EVER
European Association for Vision and Eye Research
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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 toxoplastic 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 microphthalmia 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

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**Alta Eficacia Tecnologia SL, Spain, travel grant**

Alta Eficacia Tecnologia 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

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**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
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.
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.
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.
The changing roles of perimetry and perimeters in glaucoma management

HEIJL A
Lund University, Department of Ophthalmology (Malmö)
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.
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• 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 autoimmune and activation of immunity will be discussed. In addition the talk will highlight the pathways and mechanisms of tissue damage that result 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 rewire immune balance, tolerance and local homoeostasis within ocular tissues

• 1512
Classification of uveitis

ANDRONIDIS
Ismail

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 choiroid). 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. 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 L, CAPLIANO V, PIRANI V
The Eye Clinic, Polytechnic University of Marche, Ancona

Purpose
To review the symptoms and signs of anterior uveitis (AU), based on the anatomical 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 antigens and spondylarthropathies. 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. Endothelitis, high intraocular pressure, and patchy/sectoral iris atrophy are also present. Chronic flare, Koeppie and Rosacea nodules of the iris, medium-size KPs or large mutton fat KPs, peripheral anterior synchiae and broad-based posterior synechiae represent hallmarks of granulomatous anterior uveitis which tends to chronicity. Juvenile Idiopathic 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, KAHLIOLIN R
Ophthalmology, Monastir

Purpose
Posterior uveitis (PU) is an important anatomic form of uveitis in which the primary site of inflammation 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 flare 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 diffuse, involving the periphery or posterior pole. It is important to distinguish between active and inactive choroidal disease. Retinal vasculitis can occur in the setting of several PU entities involving retinal veins or arteries. It appears as focal, multifocal, or diffuse vascular clogging 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-ladder 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) 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 ischaemia, 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, Charité – 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 microscopic/cellular level. Conventional morphology (histology) requires a respective preparation that consists of tissue fixation to stop natural post mortem 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 methodological requirements, considerations and results

KNOP E, KNOP N
Ocular Surface Center Berlin, Dept. for Cell- and Neurobiology, Charité – 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
Immunoelectron 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 immunoelectron microscopy (immuno-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, keratosephalin have been demonstrated by the immuno-EM procedure. A number of cellular proteins such as keratosephalin 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
Herpetic eye disease

VASSILEVA P
SORAL “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 65 patients (77%) 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.

Treatment: medical therapy

HERGELDZHIEVA T, P
(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 debridement 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 herpes simplex virus epithelial keratitis, trifluridine and acyclovir are more effective than idoxuridine or vidarabine. The effectiveness of corneal epithelial debridement is improved by an antiviral agent. For HSV stromal keratitis, topical corticosteroids in addition to a topical antiviral agent are effective as acyclovir.

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

Treatment: surgical methods

DEKARIS I, RAKTOVIC M, PAUK M, DRACA N
University Eye Hospital Svetlost, Zagreb

Purpose: Herpetic keratitis may lead to a significant corneal scarring 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.
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<th>Course 4: Common corneal procedures</th>
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| **1541**  
Limbal stem cell transplantation techniques  
_DUA H_  
Nottingham  
ABSTRACT NOT PROVIDED |
| **1542**  
Modern pterygium surgery  
_GICQUEL JJ_  
Poitiers  
Pterygium is the most common surgically managed ocular surface disorder. The primary goals are to prevent recurrences in advanced cases and get a proper aesthetic result in younger patients with less symptomatic cases. There 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 conjunctivo-limbal autograft (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  
_MENCUCCHI R_  
Florence  
ABSTRACT NOT PROVIDED |
Indications and limitations of amniotic membrane transplantation

YEUNGA
Nottingham

ABSTRACT NOT PROVIDED
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 may be discussed for their role in the prevention of PVR.

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

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.

How to localise retinal tears?

KOROBELNIK JF
Bordeaux

ABSