kg 8-OH-DPAT or NaCl 0.9% subcutaneously injected once a day, starting 2 days before light exposure.Retinal function and anatomical integrity were evaluated by scotopic electroretinography (ERG) and optical coherence tomography, respectively, 1 and 2 weeks after induction. Outer nuclear layer thickness was measured on histological sections harvested 2 weeks after the induction.

Results Significant protection of retina from degeneration was achieved with both compounds, which effectively rescued a wave and b wave amplitudes of ERG responses and preserved photoreceptor layer thickness.

Conclusion The serotonin receptor 5-HT1a could be a valuable target for AMD and other retinal degenerative diseases.

Commercial interest

• S064
Effect of Resvega in a model of choroidal neovascularization in mice

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Purpose We aim to assess the effect of Resvega as a source of resveratrol and combined with an anti-VEGF in a diode laser-induced choroidal neovascularization (Li-CNV) model in mice.

Methods Sixty C57BL6/J mice underwent a diode Li-CNV model, and were divided into 4 groups (n=15): Control group: vehicle by oral gavage. NA group: daily oral Resvega (NA). C-VEGF group: vehicle and intravitreal anti-VEGF. NA-VEGF group: NA and intravitreal anti-VEGF. Oral treatments (100 µL) were administered 10 days before laser until 28 days post-laser. Intravitreal injections (7 µl) were performed 48 hours after laser. CNV evolution was assessed weekly through fluorescein angiography (FA) for 4 weeks. CD-31 immunofluorescence was assessed in choroidal flat mounts after sacrifice. Gene and protein expression of VEGF was analyzed with RT-PCR and western-blot, respectively. Results were analyzed with SPSS 15.0.

Results FA showed a significant decrease in fluorescein leakage from second week in NA and NA-VEGF groups compared with their respective controls ($p<0.05$). The lowest CNV area measured by CD31 was observed in NA group compared with control group with statistically significant differences ($p<0.05$). RT-PCR and western-blot analysis showed a significant decrease in VEGF expression in NA and NA-VEGF groups ($p<0.05$).

Conclusion Our data show that oral Resvega administration reduces CNV area and expression of proangiogenic VEGF expression. These results suggest that Resvega could be considered as potential preventive therapy against CNV.Supported in part by Thea Laboratoires and Grant RETICS RD 07/0062, Ministerio de Ciencia e Innovación.

• S065

Cytomegalovirus retinitis (CMVR) with and without extra-ocular CMV (EO-CMV) Infection – a comparative analysis of outcomes in HIV patients

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Purpose To compare the characteristics and treatment outcomes of HIV patients with cytomegalovirus retinitis (CMVR), with and without extra-ocular CMV (EO-CMV) infection in Singapore.

Methods This is a retrospective cohort study. All HIV patients diagnosed with CMVR at the Singapore Communicable Disease Centre from January 2005 through November 2009 were included.

Results 101 patients (138 eyes) were included. 92% were male, with a mean age of 48.6±10.4 years. Median follow-up was 8 months (range 0.5-58). 11% defaulted at a median of 6 months, and overall mortality was 24% at a median of 4 months. There were 68 patients (88 eyes) with only CMVR and 33 patients (50 eyes) with CMVR and EO-CMV. 36% had multiple sites of EO-CMV infection. In the EO-CMV group, 24% developed EO-CMV after CMVR, of which 6 were diagnosed with EO-CMV infection within 3 months after initiation of anti-retroviral therapy. Bilateral CMVR was significantly higher in the EO-CMV group (52% versus 29%; p=0.03). Patients with EO-CMV were less likely to develop immune reactivation uveitis (OR 0.8; CI 0.3-2.4), although mortality was higher (42% versus 15%, p=0.002). Multivariate logistic regression analysis showed that a longer duration of prior anti-CMV treatment had higher odds (OR 1.127, p=0.037) of CMVR recurrence, but no significant difference between both groups (OR 0.886, p=0.866).

Conclusion EO-CMV infection was significantly associated with increased mortality, bilateral CMVR disease and can manifest as CMV-associated immune reconstitution inflammatory syndrome. Our results also suggest that CMVR recurrence is multi-factorial and cessation of anti-CMV therapy should be tailored to an individualized risk factor profile.

• S066

Aqueous flare and choroidal thickness in patients with chronic hepatitis C virus infection

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Purpose To investigate the status of blood-aqueous barrier and to evaluate the subfoveal choroidal thickness (SCT) in patients with chronic never treated hepatitis C virus (HCV) infection without any anterior or posterior ocular disease.

Methods A total of 80 eyes of 20 naive HCV patients (M:F=12:8; mean age: 46.9±7.23 years) and 20 healthy controls (M:F=10:10; mean age: 48.2±8.71) were examined. Partecipants underwent a complete ophthalmologic examination. Aqueous flare was objectively quantified by using the non-invasive laser flare cell meter FC 1000 (Kowa, Tokyo, Japan), while SCT was evaluated by using enhanced depth imaging optical coherence tomography (Spectralis OCT; Heidelberg Engineering GmbH). An unpaired t test with Welch correction was performed to compare flare values and SCT between HCV patients and controls, considering significance a $p<0.05$ and a Spearman's rank correlation test was used to assess the relationship between aqueous flare and SCT in HCV subjects.

Results HCV patients showed significantly higher aqueous flare (photon counts/ms) values (8.37±2.25 vs. 4.56±1.45; p=0.0001) and a significant increased SCT (μm) (362.7±46.5 vs. 320.25±32.82; p=0.002) than normal controls.Statistical analysis revealed that there was a positive correlation between aqueous flare values and SCT in HCV patients (r=0,688; $p<0.0001$).

Conclusion These findings strongly indicate that impairment of the blood-aqueous barrier and thicker choroids are features of HCV patients even if they have no ocular symptoms, and that choroidal thickness increases as the degree of subclinical inflammation of the anterior chamber increases.

• S067

Macular involvement in non infectious intermediate, posterior and panuveitis

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Purpose To study macular involvement in non infectious intermediate, posterior and panuveitis.

Methods The data of 201 eyes in 118 patients with diagnosed non infectious intermediate, posterior or panuveitis examined between January 2007 and June 2012 were retrospectively reviewed. All patients underwent complete ophthalmic examination with fluorescein angiography and optical coherence tomography (OCT) to assess macular involvement.

Results Uveitis was due to behcet's disease in 62 eyes(30.8%), sarcoidosis in 22 eyes (10.9%), VKH in 24 eyes (11.9%), sympathetic ophthalmia in 1 eye (0.5%), birdshot chorioretinopathy in 2 eyes (1%), and multiple sclerosis in 2 eyes (1%). At initial examination, 54 eyes (27.2%) demonstrated macular involvement which consisted in macular edema (ME) in 32 eyes (15.9%), serous retinal detachment in 29 eyes(14.4%), epiretinal membrane (ERM) in 8 eyes (3.9%), macular atrophy in 2 eyes (1%), vitreo-retinal traction in 1 eye (0.5%), macular hole in 1 eye (0.5%) , and active macular chorioretinitis in 1 eye (0.5%). During follow up, 16 eyes (8%) developed macular complications including ME in 6 eyes(3%), ERM in 5 eyes (2.5%), and macular atrophy in 5 eyes (2.5%).

Conclusion Macular involvement,especially macular edema, is common in non infectious intermediate, posterior and panuveitis. It may lead to irreversible visual impairment. Thus, recognition of macular morphological characteristics by performing both OCT and fluorescein angiography in uveitic disease may facilitate earlier diagnosis and the initiation of specific treatment.

• S068

Ocular manifestations of Takayasu arteritis

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Purpose Takayasu arteritis is an inflammatory vascular disease of aorta and its branches. Ophthalmologic manifestations can occur up to 68% of patients and can be inaugural. The objective of this series is to describe the typical and atypical ocular manifestations of the disease

Methods Bicentric (Pitié-Salpêtrière and Lariboisière Hospitals) and multidisciplinary retrospective study conducted between 2004 and 2012, describing ocular manifestations of patients with Takayasu arteritis.

Results Seven patients, 3 men and 4 women, were included. Mean age was 51(range:31-70 years). Five patients had previously a confirmed diagnosis of Takayasu (71% type V) and 2 presented with inaugural ocular involvement. Most of the patients were asymptomatic(42%). We identified 5 typical manifestations , including 3 Takayasu retinopathy (42%),1 hypertensive retinopathy(15%) and 1 mixed retinopathy (15%). Atypical manifestations included a bilateral central retinal artery occlusion, a branch retinal vein occlusion and a transient monocular blindness. Treatment consisted of systemic administration of corticosteroids and immunosuppressors, symptomatic and secondary preventive therapy (laser photocoagulation on ischemic areas). Takayasu arteritis causes various ophthalmic manifestations such as traditional hypoperfusion retinopathy and hypertensive retinopathy. Atypical cases have been described, such as venous or arterial occlusions, ischemic neuropathy, and for the first time in our series a case of inaugural bilateral central retinal artery occlusion.

Conclusion Takayasu arteritis should be considered in young patients with atypical vascular or inflammatory retinal manifestations. Collaboration with internists is mandatory in order to diagnose systemic involvement and propose the best therapeutic approach.

• S069

Acute worsening of retinal lesions during oral steroid treatement in a case of intracular lymphoma

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Purpose Diagnosis and treatment of intraocular lymphoma remains a clinical challenge. Herein, we present a complicated case in which the diagnosis was made after the acute worsening of retinal lesions during oral steroid treatement.

Methods A 49 year old woman complaning of progessive visual acuity decrease was referred with visual acuity of hand movements in the right eye accompanied by vitritis and two peripheral white retinal lesions with vasculitis. Futher examinations excluded the diagnosis of the main causes of infectious and non infectious uveitis and pathological examination of vitreous cells was not compatible with the diagnosis of lymphoma.

Results Systemic steroid treatment were given with an initial improvement of the inflammatory conditions. However, a week later an acute worsening of the retinal lesions occured, taking the appearence of a very severe retinal necrosis. Another vitrectomy was thus performed to exclude again infectious causes but was negative for virus and toxo. Finally, the diagnosis of intraocular lymphoma was made on a 3rd diagnostic vitrectomy with retinal biopsy. The patient was treated with a series of intravitreous methotrexate injections followed by chemo- and radiotherapy.

Conclusion Systemic administration of corticosteroids in patient with intraocular B lymphoma may lead to dramatic lesion extention preceeded by temporal clinical stabilisation or improvement.

• S070

Ocular effects of combined therapy with pegylated interferon (PegINF) and ribavirin (RBV) in hepatitis C

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Purpose To evaluate ocular effects of combined therapy with pegylated interferon and ribavirin in hepatitis C.

Methods 18 patients (36 eyes) received combined therapy based on the presence of HCV antibodies in the serum and positive RT – PCR test results for HCV RNA. Patients were examined at baseline, months 1, 3, 6 after initiation and 6 months after completion of antiviral treatment. Primary outcome was best corrected visual acuity (BCVA) and secondary outcomes were slit lamp examination, intraocular pressure, foveal thickness, and P1 Multifocal Electroretinography(mfERG) amplitude.

Results 13 patients (26 eyes) completed the study. 2 of 13 (15%) patients had exacerbation of dry eye syndrome and 2 of 13 (15%) developed retinopathy. Therapy was discontinued in patients with retinopathy with remission of retinal changes after 3 months. No significant changes in other parameters were observed.

Conclusion Patients treated with PegINF-RBV have a potential risk of ocular complications and require a regular ophthalmic examination. We suggest ocular examination and follow up protocol for patients treated with interferon-ribavarin therapy to limit potential side effects.

• S071

Diagnosis of tuberculosis uveitis

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Purpose Tuberculosis uveitis are difficult to diagnose because of their polymorphism of clinical presentations. As a consequence, a diagnostic delay is often observed in this pathology. The goal of this study is to determine the clinical features and the investigations leading to the diagnosis of tuberculosis uveitis.

Methods It is a retrospective study at the Saint Roch University Hospital in Nice. We followed eight patients (thirteen eyes) between September 1997 to March 2011, who presented with unilateral or bilateral tuberculosis uveitis.

Results A slit-lamp examination revealed an anterior uveitis in twelve eyes. Six eyes presented granulomatous keratoprecipitates, five had posterior synechia.Funduscopy showed twelve eyes with vitritis, seven eyes presented snowball vitreous opacities, and four eyes were affected by a papillitis. Optical coherence tomography showed a macular oedema in six eyes. Fluorescein angiography revealed five cases of retinal vasculitis. We observed three exsudative retinal detachments, and four choroidal or retinal granulomas.Five tuberculin skin test were performed, and four were positive. Three interferon-gamma release assays were realized, and were all positive. Six analysis of aqueous humor were negative, one vitreous sample was negative.All the patients were treated with anti-tuberculosis therapy as well as systemic steroids with a favorable clinical outcome without any recurrences observed.

Conclusion Our case series shows that tuberculosis uveitis were mostly anterior granulomatous uveitis, associated with an intermediate uveitis. Some patients presented a posterior affection. Tuberculin skin test and interferon-gamma release assays were efficient tests while analysis of intraocular fluid was less helpfull.

• S072

Werner syndrome accompanied with refractory CME and WRN proteins expression in human retinas

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Purpose To present a case of Werner syndrome accompanied with refractory cystoid macular edema (CME), and analyze the expression and the distribution of WRN proteins in human retinas.

Methods A 35-year-old individual with Werner syndrome exhibited CME after YAG laser treatment. Optical coherence tomography (OCT) scans were indicative of CME in the right eye. The patient received topical eye drops (0.1% bromfenac sodium hydrate twice daily and 1% dorzolamide hydrochloride thrice daily), sub-Tenon triamcinolone injection thrice, intravitreal bevacizumab injection twice, and pars plana vitrectomy in the right eye. Genetic analyses were performed to conduct diagnosis of the individual. To examine the expression and distribution of WRN proteins in the retinas, immunohistochemistry for WRN proteins in human retinas was performed.

Results CME in the right eye could not be improved by any of the treatment. During the follow-up period, CME developed in the left eye. Genetic analyses detected compound heterozygosity of Mut4 and Mut11 in WRN gene and the individual was diagnosed with Werner syndrome. Immunohistochemical analysis of WRN proteins expression in human retinas indicated that WRN proteins were expressed in Müller cells of the inner nuclear layer and the outer nuclear layer.

Conclusion Patients with Werner syndrome may develop severe CME. A pathological link may exist between the potential mutation in WRN gene and the development of CME in patients with Werner syndrome.

• S073

Effect of hemodialysis on the ophthalmologic findings in chronic renal failure patients

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Purpose The aim of this study is to evaluate the short-term changes in the ophthalmologic findings including retinal thicness measured by SD-OCT after HD.

Methods Thirty eyes of 30 patients with chronic renal failure(CRF) undergoing HD were analyzed. The subjects were categorized into two groups according to the cause of CRF. Detailed ophthalmologic examinations were performed immediatelybefore and after HD. The relationships between the systemic hemodynamic changes and the ophthalmologicchanges during a single HD session were evaluated.

Results The mean intraocular pressure decreased after HD with a mean decrease of 2.4±2.1 mmHg and the central corneal thickness decreased with a mean change of 6.9±5.4 μm. After HD, the ocular surface changed significantly; the tear break-up time and basal tear secretion (Schirmer's test) decreased, whereas the keratoepitheliopathy score increased. The macular thickness measured by spectral domain optical coherence tomography decreased after HD. The mean decrease in the central subfield thickness was 7.4±9.9 μm. The ocular surface changes after HD affected the visual acuity and examination quality. A significant correlation was found between the changes in the systemic hemodynamic parameters and those in the ophthalmologic findings, except for the retinal thickness.

Conclusion HD can affect the ophthalmologic findings in a short period of time. These changes correlated with the increase in plasma colloid osmotic pressure. In addition, for good examination quality, it is recommended that an ophthalmologic examination in CRF patients be performed on a non-dialysis day or prior to HD on a dialysis day.

• S074

Danger of research in lasers: about two examples of retinal impacts in senior researchers

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Purpose We report two cases of accidental retinal lesions made by diode and femtosecond lasers in senior researchers in optics.

Methods The first case concerned a 29-year old caucasian woman exposed to a 1053 nm wavelength femtosecond laser (0.5 mW) during mirror alignment. Immediately after exposure, she felt blurry central vision and scotoma in her left eye. Visual acuity was 20/60. Clinical examination showed yellowish dots in foveal region. No treatment was given. Two years later, visual acuity remained low. The second case was a 40-year old causasian woman exposed to 670 nm wavelength diode laser (3 mW) in both eyes during repeated experiments. The patient had no symptoms. Visual acuity was 20/20 without central scotoma. The fundus revealed several extrafoveal macular white and yellow impacts of different ages. Ten years later, no neovascular complication was observed

Results These two different cases illustrate the danger of any type of laser. Thermic or blast effect can caused permanent damage to the retinal pigment epithelium affecting the fixation point with permanent visual acuity decrease. Choroidal infarction has been described in the literature. Main risks are neovascularization and enlargement of the impacts involving the fovea. When patient does not consult immediately after accidental exposition, differential diagnosis of white retinal infiltrates, as multifocal choroiditis, should be ruled out.

Conclusion Whatever their skill, researchers and workers exposed to any type of lasers should be reminded the importance of wearing suitable eye protections. Considering the possibility of asymptomatic lesions, a periodical screening remains justified.

• S075

Pathologic findings for patients with acute and symptomatic floater

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Purpose To evaluate and establish the rate of pathologic findings for patiens with acute and symptomatic floater

Methods Retrospectively records of 3377eyes(2649 patients) with acute, symptomatic floater who visited Kim's Eye Hospital from January 1, 2011 to December 31, 2011 were evaluated. Patients with previous retinal detachments resulting from other ocular pathologic features, direct ocular trauma, or previous vitreoretinal, cataract surgery were excluded.Their standard examination included visual acuity, IOP, anterior segment examination, and dilated fundus examination using a slit-lamp and indirect ophthalmoscop

Results The incidence of floater symptom was common in female than male respectively($p<0.05$). And the most common cause of floater was posterior vitreous detachment(10.4%). The incidence of retinal tear was 0.8%(28 eyes) and 27eyes of them were undergone barrier laser. The incidence of lattice degeneration was 1.8%(61 eyes) and 36 eyes of them were treated with barrier laser. 3 cases of all showed retinal detachment. 2 cases of them were managed with barrier laser, 1 case was treated with scleral buckling and cryotherapy. And the incidence of retinal hemorrhage and vitreous hemorrhage was 0.4%(15 eyes), 0.02%(8 eyes) each. Other pathologic findings include epiretinal membrane(0.5%, 19 eyes), uveitis(0.4%, 14 eyes), and endophthalmitis(1 eye)

Conclusion The study revealed that the pathologic findings of floaters may be encountered: retinal detachment, retinal tears, lattice degeneration, vitreous hemorrhage, retinal hemorrhage, uveitis and endophthalmitis. Patients with an acute, symptomatic floater should be examined closely and if the results of an initial examination are negative for pathologic finding, the necessity of early follow-up should be needed.

• S076

Value of fundus autofluorescence imaging in a rare case of clonazepam associated retinopathy

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Purpose Many unwanted ocular effects have been described after the ingestion of psychotropic drugs. Clonazepam is an anticonvulsant and anxiolytic agent belonging to the family of benzodiazepines. Our aim is to report a case of toxic retinopathy associated with prolonged administration of clonazepam.

Methods We present a case of a middle-aged woman, with no significant ocular or familial ocular history, who complained of bilateral blurred vision and photophobia. She had a long-lasting anxiety disorder and underwent clonazepam for the previous 8 years. We carried out a complete ophthalmological examination including visual acuity and color vision testing, funduscopy, fluorescein angiography, electrophysiologic retinal testing, optical coherence tomography and fundus autofluorescence (FAF). We found multiple retinal mild depigmentation dots in the posterior pole of both eyes that showed a clear hyperautofluorescence and slightly reduced electrophysiologic responses. Other possible diagnoses were ruled out as multiple evanescent white dot syndrome or macular dystrophy associated with hyperautofluorescence.

Results A large variety of drugs may have toxic effects on the human retina. Thus, retinopathy has been shown to be related to high doses of typical antipsychotics, mainly chlorpromazine and thioridazine, but only two cases of retinal toxicity by benzodiazepines have been described. To our knowledge, this is the first reported case of FAF imaging findings in a retinopathy associated with clonazepam.

Conclusion Neurologists and ophthalmologists should be aware of the possible retinal toxicity of clonazepam and FAF should be considered as a complementary imaging modality in the diagnosis of toxic or drug-induced retinopathy.

• S077

Dramatic effect of bolus cyclophosphamide in a severe case of lupus retinopathy

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Purpose To report the dramatic effect of bolus cyclophosphamide in a severe case of lupus retinopathy.

Methods A 31-year-old woman with active systemic lupus erythematosus (SLE) consulted for asymmetric rapidly progressive decreased visual acuity (8/10 P2 OD, 1/20 P14 OS).Fundus examination disclosed bilateral macular oedema, numerous peripapillary cotton wool spots and hemorrhages suggestive of the diagnosis of lupus retinopathy. Clinical and biological criteria allowed the diagnosis of severe multi systemic SLE with lupus glomerulonephritis. Treatment based on oral 1mg/kg daily steroids and 6 intravenous cyclophosphamide cures (100mg/m2). Rapid improvement in systemic and biological signs of SLE was observed with parallel disappearance of retinal signs. Full recovery of visual acuity was obtained within 6 months.

Results Prevalence of SLE varies between 10 and 50 p 100,000. Presence of ophthalmological manifestations is estimated between 5 and 50% of the patients depending on the series, and the most frequent one is lupus retinopathy. First line treatment is usually based on oral corticosteroids. Immunosuppressive drugs may be used as part of a steroid-sparing strategy or for resistant forms of the disease. In case of severe acute cases, as in our patient, intensive treatment combining steroids and cyclophophamide cures enables regression of retinal signs and improvement of visual acuity, along with clinical and self-immune and inflammatory tests.

Conclusion In severe forms of SLE a treatment combining cyclophosphamide cures and steroids is mandatory to obtain not only improvement of systemic manifestations but also complete visual recovery.

• S078

High-altitude retinopathy

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Purpose To report the clinical characteristics of 3 cases of high altitude retinopathy (HAR) and a review of the literature.

Methods We report 3 cases of patients consulting for HAR after high trekking above 7000m.

Results Patient 1 was a 27 years-old man, high level sportsman, coming back from a GASNERBRUM expedition (7600m) and complaining of right eye central scotoma. Fundus examination revealed 2 haemorrhages : one next the fovea and one on the temporal arcade vessel. Patient 2 was a 52 years-old man, high mountain guide, coming back from EVERSEST ascent (8000m) and complaining of left eye central scotoma and visual acuity deficit. Fundus examination found one parafoveal haemorrhage in the left eye and paramacular haemorrhages in the right eye. Patient 3 was a young 25 years-old military doctor coming back from a high altitude expedition (7000m), he was complaining of right eye central scotoma during the descent and headache.Fundus examination found three macular haemorrhages and one on the inferior temporal arcade vessel. Only one of the three patients presented other symptomes of high altitude illness. All of us presented a positive outcome with complete functional and anatomical resolution of HAR, less than 2 month, without sequela.

Conclusion The real incidence and physiopathology of HAR are not very well known. Retinal haemorrhages after a high trekking are an early manifestation of HAR and more generally high altitude illness. It usually occurs at altitudes above 4000m. While macular involvement or retinal vein occlusion may result in permanent visual acuity deficit, these haemorrhages are generally asymptomatic and spontaneous regressive.

• S079

Experimental study of the effect of femtosecond laser radiation on eye fundus and sclera morphology

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Purpose To study the macro- and microscopic changes in the structures of fundus and sclera in the experiment after exposure of femtosecond laser radiation with a wavelength of 800 nm.

Methods As a source of laser radiation we used Ti: sapphire laser oscillator «Coherent», which allows to obtain a sequence of pulses of duration 130 fs and a repetition frequency of 76 MHz (wavelength - 800 nm) and femtosecond regenerative amplifier Legend F-1K-HE, which provides a pulse frequency of 1 kHz, lasting no more than 130 fs and an energy of about 2.5 mJ. In th study of eye tissues after femtosecond laser exposure was carried out on enucleated porcine and bovine eye

Results After exposure of the laser radiation with 76 MHz frequency were revealed destruction of the photoreceptor layer, the layer of retinal pigment epithelium and endothelium of blood vessels in the retina. Observed the effect of coagulation. When using the laser frequency of 1 kHz are marked changes in the fundus structures associated only with the cavitation effect of the laser. After the femtosecond laser damage to the sclera have been reported the formation of a defect of the sclera, full thickness homogenization of the collagen fibers of the sclera, the disappearance of cells, destruction of pigment cells of uveal tract and retinal pigment epithelium.

Conclusion During 130 fs laser using with 800 nm wavelength and high pulse frequency (76 MHz) marked cavitation effect in the tissues and thermal damage of retinal structures, mainly photoreceptor layer and retinal pigment epithelium. After laser radiation with low frequency (1 kHz) using dominates the mechanical cavitation effects on retinal and scleral structures.

• S080

Unilateral Terson syndrome. Outcome after early vitrectomy

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Purpose To report the clinical features and the results after an early vitrectomy of a case of a Terson syndrome following an aneurysmal subarachnoid hemorrhage

Methods 32 years old male with decreased visual acuity (VA) of the right eye (RE) of evolution difficult to determine. As recent precedent a month before stands out a subarachnoid and parenchymal hemorrhage secondary to ruptured aneurysm of the right medial cerebral artery, treated by external ventricular drainage and posterior surgical clipping with satisfactory outcome. The examination revealed visual acuity of light perception in RE and funduscopy shows widespread vitreous haze with impossibility of glimpse the retina, with fibrinous-looking condensations

Results Suspecting Terson syndrome a pars plana vitrectomy is performed with aspiration of subhyaloid bleeding in the posterior pole. The patient achieved a VA of 0.9 and the funduscopy shows the demarcation zone of ancient bleeding in the posterior pole

Conclusion Terson's syndrome is the combination of intraocular bleeding and subarachnoid hemorrhage secondary to rupture of an aneurysm. The bleeding can be intraretinal, subretinal or vitreal. It is a commonly underdiagnosed pathology. It is associated with worse neurological prognosis with higher rates of morbidity and mortality. However, vitreous hemorrhage is usually resolved spontaneously within a few months, and generally has good long-term visual prognosis. But early vitrectomy is indicated in bilateral cases, persistent bleeding or proliferative vitreoretinopathy

• S081

An unusual case of visual disturbance in a young boy

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Purpose To describe an unusual case of visual disturbance in a young boy.

Methods A 14-year-old boy described a 3 week history of blurred vision in his right eye. He was otherwise fit and well and on no regular medication with no family history of ophthalmic disease. There was no history of drug taking, sun gazing or eclipse viewing.Best-corrected visual acuity was 6/9.5 right eye,6/5 left eye and on Amsler grid testing there was evidence of right central distortion. Ocular examination revealed a right foveal yellow deposit; otherwise dilated fundoscopy was unremarkable. Autofluorescence imaging was within normal limits. Spectral domain optical coherence tomography, revealed a focal disruption of the junction between the foveal photoreceptor inner segments and outer segments with a central sub-retinal deposit in the right eye.Electrophysiological assessment revealed no evidence of generalised retinal dysfunction or significant macular dysfunction. Multifocal electroretinography was suggestive of very mild localised inferior macular dysfunction bilaterally.

Results The patient has been reviewed a year later and found to have improved visual acuity with 6/5 in both eyes. OCT findings are unchanged.

Conclusion The OCT can detect significant foveal changes in the majority of affected eyes with a characteristic outer retinal defect. OCT can improves the diagnosis and assessment of the degree and nature of foveal damage in patients with solar retinopathy and may be an important tool in identifying foveal damage not detected by standard fluorescein angiography.Nevertheless, the underlying aetiology of the unilateral abnormality detected in this child remains uncertain.

• S082

Peripheral exudative haemorrhagic chorioretinopathy complicated with acute onset of visual loss

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Purpose To report a case of unilateral peripheral exudative haemorrhagic chorioretinopathy (PEHCR) complicated with acute onset of visual loss.

Methods A 64-year-old female presented with a one week history of sudden onset of visual loss in her left eye. There was no other relevant medical or family history. Best corrected Snellen visual acuity (BCVA) was documented and full ophthalmic examination was performed.

Results BCVA was 1.0 in her right eye and hand movements in the left eye. Complete ophthalmic examination of her right eye was normal. Anterior segment examination of her left eye was unremarkable. There was no view of her left fundus. B-scan ultrasonography revealed vitreous haemorrhage with no evidence of retinal detachment. Pars plana vitrectomy was performed few weeks later. At follow up examination fundoscopy revealed extensive subretinal and sub-RPE haemorrhage in the retinal periphery temporal to the macula. Fundus fluorescein angiography (FFA) revealed patchy blockage of the background choroidal fluorescence corresponding to the suretinal/sub-RPE haemorrhage. Indocyanine green angiography revealed no further pathology. Visual acuity was finally improved to 1.0 and disciform retinal degeneration was documented at the temporal periphery. Seventeen months later the patient remained stable.

Conclusion PEHCR is a haemorrhagic retinal degenerative process, which can be complicated with vitreous haemorrhage and sudden visual loss. Differential diagnosis from choroidal melanoma or other vascular lesion is of major importance.

• S083

Subretinal injection of recombinant tissue of plasminogen activator and intravitreal injection in the management of subretinal hemorrhages secondary to age-related macular degeneration. A report of eight cases

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Purpose Complicated forms of AMD are the final stage of a disease leading to deep and permanent visual loss.All current therapeutic advances are opening up real prospects but no consensus has been established despite the efficiency of the subretinal injection of fibrinolytic un macular hematoma.We aimed to assess subretinal injection of rt-PA associated with anti-VEGF in the hematoma as a complication of AMD and to establish predictors of efficacy in order to identify target patients.

Methods Inclusion criteria were patients with subretinal hematoma as a complication of AMD active for less than 15 days and treated with the same surgical technique: vitrectomy, subretinal injection of rt-PA, intravitreal gas and anti-VEGF injections.Data from preoperative clinical exam at 3, 6 and 12 months postoperative were recorded.

Results Eight patients with extensive hematoma were included. 62 % patients showed significant improvment at 6 months (p=0,04) contrary to the one year results. Displacement of hematoma was observed in all patients and no complication during the surgery is noted. The mean dose of rt-PA is 50 µg/ml. All patients received locoregional anesthesia. Postoperative complications were cataract (25%), recurrent hemorrhage (25%), and ocular hypertension (12%). No cases of endophtalmitis or retinal detachment is observed.

Conclusion The extensive recent hemorrhage with underlying healthy macula appears to respond to treatment contrary to the old hematoma with pigment epithelium rupture and the hematoma after anti-VEGF injections responsible of large pigment epithelium detachment.

• S084

20 versus 23 Gauge sclerotomies for silicone oil extraction in vitreoretinal surgery

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Purpose The visco-elastic features of silicone oil are a limiting factor transconjunctival vitreoretinal surgery. The flow resistence increases with the reduction of the inner diameter of the extrusion canula. Thise increases the duration of silicone oil extraction. The purpose of this study was to compare 2 surgical procedures for silicone oil extrusion: 20 versus 23 Gauge.

Methods A retrospective pilot study compared two groups of patients scheduled for silicone oil extraction. In the first group silicone oil extraction was performed through a 20 Gauge scllerotomy after conjunctival dissection whereas a 25 Gauge tranconjunctival sclerotomy enabled saline infusion. In the second group both infusion and silicone oil extraction was performed through 23 Gayge transconjunctival sclerotomies. The duration of each procedure was the main outcome measure.

Results The mean duration of the 23 Gauge procedure was 42 minutes compared with 22 minutes in the combined 20/25 Gauge procedure. Transitory intraoperative hypotonia was encountered in two patients, one in each group. During the post-operative follow up, a vitreous hemorrhage occurred in one patient of the 23 Gauge procedure group.

Conclusion Comparing two surgical procedures for silicone oil extraction, the conjunctival dissection time in the 20/25 Gauge group seems to be largely counterbalanced by the rapidity of the silicone oil extraction through a larger sclerotomy. The use of a combined 20/25 Gauge full transconjunctival procedure could probably reduce furthermore the duration of surgery .

• S085

Early reactional hyperplasia and neuronal differentiation of the ciliary epithelium (CE) in experimental retinal detachment (RD) with proliferative vitreoretinopathy (PVR) in the porcine eye

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Purpose Rare quiescent retinal progenitor cells (RPCs) have been isolated in the adult mammalian (including human) CE. We have reported a CE proliferation with retinal neuronal and photoreceptor cell (rhodopsin+) differentiation in three human eyes eviscerated for longstanding RD and PVR. The CE strongly expressed EGFR. We have hypothezised that the disease RD and PVR might stimulate a dormant population of RPCs in the CE in presence of a niche constituted by EGF. The aim of the present work was to study the CE in the porcine eye with experimental DR and PVR.

Methods Two porcine eyes with experimental surgical RD and PVR enucleated at Day 15 and Day 35 were studied with light microscopy and immunocytochemistry with antibodies against EGFR, Ki67, CD133, NSE, rhodopsin, GFAP. The fellow porcine eyes, one non operated porcine eye, and one human eye exenterated for orbital tumor served as controls

Results Wwe observed in the CE of both porcine eyes a discrete hyperplasia of the non pigmented CE with an overexpression of EGFR and an expression of NSE. All CE controls were negative for NSE. Ki 67, CD133, GFAP and rhodopsin were negative in the CE of the eyes with RD and of the control eyes

Conclusion The CE of the porcine eye in vivo with shorter duration experimental RD and PVR showed hyperplasia with neuronal differentiation, in presence of an overexpression of EGFR, as in the human eye with longer duration RD. Photoreceptor differentiation was not observed in the porcine CE at this stage.

• S086

Traumatic macular hole revealing a retinitis pigmentosa: a case report

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Purpose To report a case of traumatic macular hole revealing a retinitis pigmentosa.

Methods A 33-year old man without past medical history complained of visual loss after direct trauma of his left eye. Visual acuity was 20/50 RE and 20/400 LE. Anterior chamber examination was normal and fundus examination revealed a large macular hole associated with optic atrophy in his left eye. Right eye funduscopy showed a cystoid macular edema and optic nerve palor (RE). Many pigment deposits were present in retinal mid-periphery of both eyes. Optical coherence tomography showed cystoid macular edema (517 microns) RE and a large macular hole (3100 microns) LE. Typical visual field defects and extinguished electroretinogram responses confirmed the diagnosis of retinitis pigmentosa.

Results Macular diseases are well-known complications of retinitis pigmentosa, especially macular edema. Vitreomacular tractions, epiretinal membranes and macular holes are less frequent. These complications may be explained by pigment epithelium disorders that may compromise ionic drainage of the retina. Causes of macular hole in retinitis pigmentosa remain uncertain. In our patient, development of a macular hole may be explained by occurrence of trauma in an eye with pre-existent macular edema secondary to the unknown retinitis pigmentosa.

Conclusion Despite macular complications of retinitis pigmentosa are relatively common, a traumatic macular hole as a revealing symptom is exceptional.

• S087

Age macular degeneration-Alzheimer disease: relevance and interest of ophthalmologic exam in detection and follow-up of Alzheimer disease

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Purpose To evaluate the impact of AMD on Alzheimer disease and their in-between visionary correlation.

Methods 285 patients, 95 men, 190 women, with AMD.3 Groups A,B,C: A, 90 patients with first stage AMD (drusen, drusenoid PED, pigment, small atrophic areas);B:80 patients with predominant atrophic areas;C,115 patients with Neovascular AMD. AMD evaluation included ETDRS visual acuity (VA), complete ophthalmic examination, autofluorescence imaging (FAF), optical coherence tomography (OCT) and fluorescein (FA) angiography, and ICG when neovascular complication.AD was diagnosed and valuated by general practice doctors and /or neurologists.

Results 20% patients in group A , 25% in group B, 30% in group C have mild cognitive impairment (MCI). 25% in group B, 35% in group C have early stage AD. 20% in group C have symptomatic AD. AMD ophthalmologic signs are predictive and precursor for AD. Fundus examination and even more (FAF , OCT) are useful and needed to enhance AD screening and follow-up.

Conclusion The AMD-AD correlation allows us to improve detection, follow-up, screening of both AMD and AD pathologies and furthermore progress in etiopathogenic knowledge and therapeutic prospects.

• S088

Long term evolution of combined hamartoma of the retina and retinal pigment epithelium: a report of two cases

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Purpose To show the long-term evolution of two cases of Combined Hamartoma of Retina and Retinal Pigment Epithelium (CHRRPE), one managed by vitrectomy, and other managed conservatively.

Methods A 46-year-old male and a 35-year-old female, diagnosed as having a CHRRPE, were observed during four years. One of them underwent pars plana vitrectomy due to an extense associated epiretinal membrane (ERM), and the other patient declined surgery. Full clinical examination, including Best Corrected Visual Acuity (BCVA), funduscopy examination and Optical Coherence Tomography (OCT) was performed.

Results For the patient who underwent vitreoretinal surgery, the evolution was initially satisfactory, with anatomic improvement (assesed by funduscopy and OCT examination) and visual acuity stabilization. However, four years later he presented with a complaint of visual loss, and severe macular distorsion was confirmed by OCT. The patient who asked for a conservative management, showed no visual nor funduscopic changes during the follow-up.

Conclusion Vitreoretinal surgery for CHRRPE can improve retinal architecture and visual acuity, but in the long-term functional recuperation is frequently not possible, with similar visual outcomes to those managed conservatively.

• S089

Intraretinal brilliant blue infiltration during membrane limiting intern peeling: a case report

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Purpose Surgical treatment of epiretinal membrane (ERM) have been facilitated by use of dyes such as brilliant blue G (BBG) whose harmlessness by intravitrael injection have been fully reported.

Methods We describe the case of a seventy-two year old female patient addressed for surgical treatment of left idiopathic ERM that caused metamorphopsia and a decrease of visual acuity. Pars plana vitrectomy and ERM peeling staining with BBG was performed.

Results During the procedure, an unusual complication occurs: intraretinal BBG infiltration. The area was limited (under a disc diameter) located in macular area, in temporal and superior to the fovea; the infiltration reached all retinal layers according to our OCT images. A defect in retina nerve fiber layer seems to be the origin of that staining. No damage in the field or in fluorescein and indocyanine angiography were observed. A progressive resorption of the staining appeared with atrophy of the inners retinal layers as aftereffect. Visual acuity reached 9/10 Pa2 a month and a half after the surgery.

Conclusion In spite of the benefits of vital dyes in vitreoretinal surgery which are widely used, this case remains us the damage that can occur.

• S090

Bilateral macular coloboma in a patient with retinitis pigmentosa like changes

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Purpose To report a case with bilateral macular coloboma and RP (retinitis pigmentosa) like changes.

Methods A 46-year-old female presented with macular coloboma in both eyes. There was a history of strabismic amblyopia in her right eye but no other contributory medical or family history.Best corrected Snellen visual acuity (BCVA) was measured and full ophthalmic examination was performed. Visual field testing, optical coherence tomography (OCT) and international-standard electrophysiological (ISCEV) evaluation, including pattern and full-field electroretinography (PERG and FFERG), were also performed.

Results BCVA was hand movements in the right eye and 0.5 in her left eye. Fundoscopy revealed an oval sharply- demarcated defect at the macula with bare sclera at its base and pigment clumping, mainly in the right eye, resembling macular coloboma. There were also severe retinal vessel attenuation and scattered retinal pigmentary changes, occasionally resembling bone spicule RPE changes, in the retinal periphery in both eyes. Optic discs were pale bilaterally. Visual field testing demonstrated bilateral scotomas. OCT revealed a crater-like depression at the macula with atrophic neurosensory retina and absence of retinal pigment epithelium (RPE) and choroid, more extensive in her right eye, where scleral excavation was also documented. Pattern ERG as an indication of macular function was extinguished in the right eye and severely affected in her left eye. Full field ERG was extinguished bilaterally for both scotopic and photopic responses.

Conclusion Bilateral macular coloboma associated with RP like changes, an abnormal electroretinography and no relevant family history, may be indicative of a developmental retinal abnormality.

• S091

Priminary observations of the effects of ACE inhibitor ramipril in patients with Stargardt's disease

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Purpose to assess the effect of Ramipril 2% eyedrops on visual function in patients with Stargardt's disease.

Methods We conducted a prospective, interventional, open label pilot study. 12 eyes of 6 consecutive patients in whom Stargardt's disease had been diagnosed were treated with Ramipril 2%, one drop three times a day in both eyes. Four follow-up visits were performed over 3 months. Retinal imaging workup was performed at baseline to confirm diagnosis. During follow up, best corrected visual acuity, fundus examination, static perimetry and electroretinogram were performed to assess safety and efficacy.

Results Treatment was well-tolerated in all cases. Mean BCVA improved from 40 +/- 20 letters to 51 +/- 17. Mean sensitivity improved from 20.6 +/- 3.2 dB to 22.5 +/- 3.7dB.

Conclusion Ramipril demonstrated a good local and systemic safety profile as well as efficiency in terms of BCVA improvement and retinal sensitivity in patients with Stargardt's disease. These results encourage us to further describe the effects of Ramipril used as a NO-donating and antioxidative drug in ophthalmology.

Commercial interest

• S092

Recurrent retinal detachment secondary to hereditary congenital collagen disease

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Purpose Hereditary progressive arthro-ophthalmopathy, also called Stickler syndrome, is an autosomal dominant genetic disease affecting connective tissue collagen. It is considered the leading cause of inherited retinal detachment in all ages and produces multisystem manifestations such as premature arthritis, micrognathia or eye disorder.

Methods A 31-year-old man reports hereditary progressive arthro-ophthalmopathy. He presented degenerative myopia, congenital cataract and bilateral recurrent retinal detachments during childhood. At birth, he presented craniofacial anomalies, hearing loss and flat feet. When he was 6 years old, he suffered a retinal detachment associated with giant tear, which was treated with 20G pars plana vitrectomy and injection of silicone oil. At 22 years, the right eye presented another retinal detachment that was treated with silicone band placement, cryotherapy and C3F8 gas intravitreal injection. Two months later the retinal detachment recurred in right eye, needing 23 G pars plana vitrectomy and intravitreal silicone oil implantation.

Results The patient presented several ophthalmic complications such as post-surgical ocular hypertension and retinal tears requiring selective photocoagulation with argon laser in the right eye. Recently, genetic diagnosis was confirmed by COL11A1 gene mutation.

Conclusion Development, prevention and therapeutic management of ophthalmic complications during 26 years follow-up are presented. The importance of early diagnosis and follow-up by a vitreoretinal surgeon are also emphasized.

• S093

Changes in chronobiological function related to retina degeneration P23H line 1 transgenic rats

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Purpose To evaluate and determinate changes in the circadian rhythms related to retinal degeneration in P23H line 1 rats.

Methods Male rats homozygous for the P23H rhodopsin mutation line 1 and male SD rats were evaluated during a 12 months period. All of them were individually housed and maintained during this time under controlled humidity (60%), temperature (23 ± 1°C) and under a 12-h light/dark cycle. Locomotor activity (LA) was monitored throughout the experiment by an intraperitoneal transmitter. Electroretinograms (ERG) were used to evaluate retinal function and retinas were evaluated by ICC looking for the degeneration pattern.

Results The LA recordings from wild type and mutant animals showed no differences in the pattern of the mean waveform and the periodogram. However, a progressive decrease in the amplitude of the LA rhythm was observed in P23H rats, when compared to wild-type animals. The nonparametric analyses of the data showed a gradual decrease in the coupling strength of the LA rhythm to environmental zeitgebers (inter-daily stability, IS) and an increased rhythm fragmentation (intra-daily variability, IV) in P23H rats, as compared with wild type animals. The circadian changes are related to the rate of the degeneration. In 6 months P23H line 1 rats, the only remaining photoreceptor were cones, distributed in a disrupted single layer. B-wave amplitude was declined at this age.

Conclusion Vision loss in P23H line 1 rats produces a progressive fragmentation of their circadian patterns.

• S094

Bilateral intermediate uveitis asociated with retinosis pigmentosa

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Purpose Retinitis pigmentosa (RP) is a group of inherited dystrophies with great clinical genetic and evolutionary heterogeneity.We report a patient with retinitis pigmentosa who presented a bilateral intermediate uveitis with cystoid macular edema associated and no other systemic disease.

Methods A 16 year old man with a history of Retinosis pigmentosa since birth presented blurred vision associated with a bilateral intermediate uveitis. The visual acuity was 0,4, Tyndall ++, and intense vitritis with snowballs in both eyes. All systemic examinations were normal (analytics, autoimmunity and serology tests).

Results Patient was treated with orals corticosteroids maintained in decreasing doses. Response to treatment was favorable, but then macular edema appeared. Due to the inability to control uveitis symptoms with steroids, azathioprine was associated and response has been favorable with resolution of macular edema and decreasing inflammation.

Conclusion RP includes a large group of degenerative and hereditary diseases that may be associated with a number of ocular complications. Intermediate uveitis is a rare complication described but can cause decreased vision and requiring monitoring and appropriate treatment for their control.

• S095

Ischemic maculopathy with temporal macular thinning on spectral-domain optical coherence tomography in sickle cell retinopathy: about three cases

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Purpose Ischemic maculopathy with temporal macular thinning was recently described on OCT in patients with sickle cell disease. In the current study, we describe the features on Spectral Domain OCT(SD-OCT)in three patients.

Methods We report 3 cases of sickle cell patients presenting ischemic maculopathy documented by ophthalmologic clinical evaluation, fluorescein angiography (FA),and SD-OCT.

Results The three patients present stage 3 sickle cell peripheral ischemic retinopathy (Goldberg classification) and bilateral enlargement of ACV in FA. The first patient is a 35 year old man. SD-OCT shows bilateral thinning in temporal macula retina. Thickness measurement is respectively in right and left eye, 271µm and 219 µm in foveolar region, 275µm and 302µm in temporal perifoveolar region, 203µm and 265 µm in temporal parafoveolar region. The second patient is aged 15. Angiograms reveal a small arteriolar occlusion in the right temporal macula. On SD-OCT retinal thickness measurement is decreased in both temporal macula: 240µm and 261µm in foveolar region, 233µm and 265µm in temporal perifoveolar region vs 276µm and 358µm in nasal perifoveolar region, 199µm and 230 µm in temporal parafoveolar region vs 292µm and 319µm in nasal parafoveolar region (respectively in right and left eye). The third patient is aged 19 and present the same OCT aspect. Temporal retinal thinning is predominant in inner layers in the three patients.

Conclusion Sickle cell retinopathy can affect macular area through the same process of peripheral terminal vascular occlusion. SD-OCT provides high resolution images that shows temporal macular thinning which is predominant in the retinal inner layers.

• S096

Ocular sarcoidosis: when should labial salivary gland biopsy be performed ?

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Purpose To assess the usefulness of a labial salivary gland biopsy (LSGB) in subsets of patients with uveitis.

Methods A retrospective study of 116 consecutive patients with uveitis for whom a LSGB had been done because of suspected ocular sarcoidosis (n=87) or unexplained uveitis (n=29). Eighty six patients had a suspicion of ocular sarcoidosis because of ocular features (n=67), an elevated angiotensin converting enzyme (ACE) (n=30) or because of CT findings (n=33) suggestive of sarcoidosis. The biopsy results were analyzed together with their ophthalmological features and the results of other relevant examinations, such as the serum levels of ACE and a chest radiography or a CT scan.

Results Six of the 116 patients (5.2%) with uveitis had sarcoid granulomas on the LSGB. At the end of the study, 32 patients had proven sarcoidois while 23 patients were considered as having either indeterminate or presumed sarcoidosis, according to the criteria of Abad et al. A raised ACE (p=0.033) and a compatible radiology (p=0.019) were related to a positive LSGB test but not to the features of uveitis. Granulomas were only found in the LSGB of the patients with an elevated ACE or compatible CT scans.

Conclusion In this study, the LSGB sensitivity (18.75%) in the patients with proven sarcoidosis appears to be lower than in other reports. Our results suggest that this investigation should be limited to the patients with a raised ACE and/or CT scans pattern compatible with sarcoidosis and should not be performed in patients with unexplained uveitis or because of ophthalmological features.

• S097 / 2717

Atrophic areas and/with neovascular AMD. Characteristics, evolution of atrophic lesions associated to neovascular AMD treated by series of 3 Ranibizumab IVT protocol, 4 years follow-up

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Purpose To evaluate atrophic areas characteristics, at the first time, their change, evolution and correlation or no with and during the follow-up of neovascular AMD treatment by series of 3 Ranibizumab IVT

Methods 102 eyes of 91 patients, 28 men, 63 women, with retrofoveolar neovascularisation complicating AMD. Atrophic areas were evaluated by autofluorescence imaging Spectralis (in particular with region finder software), OCT (notably choriocapillary depth), FA, ICG. We evaluate the size, characteristics, topography of the lesions, their growth way. The areas themselves, their edge and rim were considered and evaluated. Each element was studied, compared cut to cut and time to time to itself and to each other data, every 2 months. The impact of AMD and / or this treatment protocol on the evolution of atrophic areas is also valuate.

Results VA improved in 85% cases, stabilized in 15%. AF imaging and their region finder analyze were the main elements of the atrophic lesions' study. The surface of the atrophic area grows by 17%, the edge changes in 20%. Speed growth was in average 1,15mm2/ year. At OCT, thickness of photoreceptor, pigment epithelium layer diminished about 25% and 35% at the area's edge. Choriocapillary depth values, FA and ICG data were mainly significative in the large atrophic areas and less than AF indications. This protocol has a little impact on the evolution of atrophic areas, apparently less than monthly IVT, and the same as AMD by itself.

Conclusion The study of atrophic process and its progression is a main question in the AMD follow –up, the evaluation of the protocol treatments and their safety too.

• S098 / 2716

Assessment of different methods for inter-individual registration of OCT topography for statistical analysis

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Purpose Assessment of OCT topography is subjective. A statistical method of analysis would be helpful to aid interpretation. This requires the generation of accurate normative topography which in turn requires accurate alignment of normal OCTs. This study assesses 9 methods of alignment.

Methods Normal topography maps were exported from a spectral domain OCT system. Code was written to perform image registration using different methods: User selection of foveal centre, cross-correlation to a difference of two Gaussian macula template, finding of the thinnest central point and automatic fovea-finding using Gaussian convolution and centroiding for the red, green and blue channels of the image respectively.

Results Data from 127 left and 110 right eyes were analysed. Mean and total standard deviation across the central 400x400 pixels of the aligned maps were calculated. The lowest standard deviation was achieved by the cross-correlation method (38.9 microns), followed by the blue channel centroiding method (40.4 microns), the thinnest central point (40.5 microns) and the user-selected foveal centre (40.6 microns). Convolution with a Gaussian to identify the fovea produced the worst results with mean SD of 49.9-64.8 microns.

Conclusion Cross-correlation with a difference of two Gaussian macula template appears superior for inter-individual topography registration in OCT in comparison with fovea-finding methods. Blue centroid and thinnest point were the best other methods. The cross-correlation technique will lead to the most accurate normal maps for statistical comparison with data from pathological OCT topography.

• S099 / 2616

Influence of cataract in reproducibility of Optical Coherence Tomography measurements

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Purpose To evaluate the effect of lens opacities in quality of images and reproducibility of retinal nerve fiber layer (RNFL) thickness measurements using Spectralis Optical Coherence Tomography (OCT).

Methods Fifty eyes of 50 subjects (25 men and 25 women; aged from 62 to 88 years) underwent three 360° circular scans centred on the optic disc by the same experienced examiner using the "RNFL Fast" Glaucoma Application and the "RNFL-N Fast" Axonal Application of Spectralis OCT instrument one month before and one month after cataract surgery. Comparison between the two visits and changes in reproducibility (using intra-class correlation coefficients and coefficients of variation) were analyzed. The quality of images was also compared between both visits.

Results RNFL and RNFL-N differences were detected between both visits for average thickness, temporal and nasal quadrants ($p<0.05$) using Glaucoma Application and for inferior and nasal quadrants ($p<0.05$) with Axonal Application. RNFL average thickness was 99.6 µm in pre-surgery visit and 102.4 µm in post-surgery visit using Glaucoma Application; and 94.3 and 94.7 µm, respectively, with Axonal Application. Reproducibility shows better values in post-surgery evaluation (mean coefficient of variation of 5.55% in pre-surgery visit vs 4.32% in post-surgery). Intra-class correlation coefficients were higher than 0.834 in all visits and parameters, so reliability of Spectralis measurements was high with both Spectralis OCT applications. The quality of images was better in post-surgery evaluations.

Conclusion The measurements of RNFL thickness and the reproducibility of Spectralis OCT are affected by lens opacity.

• S100 / 2617

Subfoveal choriodal thickness: the Beijing Eye Study

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Purpose To study subfoveal choroidal thickness (SFCT) in adult Chinese subjects

Methods The population-based Beijing Eye Study 2011 included 3468 individuals. Spectral-domain optical coherence tomography (SD-OCT) with enhanced depth imaging was used for measurement of SFCT.

Results Mean SFCT was 253.8 ± 107.4µm (range: 8µm to 854µm). In multivariate analysis, SFCT increased with younger age ($P<0.001$), shorter axial length ($P<0.001$), male gender ($P<0.001$), deeper anterior chamber depth ($P<0.001$), thicker lens ($P<0.001$), flatter cornea ($P<0.001$) and better best corrected visual acuity ($P=0.001$). In multivariate analysis, SFCT was not significantly associated with blood pressure, ocular perfusion pressure, intraocular pressure, cigarette smoking, alcohol consumption, serum concentrations of lipids and glucose, diabetes mellitus and arterial hypertension. In the myopic refractive error range of more than -1 diopters, SFCT decreased by 15µm (95%confidence interval (CI): 11.9, 18.5) for every increase in myopic refractive error of one diopter, or by 32µm (95%CI: 37.1, 26.0) for every increase in axial length of one millimeter. For each year increase in age, the SFCT decreased by 4.1µm (95%CI: 4.6, 3.7) (multivariate analysis).

Conclusion SFCT with a mean of 254±107µm in elderly subjects with a mean age of 65 years decreased with age (4µm per year of age) and myopia (15 µm per diopter of myopia). It was additionally associated with male gender and the ocular biometric parameters of a deeper anterior chamber and thicker lens. The association between SFCT and best corrected visual acuity strongly points towards a functional aspect of SFCT

• S101 / 4225
Ocular prognosis of congenital toxoplasmosis (genotypes II and III)

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Purpose There are in France 3 main strains of T. gondii (genotypes I, II and III). Ocular lesions of congenital toxoplasmosis have been reported in 80% of untreated, infected children. But no data were available in Europe on the genotype, on the prevalence of the different strains of T. gondii and on their virulence. Our purpose was to investigate the genotype of strains and the outcome of babies born with congenital toxoplasmosis in our university hospital.

Methods From 1980, every newborn with congenital toxoplasmosis was prospectively referred to the Parasitology Department. Date of birth, sex, time of congenital contamination, pre- and post-natal treatment were recorded. We designed a retrospective follow-up of all these children. Fetal infection was detected using serologic analysis and parasitologic investigations, such as mice inoculation and PCR from samples of amniotic fluid or placenta. For 43 newborns, genotyping of T. gondii strains was performed, using multilocus analysis.

Results The median follow-up was 38.6 months. 28,2% of 78 infected children were treated in-utero upon detection of the maternal infection. 66.1% of 71 alive new borns underwent a post-natal treatment.Genotype of T. gondii was analysed for 55% of infected children. 41 strains were identified as genotype II and 2 strains as genotype III. Among the 10 children with at least 1 retinochoroidal lesion, 5 strains were analyzed: 4 were genotype II (2 peripheral lesions, 1 macular, 1 peripapillar) and 1 was genotype III (1 macular lesion).

Conclusion Genotype II is confirmed to be the most common strain in France. Percentages of ophthalmological lesions accorded to the literature. No prognostic factor was identified for the occurrence or the seriousness of retinal lesions.

• S102 / 4226
Circadien cycle and chronic central serous chorioretinopathy

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Purpose Chronic central serous chorioretinopathy (CSCR) is a multifactorial disease. The present study was designed to evaluate the prevalence of circadian disturbance and corticosteroid treatment in patients treated with chronic CSCR.

Methods Patients presenting with chronic CSCR between 01/01/2009 and 30/11/2011 were prospectively enrolled. A history of corticosteroid treatment, sleep disturbances and irregular working hours was noted. Two questionnaires (PSQI and Epworth) regarding sleeping distrurbancies were applied. After a follow up of 3 months, the patients with persisting fluid and visual acuity below 20/40 were treated with photodynamic therapy (PDT).

Results During the period of inclusion, among 26 included patients, 19 were treated with PDT (73%). A history of corticosteroid tretment was found in 12 patients (19%), 4 currently used psychopharmacologic drugs (15%) and 8 had irregular working hours (30%). The analysis of the Epworth questionnaire enabled to record moderate sleeping disturbances in 11 patients (42%), none of the patients were classified as having severe sleeping disturbances.

Conclusion It is likely that general factors such as the existence of a corticosteroid treatment or a disruption of the circadian cycle are involved in the occurrence of patients with CSCR.

• S103 / 4227
Comparative study of post-natal retinal vascular development in mice models of iPLA2 inhibition and plasmalogen deficiency

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Purpose Plasmalogens are particular phospholipids characterized by the presence of a polyunsaturated fatty acid (PUFA) at sn-2 position of glycerol. Plasmalogen deficiency in mouse leads to developmental abnormalities in retinal vasculature. We propose that liberation of PUFA by the specific calcium-independent phospholipase A2 (iPLA2), is involved in the mechanism by which plasmalogens control retinal vascular development. To confirm this hypothesis, we performed a comparative study of retinal vascular development in a mouse model of retinal iPLA2 inhibition and a model of plasmalogen deficiency.

Methods Vessel and astrocyte networks were visualized on flat-mounted retinas through immunostaining methods.

Results Similar abnormalities were observed in retina of both mouse models. They consisted in an increased number of vessel ramifications at PN14, and in an abnormal glial cells migration from the optic nerve, at PN14 and at PN21. An activation of microglial cells was also observed at adult age.

Conclusion These results confirm the implication of plasmalogen in the control of retinal vessel development through PUFA release from their sn-2 position.

• S104 / 4615
A retrospective data collection study in patients receiving two or more OZURDEX® injections for macular oedema secondary to retinal vein occlusion

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Purpose This retrospective study was designed to investigate the re-injection interval, efficacy and safety of OZURDEX® in routine clinical practice.

Methods This analysis contains data from 87 patients from 10 sites in Germany who had received at least 2 OZURDEX® injections. Data was collected from the time of the patients' first injection until 3 – 6 months following their latest OZURDEX® injection.

Results The mean time to OZURDEX® re-injection between 1st and 2nd treatments was 141 days (5.03 months) in the overall population. Mean time intervals for the BRVO and CRVO sub-populations were 153 days (5.46 months) and 127 days (4.52 months) respectively.In the overall population, a mean LogMAR BCVA improvement from 0.68 to 0.51 was recorded following the last OZURDEX® injection (mean time of 11.0 weeks post-injection). For BRVO, mean improvement was from 0.54 to 0.43 (mean time of 10.5 weeks post injection) and for CRVO, 0.83 to 0.58 (mean time of 11.5 weeks post injection). Reductions in central retinal thickness were also observed.Intraocular pressure measurements over 25mmHg were reported in 19.5% of patients. No glaucoma surgeries were reported. 5 patients underwent cataract surgery during the course of the study (4 had known lens opacity at baseline and opacity status data from the 5th was missing).

Conclusion In this real life study, OZURDEX® was found to be safe and effective with repeat treatments. The mean re-injection interval for RVO patients was 5.0 months.

• S105 / 4616
Dexamethasone drug delivery system (Ozurdex) for the treatment of refractory diabetic macular oedema: retrospective case series analysis

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Purpose The purpose of this study is to report the clinical outcome of the treatment of DME patients with the Dexamethasone Drug Delivery System (Ozurdex) in clinical practice.

Methods This retrospective case series study included 25 consecutive patients (25 eyes) with refractory DME. This preliminary report includes 10 patients who completed a 12 months follow-up. VA (EDTRS), CRT (OCT) and IOP were assessed at baseline, 7 days, and 1, 6 and 12 months after Ozurdex injection. If necessary, a second implant was injected at 6 and/or 12 month.

Results The mean duration of diabetes at baseline was 18.6 years with a mean HbA1c level of 8.97. At baseline the mean VA was 52 letters, mean CRT 467µm and mean IOP 15.9 mmHg. At day 7, the mean VA increased to 62.22 letters (+ 10.22 letters) and the mean CRT decreased to 290.25µm with a mean IOP level of 16.66 mmHg.At month 1: mean VA was maintained to 58.66 letters (+ 6.66 letters) and the CRT continued to decrease to 201µm.The mean IOP slightly increased to 17.83 mmHg (we had 1 case at 24 mmHg)At month 6: mean visual acuity continued to increase to 64.33 letters (+12.33 letters gain). The mean CRT was 281µm with an IOP level of 15.16 mmHg.At month 12: mean visual acuity was maintained to 65.41 letters (2-line gain: + 13.41 letters), mean retinal thickness and IOP level were normal (200µm and 16.81 mmHg respectively). At month 12: 5 patients (50%) had an improvement of more than 15 letters.50% of the patients underwent a second injection, and 33% of them

Conclusion The present clinical study suggests that intravitreal injection of the dexamethasone drug delivery system (Ozurdex) seems to be effective and well tolerated in eyes with refractory DME

• S106 / 4617
Pars plana vitrectomy for valsalva retinopathy: a case series

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Purpose To investigate the utility of pars plana vitrectomy in a series of patients with Valsalva retinopathy.

Methods A retrospective, case series study that includes five patients with sudden visual acuity loss owing to Valsalva retinopathy with too dense premacular hemorrhages, treated in our hospital in the last three years. The etiology of the premacular hemorrhage was: vomiting (cases 1, 2 and 3), trauma (case 4) and vigorous dancing (case 5). Mean age was 33±19 years. After a period of observation ranging between three and four weeks, all patients underwent 23-gauge pars plana vitrectomy. The internal limiting membrane (ILM) was released and the hemorrhage was cleaned. The sub-ILM localization was confirmed in all cases during vitrectomy. One patient suffered an accidental break during peribulbar anaesthesia which was resolved successfully with laser photocoagulation. Full clinical examination including best-corrected visual acuity (BCVA) (Snellen chart), intraocular pressure, fundus examination, and Optical Coherence Tomography (OCT) was performed at baseline and at last examination in all patients. The mean follow-up was 16.1 (3-32) months.

Results BCVA was 10/10 in all patients one month after surgery and it remained unchanged during the follow-up period. Funduscopy appearance was excellent in all eyes.No postoperative complications were found.

Conclusion Valsalva retinopathy is a very rare condition that causes sudden visual acuity loss. In those cases with too dense hemorrhages it is necessary to perform vitrectomy, with excellent visual outcomes, as these hemorrhages are highly unlikely to resolve spontaneously.

• S107 / 4618
Retinal vascular reactivity over extended vessel segments

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Purpose To assess the impact of vessel segment length when analysing retinal vessel responses to flicker light provocation in healthy individuals.

Methods 12 healthy individuals (mean age 30±6) underwent digital sphygmomanometry (UA-767, A&D Instruments, UK), non-contact tonometry (Keeler Pulsair, UK) and dynamic retinal diameter assessment using the retinal vessel analyser (Imedos Systems, Germany) in order to evaluate the influence of segment length on flicker light induced dilation of retinal arterioles and venules. Up to seven segments of each superior artery and vein, were extracted off-line from video recordings of each subject within a minimum distance of 1 disc diameter (DD) from the rim of the optic nerve head and up to a maximum of 4 DD away from the rim.

Results Retinal arteriolar and venular dilation amplitude were independent of segment length, blood pressure and intraocular pressure.

Conclusion Independence of segment length is essential as retinal vessel anatomy is highly variable, some individuals having numerous vessel crossings and bifurcations making it difficult to measure long vessel segments.

• S108 / 4725
A novel co-culture model of the blood-retinal barrier based on primary retinal endothelial cells, pericytes and astrocytes

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Purpose Loss of blood-retinal barrier (BRB) is an important cause of diabetic macular edema (DME), but cellular mechanisms underlying BRB dysfunction are poorly understood. Therefore, we developed and characterized a novel in vitro BRB model.

Methods The model is based on primary bovine retinal endothelial cells(BRECs).These cells were shown to maintain specific in vivo BRB properties by expressing high levels of endothelial junction proteins and specific BRB transporters. To investigate the influence of pericytes and astrocytes on BRB maintenance in vitro, we compared five different co-culture BRB models, based on BRECs, bovine retinal pericytes (BRPCs) and rat glial cells.

Results Co-cultures of BRECs with BRPCs and glial cells showed the highest trans-endothelial resistance (TEER) as well as decreased permeability of tracers, even after vascular endothelial growth factor (VEGF) stimulation, suggesting a major role for these cell types in maintaining barrier properties. To mimic the in vivo situation of DME, we stimulated BRECs with VEGF, which downregulated MDR1 and GLUT1 mRNA levels, transiently reduced expression levels of endothelial junctional proteins and altered their organization, increased the number of intercellular gaps in BRECs monolayers and influence the permeability of the model to differently-sized molecular tracers. Moreover, as has been shown in vivo, expression of plasmalemma vesicle-associated protein (PLVAP) was increased in endothelial cells in the presence of VEGF.

Conclusion This in vitro model is the first co-culture model of the BRB that mimicks in vivo VEGF-dependent changes occurring in DME.

• S109 / 4726

Measurement of subfoveal choroidal thickness before and after cataract surgery using enhanced depth imaging optical coherence tomography

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Purpose To compare subfoveal choroidal thickness (SFCT) before and after cataract surgery using enhanced depth imaging optical coherence tomography (EDI OCT)

Methods Cross-sectional observational prospective study. Spectral-domain EDI OCT was performed with a Heidelberg Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) using a standardized protocol. SFCT of 67 patients was measured manually from the posterior edge of the retinal pigment epithelium to the choroid/sclera junction before surgery, 1 day, 7 days, 1 month, 3 month after. Choroidal thicknesses were independantly assessed by two masked graders. Statistical analysis was performed to evaluate variations of choroidal thickness before and after cataract surgery.

Results Eighty four eyes of 67 patients who had cataract surgery were included. Mean SFCT ± SD was 215,9 ± 69,4 µm before surgery, 213,3 ± 67,3 µm at Day 1, 221,9 ± 67,8 µm at Day 7, 226,5 ± 68,9 µm at 1 month and 230 ± 62,2 µm at 3 months. Mean SFCT increased significantly between before and 3 months after surgery ($p<0,04$). For diabetic patients mean SFCT increased in the same proportion as in general population but later (Day 7 versus Day 30). No significative difference was observed between group with Diabetic Retinopathy (DR) and group without. For the only patient who developed an Irvine Gass Syndrom, SFCT increased.

Conclusion Mean SFCT seems to increase after phacoemulsification. EDI OCT can be used to evaluate choroidal changes after cataract surgery in diabetic patients, and to detect patients who would develop an Irvine Gass syndrome.

• S110 / 4727

Subthreshold micropulse photocoagulation with true yellow 577nm diode laser for macular oedema

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Purpose Subthreshold, or tissue sparing, Diode Micropulse Photocoagualtion (SDM) is a treatment used to produce a therapeutic effect without inducing detectable intraretinal damage. Actually treatment options are available for diabetic macular edema (DME), proliferative diabetic retinopathy (PDR), central serous chorioretinopathy (CSR), macular edema secondary to branch retinal vein occlusion (BRVO), and even glaucoma.

Methods We used micropulse technology with 577nm yellow diode laser to produce a therapeutic effect without inducing intraretinal damage detectable on clinical examination during or after the treatment. All patients were affected by clinically significative macular edema (CSME) due to diabetic retinopathy, venous branch retinal occlusion and central serous retinopathy.

Results Controls prefomed at 1, 3 and 6 months showed no detectable retinal scars in any case. Foveal thickness decreased in all patients, visual acuity remained stable (<10 ETDRS letters) or improved (≥10 ETDRS letters).

Conclusion The results of our study indicate that, in the treatment of CSME due to PDR, BRVO and CSR,SDM photocoagulation is at least as effective as conventional photocoagulation without any clinically discernible evidence of laser-induced iatrogenic damage.

• S111 / 4728

Peripheral capillary network enlargement in diabetic maculopathy

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Purpose Diabetic macular edema has been associated with increased intravitreal levels of VEGF. Therefore, ischemia is probably part of the physiopathology. The purpose of this study is to evaluate the rarefaction of peripheral capillaries.

Methods A retrospective analysis of large field angiographic images with a scanning laser ophthalmoscope (OPTOS, Edinburgh, Scotland) was performed between Novembre 2011 and March 2012was performed. After excluding patients with previous panretinal laser photocoagulation and those with peripheral non-analyzable images, the peripheral area on early phase images in 112 patients were evaluated. 38 had a diabetic maculopathy and 78 served as non diabetic controls. The enlargement of the peripheral capillary network was graded from 1 to 3 (1: normal, 2: moderate, 3: severe).

Results A total of 43 patients were excluded because of panretinal photocoagulation in the diabetic group, possible VEGF involvement in the control group and poor image quality in either group.When comparing the remaining patients of the two groups, no significant difference in peripheral capillary network changes was observed.

Conclusion The peripheral capillary rarefaction is difficult to analyze on conventional angiography (peripheral images are usually obtained in the late phase). This angiographic finding is probably not encountered more often in diabetic maculopathy than other retinal diseases. It remains to be demonstrated in which cases peripheral capillary rarefaction should be considered as significant and whether targeted laser treatment as a part of diabetic macular edema therapy should be discussed.

• S112

Cationic amino acid transport activity and detection of B-defensin-1 in canine lens epithelial cells

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Purpose The aim of this study is to investigate the cationic amino acid transport activity in canine lens epithelial cells line (cdLEC).B-defensins are small cationic peptides possessing a broad range of antimicrobial and physiological activities. The mucosal physical barrier is an important component protecting luminal surfaces from bacteria. Expression of B-defensins was also examined.

Methods Na-independence of arginine transport activity was measured, and N-ethylmaleimide (NEM)-sensitive uptake of arginine was investigated. cDNA sequence of cationic amino acid transporter 1 (CAT1) was determined based on human and mouse CAT1 sequences. RT-PCR analysis of B-defensins was carried out.

Results NEM-sensitive component of arginine uptake was detected. cDNA sequence of CAT1 was determined from the cdLEC. The sequence was 2589 bp long and was predicted to encode the 629 amino acid polypeptides. The deduced amino acid sequence showed similarities of 92.1% and 88.6% to those of human and mouse, respectively. Western blot analysis indicated the single band at 70 kDa in membrane protein sample of cdLEC. RT-PCR analysis confirmed that CAT1 was ubiquitously detected in all tissues examined. Among the B-defensins, B-defensin-1 but not -2 and -3 were observed in cdLECs and primary culture of lens epithelial cells.

Conclusion Lens epithelial cells possess CAT1, and CAT1 may provide substrates for synthesis of B-defensin-1.

• S113
The lipids of lens in the aging and in cataractogenesis

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Purpose to study influence of lens's lipids on its optical properties

Methods 40 patients at the age from 60 to 90, with cataract were examined. The lens tissue after phacoemulsification was investigated. The cataract maturity, color characteristics of lens were estimated. Laboratory researches of crystalline lens' tissue were included: researching of lipid peroxidation's level; studying of lipid peroxidation's products; researching of the higher fatty acids' composition

Results Concentration of the free oxidations' primary and secondary products were gradually decreased in about 5 times with the age. The finite products of the free oxidations had a similar tendency. The chemiluminescence level also was decreasing during the period from 50 to 70 years. In contrast to the other groups in 80 years slight increase of lipid peroxidations processes in comparison with group of 70 years, except for malonic dialdehyde was observed. When the cataract was developing in the changes of the free-radical oxidation had differences: at initial changes in lens there was a sharp intensification of free-radical activity and then the level of lipid peroxidation was on the high level. The polyunsaturated fatty acids and the palmitic acid had max percent of content in lens, the min – lauric and linolenic. The content of saturated and polyunsaturated fatty acids was approximately identical. When cataract was developing the composition of the higher fatty acids was changing considerably: the content of palmitic acid was increasing, the correlation factor was 0.52(R<0.05); the content of linoleic acid was decreasing, the correlation factor was -0.6(R<0,05)

Conclusion The differences between the lipid peroxidation in the aging and the lipid peroxidation in cataractogenesis were revealed

• S114
Age-related oxidation of lipids and proteins in rats' crystalline lens

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Purpose estimation and comparison of age-related intensity of oxidation of lipids and proteins of rats' crystalline lens

Methods Experiments are carried out on 25 Wistar line rats males of four age groups: 5 (n=6), 12 (n=7), 24 (n=6) and 36 (n=6) of months. Homogenate of crystalline lens tissue was used. The level of the general lipids, the contents of diene and triene conjugates, level of the Schiff bases and TBA-test were estimated. The received results were rated to amount of lipids and expressed in relative units. Extent of oxidizing proteins modification, the content of the general protein was defined. The level of oxidizing proteins modification was rated to amount of proteins. Potential possibility of oxidation was estimated by method of the induced chemiluminescence with use of Fenton's reaction

Results In adult animals' crystalline lenses (12 months) the raised level of products of lipids oxidation was observed. Then, the level of trienic conjugates were decreasing in the interval of 12-24 months. The comparative content of carbonyl derivative of proteins had tendency to decrease with age. At groups of age 12, 24 and 36 months in comparison with group of 5 months were determined the decrease of the hemiluminescence level. It corresponds to decrease of level of the medium for free radical oxidation

Conclusion On the basis of results, we can assume that, together with the intermolecular interaction of proteins with each other and with low-molecular metabolites, the free-radical processes of lipids proceeding on membranes, also contributes to formation of age-related changes of lens in rats

• S115
Effect of Crocus sativus stigmas (saffron) extract on sodium selenite induced cataract formation

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Purpose To study the effect of Crocus sativus (CS) stigmas (saffron) extract on sodium selenite induced cataract formation in vivo.

Methods Twenty-four Wistar rat pups were randomized into 3 groups (n=8/group). Control group received subcutaneous injection of normal saline on postnatal day 10. Selenite and CS treated group received a subcutaneous injection of sodium selenite (20 µmol/kg body weight) on postnatal day 10. CS group also received intraperitoneal injections of CS extract (60 mg/kg body weight) on postnatal days 11 and 12. On postpartum day 21, rats were sacrificed and the lenses were isolated and examined for cataract formation. Activities of superoxide dismutase (SOD) and catalase (CAT) and levels of reduced glutathione (GSH) and glutathione disulfide (GSSG) in the isolated lenses were measured. SDS-PAGE of lens water soluble protein fraction (WSF) was done.

Results Selenite resulted in significant cataract formation compared to control group, p<0.001. In the CS group, cataract formation was significantly prevented compared to selenite group, p< 0.0001. The mean activities of SOD and CAT were significantly increased in the CS group compared to the selenite group (p=0.025 and 0.0009 respectively). The GSSG/GSH ratio was significantly decreased in the CS group compared to selenite group (p=0.001). CS prevented selenite induced proteolysis of the lens WSF.

Conclusion CS extracts prevented selenite induced cataract formation in Wistar rats possibly by enhancement of antioxidant status and inhibition of proteolysis of the lens WSF.

• S116
Gaps between lens epithelial cells due to contractions

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Purpose The purpose of the study was to characterize the contractions of human anterior lens capsule epithelial cells that create gaps between cells, and to assess the physiological mechanisms and a possible association of the contractions with cataract formation.

Methods Lens capsules obtained during cataract surgery were stained with fluorescent dye Fura-2. Its fluorescence, upon excitation at 360 and 380 nm, was imaged to monitor changes in cell morphology and cytosolic free Ca2+ concentrations ([Ca2+]i) in response to pharmacological stimulation by acetylcholine and to mechanical stimulation. Contractions were also studied by scanning electron microscope.

Results Epithelial cells contracted in about a third of preparations after stimulation. Contractions started either before or at best simultaneously with the rise in [Ca2+]i. They also occurred when there was hardly any change in [Ca2+]i upon application of physiological saline alone. The probability of contractions occurring did not differ significantly among cortical, nuclear and combined cortical+nuclear cataract.

Conclusion The contractions of the anterior lens epithelial cells occur in significant part of human lens anterior capsule postoperative preparations. They can be mechanically induced, are localized and reversible, have a fast response and did not differ among different types of cataract. They are at least partly independent of changes in [Ca2+]i. This mechanism could represent physiological basis of cataract formation in phakic intraocular lenses that touch the crystalline lens.

• S117

FYCO1 mutation hotspot in congenital cataract

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Purpose To report on the molecular origin of congenital cataract in an Egyptian family.

Methods We performed a genome-wide SNPs array analysis in a consanguineous family of Egyptian origin with two affected and one unaffected children with congenital cataract. Systemic and ophthalmic examinations were performed.

Results The two affected patients, a 3 month old boy and a 7 year old girl with cataract and nystagmus were studied. Lensectomy was performed on both patients with IOL implantation in the older patient. A homozygous region of 12Mb on chromosome 3 was identified. This region contained the previously reported FYCO1 gene. Molecular analysis revealed a homozygous c.2206C>T mutation (p.Gln736X) in the affected patients. SNP analysis around the gene indicated that the mutation arose on a different genetic background than that reported by Chen et al. (AJHG 2011).

Conclusion Mutations in FYCO1 are also present in the Egyptian population. We have shown that it developed de novo in this family thus indicating that this nucleotide is a hotspot for mutation and does not represent a founder effect.

• S118

Sunflower cataract in Wilson's disease : transmission electron microscopic study

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Purpose To report ultramicrostructures of anterior capsule of sunflower cataract by the transmission electron microscopic study (TEM)

Methods A 37-year-old male with liver cirrhosis was referred to department of ophthalmology due to visual disturbance. She has bilateral sunflower cataract & Kayer-Fleischer ring.Her right eye underwent phacoemulsification with a CCC and intraocular lens implantation. 1. Anterior capsule preparation for transmission electron microscopic examination(TEM)2. Cross section image by energy filtered TEM 3. Elemental analysis : High-angle annular dark-field(HAADF) scanning TEM (STEM) with energy-dispersive x-ray analysis (EDAX)

Results TEM shows the multiple heterogeneous dense deposits in the anterior lens capsule.HAADF-STEM shows bright particle deposits. EDAX shows high emission peaks for copper.

Conclusion This is first report of TEM study for anterior capsule of sunflower cataract. We found the multiple heterogeneous dense deposits in the anterior lens capsule. And we confirmed that copper was a component of these particles using EDAX.

• S119

Corneal changes after a 3 incision cataract surgery by 2.2mm

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Purpose a prospective study to analyze the effects of the miniincision coaxial phacoemulsification (2.2 mm) combined with bimanual irrigation/aspiration (I/A) on the corneal optical quality characterized in terms of corneal aberrations.

Methods One hundred and eith eyes underwent mini-incision phacoemulsification, by the same surgeon. Cataract surgery was performed through a clear corneal incision of 2.2mm, placed at 130°. Two paracentesis of 1mm were performed 90° apart for bimanual irrigation/aspiration. An aberrometry (OPD scannII, Nidek®, Japan) was performed preoperatively (Day 0), 15 days after surgery (Day 15) then 1 month after (M1).

Results The corneal surgical induced astigmatism (SIA) was quite neutral : 0.091 D +/-0.428 at Day 15, and 0.065 D +/-0.86 at Day 30. Between Day 15 and D30, its variation was not significant - 0.026 D +/-0.871 (p=0.74). At 1 month: we observed a mean reduction of - 0,25D +/- 0.96 in the direct astigmatism group (n=46), and a mean induced astigmatism of + 0.23D +/- 0.94 in the inverse astigmatism group (n=37), of + 0.21D +/- 0.6 in the oblique stigmatism group (n=25).Corneal topographic astigmatism is modified in the axis : mean rotation was 29.95° +/- 27.6 between Day 0 and 30. Congenital astigmatism superior to 1,5D appears to be more stable. Corneal asphericity didn't change statistically between Day 0 and 30 (1.14 D +/- 0.5 versus 1.11 D +/- 0.49 p=0,13).

Conclusion This 3 incision procedure permits a real neutral power SIA through a 2.2 mm main incision, compared to classical coaxial procedure.The stability of refractive data between Day 15 and M1 allows early spectacles prescription and a quick return to normal life. SIA rotation could explain some undercorrections after toric IOL.

• S120

Safer posterior capsule polishing using the silicone sleeve from I/A cannula

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Purpose Removing last particles of nuclear cortex from central posterior capsule is sometimes difficult. Diamond blasted cannulas or silicone tipped needles are provided as extra material. We describe a new costless technique for capsular polish using the silicone sleeve of the Irrigation/Aspiration (I/A) cannula. It is also possible to do safer polish-aspiration of cortical masses.

Methods We used Bausch & Lomb® single use I/A cannula 85910ST with metallic tip recovered by a silicone sleeve. After standard I/A procedure, we push a little the sleeve ahead from the rigid plastic part of I/A cannula, just to put the sleeve a little ahead the metal cannula and recovering it. Then, we can scrap posterior capsule safely, by direct contact of the end of the silicone sleeve, with irrigation and none or small aspiration. For some adhesives greater parts of cortex, we place a lateral hole of the silicone sleeve just in front of aspiration hole in the metallic cannula. Then we can smoothly and safely scrap the capsula adhesive cortex and just after, when a part of cortex is free, aspire it with strong vacuum.

Results We use this method for years with different types of phacoemulsification devices. It gives a very clean scraping of posterior caspsule with great safety. As far as we can know, we never find a description of similar technique in any publication.

Conclusion This new use of silicon sleeve is very effective and free of additional costs. Compared to specific capsule polisher cannulas, this technique offers possibility to scrap capsule and do I/A in the same time. Compared to classic polishing with metallic extremity of I/A cannula, It seems more safe to do it with a soft, non traumatic silicone sleeve.

• S121
Bilateral phacoemulsification in the day: a wise decision?

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Purpose Bilateral cataract surgery is not part of the regular practice of all centers.It´s indicated only for those cases in which the patient's general condition is very poor

Methods We conducted a retrospective study of 106 patients in which visual acuity was assessed before and after surgery, complications, pre, intra and postoperative, the reason for simultaneous intervention, as well as the rate of total bilateral phacoemulsification interventions between 2007-2011

Results The best corrected visual acuity was 0.4 preoperatively half while mean postoperative visual acuity was 0.8. The rate of simultaneous bilateral phacoemulsification in that period was 0.83%.

Conclusion Our results show that simultaneous bilateral surgery is a safe and economical way to quickly rehabilitate certain patients with bilateral cataract.

• S122
Cataract surgery rationing in an age of austerity – Is a UK district general hospital compliant with regional cataract booking guidelines?

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Purpose The rate of cataract surgery in Outer North East London (ONEL) is significantly higher than the standardised admission rate (SAR) for England. Financial pressures have forced cost savings by restricting cataract operations, aiming for 22% reduction through new clinical acceptance criteria for the region since April 2011.This involves:
1. Best corrected distance visual acuity 6/10 or worse in the better eye
AND
Impaired lifestyle due to cataract:
OR
2. Severe glare, diplopia or anisometropia >/= 1.5 D Exceptions include:
• Significant posterior subcapsular lens opacity despite good vision
• If surgery is needed to help co-manage conditions such as glaucoma or for the view of the retina in patients with diabetic retinopathy

Methods Retrospective audit of cataract surgery from Aug 2010 - Dec 2011.Medisoft electronic database query identified patients with VA > 6/9 for case-note review to ascertain reasons for (non/)compliance with cataract booking criteria.

Results 1084 cataract operations were performed. Median age was 73.5 years.n=34 eyes with pre-op VA 6/9 or better; pre-April 2011 (9 cases) vs post-April 2011 (25 cases). Case-note review revealed:
• Glare (8) / Anisometropia (3): 11
• Posterior Subcapsular cataract: 4
• Co-management of other pathology: 23
Glaucoma (15), Diabetic Retinopathy (7), ARMD (1)
• Not valid: 2

Conclusion Rationing must be balanced with individual clinical needs. 99.8% of cataract operations met the new restricted criteria. This sample is an underestimate as not all cataract operations are registered on the Medisoft database.A re-audit in 6-8 months would establish compliance and feasibility as policies are tightened.

• S123
Clinical outcomes following cataract surgery in patients over 90 years old

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Purpose The aim of our study was retrospectively evaluate the effect and safety of cataract surgery and intraocular lens implantation (IOL) for patients aged 90 years or older.

Methods In the study we involved a total of 122 patients (122 eyes) with senile cataract between the ages of 90 and 100 (mean age 91,22±2,28 years and the gender distribution was 79 females and 43 males). 113 of 122 eyes had phacoemulsification (Phaco) and 9 of 122 eyes had extracapsular extraction (ECCE). Postoperative visual acuity and intraocular pressure (IOP) were observed and analysed on the first day, three months, and six months after surgery. In analysed group there were 26 of 122 patients (21,31%) with glaucoma and 54 of 122 patients (44,26%) with degeneration of the central retina.

Results The best uncorrected preoperative visual acuity was ≤ 0,1 in 94 of 122 eyes (77,05%), between 0,2-0,4 in 24 of 122 eyes (19,67%) and between 0,5-0,7 in 4 of 122 eyes (3,28%). Visual acuity improved in 102 of 122 eyes (84%) and remained the same in 20 of 122 eyes (16,39%). In our investigations we have also found statistically significant implications of cataract surgery on decreasing IOP (intraocular pressure) in the studied group of patients suffering from glaucoma, which were not found in patients without glaucoma. The most important cause of visual impairment after cataract surgery was AMD in the studied group. The central degeneration of retina was found in 54 of 122 patients (44,26%).

Conclusion We concluded that advanced age isn't a contraindication for cataract removal and we have found that cataract surgery with IOL implantation is an effective procedure in aged patients.

• S124
Improving effective lens position : comparison of femtosecond laser vs manual capsulotomy

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Purpose Every IOL formula has its limits in estimating Effective lens position (ELP). The main one is the variability in capsulotomy size and centration. Our purpose was to compare the variability and predictability in ELP based on capsulotomy created by a femtosecond laser with those using manual continual curvilinear capsulorhexis.

Methods 32 eyes from 24 patients undergoing cataract surgery had either femtosecond created 5.2 mm capsulotomy (VICTUS™ Femtosecond Laser Platform - Technolas Perfect vision) (n=16) or manual continuous curvilinear capsulorhexis performed with an attempted diameter of 5.2 mm (n=16). One surgeon performed all the surgeries during a period of one month in April 2012, at Percy military hospital, Clamart. Three type of monofocal IOL were implanted in the bag. At one month after surgery, ELP was measured by Pentacam HR and compared to preoperative estimated lens position. Accuracy to target refraction was also calculated, being the difference between target refraction with Iolmaster v5 (Haigis, SRK/T and Holladay formula) and postoperative objective refraction

Results Precision of IOL position was improved, as shown by statistically significant reduced variability of ELP (0,27 vs 0,45, p=0,03) in the laser group at one month. Better accuracy to target refraction using SRK/T formula (0,16 vs 0,5, p=0.02) and Holladay formula (0,26 vs 0,50, p=0,02) was also observed in the laser-treated eyes compared to the manual group.

Conclusion Femtosecond laser system provides a perfectly round, well-centered, and precise diameter capsulotomy. In this study, this translated to more accurate and predictable ELP and IOL power calculation in femtosecond laser group compared to manual group.

• S125

Manual rhexis vs femtosecond laser assisted rhexis in cataract surgery

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Purpose To evaluate the reproducibility and safety of capsulorhexis femtosecond laser assisted.

Methods Admitted patients for cataract surgery have been received into the "PERCY Military Hospital" refractive surgery unity.We have treated 11 eyes of 11 patients, on the Victus femtosecond laser platform.A control group (11 eyes of 11 patients) has been operated manually in the same center.The rhexis diameter measurement has been realized at one week postoperative,to the angiograph,as iris angiography,using the HRA OCT Spectralis.On the pictures,we measured the vertical diameter and the horizontal diameter.For the rhexis centration,three circles were drawn following the contour of the rhexis, the pupillary border,and the margin of limbus.We measured the position of rhexis center to pupillary center.

Results In the laser assisted group,the mean horizontal rhexis diameter was 5.35 mm +/- 0.22,and the mean vertical rhexis diameter was 5.37 mm +/- 0.22. In the control group,the mean horizontal and vertical rhexis diameters were respectively 5.3 +/- 0.28,and 5.6 +/- 0.21.We found that 85% of femtosecond laser assisted rhexis were within 0.35 mm from the programmed diameter. In the control group,only 15% have obtained the same level of accuracy.In the laser group,the three circles have the same center,and then are concentric,tell-tale of a rhexis good centration,unlike the manual rhexis.The femtosecond laser rhexis was circular,regular and covers the IOL's periphery including the haptics.

Conclusion The femtosecond laser has multiple benefits for cataract surgery, as the regular and circular capsule, the reduced variability in the effective lens position. The technique is reproducible and very safe.

• S126

Characteristics of the corneal endothelium and pseudoexfoliation syndrome in patients with senile cataract

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Purpose To describe the characteristics of the corneal endothelium in patients with and without pseudoexfoliation syndrome (PEX) over 60 years of age with senile cataract.

Methods A prospective age-matched controlled clinical study was performed on 53 patients (male = 15, female = 38) (53 eyes) with senile cataract from the period January 2012 – May 2012. Endothelial cell density (ECD), mean coefficient of variation in cell size (CV) and mean cell hexagonality were measured using automated specular microscopy. Patients were divided into two groups. 28 patients with PEX (mean age 77.1 years [range 61 - 87] and control group – 25 patients without clinical signs of PEX (mean age 76.8 years [range 62 - 86]. SPSS 21 statistical package was used for statistical analysis.

Results In the group of patients with PEX ECD was 2228.57 cells/mm2 [range 1443 – 2757] (± 290.01), hexagonal cells – 62.18 % [range 47-75] (± 7.08 %), CV - 31,04 [range 22-47] ± 5,24. In the control group ECD was 2500.96 cells/mm2 [range 2012 – 3243] (± 351.77), hexagonal cells – 59.64 % [range 45-70] (± 5.92 %), CV - 31,92 [range 25-39] ± 4,26. The mean difference between two groups with and without PEX for ECD was found to be significant (2228,57 vs 2500,96 cells/mm2, p = 0.003). There was no statistically significant difference between these two groups comparing hexagonality (62,18% vs 59,64%, p = 0,166) and CV (31,04 vs 31,92, p = 0,507).

Conclusion The endothelial cell density is significantly lower in patients with pseudoexfoliation syndrome. PEX had no impact to hexagonality and coefficient of variation in cell size.

• S127

Long-term endothelial cell loss after iris-fixated phakic intraocular lens for high ametropia

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Purpose The aim of the study is to report and to predict long-term endothelial cell outcomes after iris fixated phakic intraocular lens implantation for the correction of high refractive errors.

Methods Retrospective, non randomized study of patient who underwent surgery between January,2000 and December,2009 in the same department in the Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts. To predict long-term endothelial cell density, 2 joint regression models were fitted on ECD to individuals with at least 2 ECD measurement in time.Model-predicted parameters for endothelial cell density and survival were obtained for each patient and were used in a Kaplan-Meier method plot for predicted percentage of eyes .

Results This study consisted of 78 phakic eyes including 70 myopic eyes and 8 hyperopic eyes. 73 Verisyse/Artisan and 5 foldable Artiflex were implanted. Three eyes underwent further keratorefractive surgery (Bioptic). Two eyes were lost of follow-up. The mean follow-up was 68 months.Recent studies reported an endothelial cell loss 5 years after surgery ranged from -9 to -14%, but we found a decrease of 25% for 18 eyes. Surgery trauma is partially involved but we also found a higher endothelial cell loss one year after surgery (range from -3.5 to -9%).

Conclusion Potential complications such as progressive endothelial cell loss and risk of dislocation are major concerns in operative decision. Close follow-up with regular monitoring is necessary in patients with phakic intraocular lens.

• S128

Intraocular lens power adjustment calculator after myopic LASIK/PRK

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Purpose To develop a nomogram application for allowing simple and efficient intraocular (IOL) power calculations at the time of cataract surgery in postmyopic LASIK and PRK eyes.Keratorefractive surgery has become the most extended technique for correcting preexisting refraction defects in the last 10 years. It is anticipated that the incidence of cataract in these patients will increase over time. Technically, cataract surgery in patients with prior refractive corneal surgery has shown to be as successful as in virgin eyes. However, difficulties have been found in applying the standard methods for determining the power of the IOL in eyes that have had refractive corneal surgery. Therefore, we propose a computerized-nomogram calculator to facilitate IOL power prediction using pre-operative data if available or only postsurgical biometric measurements.

Methods After literature review, the 6 most accurate IOL power calculation formulae for myopic LASIK/PRK patients were selected: Double-K (SRKT), Feiz-Mannis, Latkany Flat-K, Modified Masket, Haigis-L formulate and Shammas. DrPhyton 3.11.3 in Linux Fedora 14 environment was used as programming language for developing an informatics application nomogram.

Results Our application provides an intuitive and straightforward computer program to achieve a simple solution for a difficult problem.

Conclusion A computerized IOL calculator is an efficient way to facilitate the selection of IOL power in patients that have had prior refractive surgery.

• S129

Visual acuity and contrast sensitivity function between spheric and aspheric intraocular lenses implanted in the same patient. A pilot study

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Purpose To analyze differences in best corrected visual acuity (BCVA) and contrast sensitivity function (CSF) between spheric (sIOL) and aspheric (aIOL) intraocular lenses with the same subjective patient criteria

Methods We evaluated 10 patients with bilateral cataract that were implanted in one eye a sn60wf aIOL, and a sn60at sIOL (Alcon, USA) in the other eye. Patients were evaluated at 3 months after surgery. We measured BCVA with an EDTRS chart, CSF with a CSV-1000 test and pupil diameter in photopic/mesopic conditions

Results We compared the differences of BCVA and photopic CSF between both eyes from the same patient, in order to ensure the same subjective response in both lenses. We used for the analysis a Mann-Whitney test with paired samples.Mean IOL power of sIOL was 23.1+3D and for aIOL was 22.9+3D,without differences (p=0.4).Mean pupil diameter was 3.1+0.6mm in photopic and 4.0+0.7mm in mesopic conditions. BCVA in sIOL was 0.02+0.03 logMAR units, and 0.01+0.02 logMAR for aIOL, without differences (p=0.13).The sIOL CSF was better than the aIOL, but we didn't found significant differences at any spatial frequency (p=0.61 for 3cpd, p=0.65 for 6cpd, p=0.27 for 12cpd and p=0.82 for 18cpd).

Conclusion VA and CSF are subjective measures to assess visual quality, because depending on the patient's subjective criteria, the responses of 2 subjects with similar optical quality may differ. We eliminate this drawback when the patient is implanted with both lenses.When we used VA and CSF to evaluate visual quality of patients,we didn't found a great improvement of aIOL. According literature, differences are significant at 6mm pupil diameter.

• S130

Customized intraocular lenses enhance binocular depth-of-focus and optimize stereoscopic vision

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Purpose The purpose of this study was to evaluate mono and binocular near vision and depth-of-focus using two different aspheric monofocal intraocular lenses (IOL) profiles after micro-incision cataract surgery.

Methods Forty eyes (20 patients) were included. The reference group (28 eyes, 14 patients) received a -0.18 µm spherical aberration (SA) aspheric IOL in each eye (Acrismart 36A®, Carl Zeiss Meditec) whereas the aspheric-customized group (12 eyes, 6 patients) received on the dominant eye an AcriSmart 36A® and on the other eye a zero-aspheric IOL (Acrismart 46 LC®, Carl Zeiss Meditec). Inclusion criteria were a 0,15-0,3 µm preoperative corneal SA and a monocular postoperative visual acuity (VA) ≥ 20/20.Reported visual outcomes were best corrected mono and binocular distance Snellen VA and uncorrected mono and binocular near VA. A binocular defocus curve was performed from +0.0 to - 4.0 Diopters (D) by -0.25D step. A corneal and total higher-order aberrations (KR1®, Topcon) evaluation was assessed. Stereoscopic vision was performed using TNO stereo test.

Results Residual postoperative spherical equivalent and best corrected distance VA was not different between the two groups (respectively p = 0,11 and p = 0,82). However, the customized group had a better near and intermediate VA during the defocus curve, for example 20/80 versus 20/125 with -4.0D of defocus ($p < 0.05$). Customized group did not have penalized stereoscopic vision while comparing frequency of patients with TNO stereo test ≥ 120 seconds.

Conclusion Differences in pseudophakic aspherical profiles of IOL in cataract surgery seemed to increase clinical depth-of-focus and near ability, without any disturbed distance vision or penalized stereoscopic outcomes.

• S131

Extraction of lens geometry in an optomechanical eye model during accommodation using automatic image processing

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Purpose To extract curvature, lens thickness and optical performance of accommodative intraocular lenses (AIOL) in an optomechanical eye model.

Methods Freshly enucleated porcine eyes with an implanted AIOL and removed cornea were placed in a cuvette with BSS (35°C) simulating physiological conditions. The ciliary body was expanded radially symmetric to stretch or release the zonula fibers effectuating pseudophakic accommodation. Dynamic accommodation and imaging quality was measured with a Shack-Hartmann-Sensor (SHS). Shape and relative lens position during accommodation was measured with an optical coherence tomograph (OCT).The 3D OCT image was processed with denoising and edge detection extracting the AIOL surface. Remaining haptic data were eliminated. Images were corrected by inverse ray-tracing for compensation of the OCT's beam divergence and refractive effects of optical surfaces. Finally the AIOL geometry was derived by a spherical fit and the center thickness was determined.

Results The algorithm allows to extract edge data from noisy OCT images and up-to-scale geometrical data. Curvature was derived from a fit of the edge points and relative lens position, lens thickness as well as optical power for the optomechanical eye model were measured at different states of accommodation. Optics with a diameter up to 6 mm could be measured with a lateral/depth resolution of 20/5 µm. The results yield complimentary data to the image quality measured with the SHS.

Conclusion The algorithms are elementary tools for the setup of the optomechanical eye model for AIOL. It is now possible to evaluate different AIOL in an experimental setup as a base for development of next generation AIOL.

• S132

Single IOL surface measurements with UV-Shack-Hartmann-Sensors

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Purpose Measuring single IOL surface topographies remains a difficult task due to reflexes from the second surface. Currently no commercially system is available for this task. The purpose of this study is to discuss the feasibility of a new and customized UV-SHS (Shack-Hartmann-Sensor) method in the field of measuring individual IOL surfaces.

Methods The WaveMaster system (Trioptics, Wedel) represents the SHS technique. It is customized to work in the UV range of light spectrum and eliminates the possibility of back surface reflections. Repeatability and reproducibility measurements are performed before measuring spherical and freeform IOLs of different radii of curvature (ROC) between 6 mm and 20 mm. For validation of the measurement system 2 criteria are applied: The correct measurement of a sample's ROC and the RMS of the residual (the topography after subtracting the best-fitted-sphere).

Results The repeatability and reproducibility measurements provide acceptable figures; a measurement of a sample's ROC takes about 5 seconds and delivers accurate results. The maximum deviation from the theoretical design ROC is about 100 µm while many results show a deviation of some µm. The results for spherical IOLs prove that the device can be applied over the whole range of ROCs. The residuals show an RMS deviation of some µm for spherical surfaces and correspondingly higher values for freeform surfaces.

Conclusion The UV-WaveMaster system is an appropriate device for measuring individual IOL surfaces for a wide range of ROCs making it applicable for quality control for freeform IOL surfaces. The acquisition of the sample's topography and ROC with its residual is fast and. Future application of the device will show its advantages and limitations in detail.

• S133

Moxifloxacin superior to cefuroxime in reducing early-phase adherence of staphylococcus epidermidis to hydrophobic intraocular lenses

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Purpose To evaluate the bacterial anti-adhesive effect of cefuroxime and moxifloxacin on the primary-attachment phase of S.epidermidis to acrylic intraocular lenses IOLs

Methods 40 single-piece SA30AT IOLs were used throughout the study. IOLs were divided into 5 groups. 2 groups were soaked in antibiotic solution,(moxifloxacin 0.5mg/0.1ml or cefuroxime 1mg/0.1ml),15 min before incubation in a S.epidermidis suspension 108 CFU/ml,t1.2 groups were incubated in the bacterial suspension for 15 min before being added with antibiotics,t2.The last group consisted in a control group. After 1 hour incubation at 37°C, for all groups, IOLs were removed from the test vial and rinsed before being sonicated and vortexed to remove the adhering bacteria. The resultant suspension was diluted and spread over a nutritive agar plate. Colonies were counted after 24-hour incubation. Comparison among groups was performed using the Wald parametric statistical test. A p-value <0.05 was considered statistically significant.

Results Mean numbers of CFU/IOL was Cef-t1:184.103[SE: 5,24 ; SD: 28,21],Cef-t2:117.103[SE: 5,74 ; SD: 30,37], Mox-t1:1,27.103[SE: 0,12 ; SD: 0,61], Mox-t2:25.103[SE:1,98 ; SD: 9,72] and Ctrl:361.103[SE: 26,9 ; SD: 107,6].There was no significant difference in antibiotic time introduction concerning cefuroxime (p=0.132). Moxifloxacin was more effective when used before incubation (p<0.001). Overall, moxifloxacin was more effective than cefuroxime (p<0,001).

Conclusion Both moxifloxacin and cefuroxime significantly reduced S.epidermidis adherence on IOLs.The anti-adhesive effect was superior with moxifloxacine. Further studies are needed to confirm results on IOLs made of other biomaterials.

• S134

Tele-ophthalmology research in post-phacoemulsification diagnostic outcomes (TORPEDO) study – preliminary results

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Purpose To evaluate the accuracy of tele-medicine in detecting post-phacoemulsification outcomes and complications at the one-month post-operative visit, as compared to a face-to-face clinical consultation.

Methods A prospective study of 30 patients who underwent uneventful phacoemulsification surgery was conducted. At the one-month post-operative visit, patients underwent a novel tele-medicine work-flow which included visual acuity testing, refraction, intraocular pressure measurement, and slit-lamp and fundus photography. Images were read by a masked investigator and the findings compared against those of a face-to-face clinical examination, performed at the same visit.

Results On clinical examination, corneal and wound-related complications occurred in 2 patients, anterior chamber inflammation of occasional to 1+ cells was noted in 4 patients and posterior capsular opacification in 1 patient. When compared against the clinical examination findings, tele-medicine detected corneal and wound-related complications with a sensitivity and specificity of 100%; anterior chamber inflammation with a sensitivity of 75% and specificity of 92.3% and the presence of posterior capsular opacification with a sensitivity of 100% and specificity of 96.6%.

Conclusion Preliminary results suggest that tele-medicine detects post-phacoemulsification outcomes and complications with a high level of sensitivity and specificity. It best detects corneal and intraocular lens-related complications; with a lower sensitivity and specificity in detecting anterior chamber inflammation.

• S135

Comparative analysis of changes in the macular region following cataract surgery by phacoemulsification with Ozil Intelligent Phaco technology according to different fluidics parameters

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Purpose To assess the change in macular thickness values following cataract surgery by phacoemulsification with Ozil Intelligent Phaco (IP) technology comparing high and low fluidics parameters

Methods A randomized, prospective, comparative trial, including 40 eyes with age-related cataracts and nuclear opalescence below 4 in the The Lens Opacities Classification System III (LOCS III). Half of the eyes were assigned to phacoemulsification with low fluidics (300mmHg vacuum and 20cc/min maximum aspiration flow), and the other half to high fluidics (500mmHg vacuum and 40cc/min maximum aspiration flow). Data were collected from the thickness map of the macular region by optical coherence tomography (OCT) prior to surgery as well as successive visits in the first postoperative month

Results All the sectors of the macular thickness in OCT were compared based on fluidics groups. No statistically significant differences in none of the 9 sectors in the macular region at both preoperative and first postoperative month were found. There was a slight increase in overall macular thickness after cataract surgery in both study groups, with no significant differences between both. However, this increase was not clinically significant

Conclusion Modifying fluidics parameters in phacoemulsification surgery with Ozil IP technology does not change the damage parameters into the macular region due to surgical trauma within the first 30 postoperative days

• S136

Intraocular scattering, a useful tool for the indication of capsulotomy?

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Purpose To evaluate the correlation between the subjective visual parameters and the objective optical quality parameters, before and after the laser YAG-Neodymium treatment in patients with posterior capsular opacification (PCO).

Methods Prospective study in 30 eyes (30 patients) referred to our service for capsulotomy, without remarkable ocular story except a non complicated phacoemulsification with intraocular implant. We quantify visual acuity (VA), contrast sensitivity (CS) and objective parameters of vision quality measured with a double pass system (Optical Quality Analysis System,

Results 78.5 ± 5.4 years was the average age of our patients, the 65.4% were women. Visual acuity values, intraocular scattering index (OSI) and Strehl ratio before the treatment were respectively: 0.4 ± 0.2; 5.84 ± 3.43; 8.89 ± 7.32; 0.06 ± 0.04. We found a moderate, inverse and statistically significant correlation between OSI values and VA before the treatment: -0.564 (p value= 0.003). And also a strong and inverse correlation between OSI values and CS values at 1.5, 3, 6 y 12 cycles per degree (cpd): -0.665 (p value < 0.001); -0.733 (p value < 0.001); -0.725 (p value < 0.001) y -0.785 (p value < 0.001) respectively.After capsulotomy, all the parameters, subjective and objective, improved significantly, except the CS at 18 cpd. However, we did not find any significant correlation between OSI and the subjective parameters after treatment.

Conclusion Tthe determination of OSI values is a useful tool to establish the indication of treatment in patients with suspicion of clinical PCO. Once eliminated the main limiting factor of visual quality, PCO, the absence of correlation indicates the influence of other limiting factors in visual quality.

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Clear lens extraction in high myopic

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Purpose To evaluate the visual results and complications in high myopic patients who underwent clear lens extraction by phacoemulsification with intraocular lens implantation.

Methods We performed a retrospective, observational and descriptive study in 61 eyes of 40 patients from HCU Lozano Blesa from Zaragoza collected between January 2002 and January 2012. We evaluated preoperative and postoperative visual acuity, visual satisfaction and early and late complications.

Results The mean age at intervention was 51,3 years. The mean visual acuity at 3 months postoperatively was 0,8. 30% of the patients needed yag capsuloyomy during the first postoperative year. 2 patients had a retinal detachment.

Conclusion The clear lens extraction in high myopia may be a reasonable option if alternative procedures are not feasible.

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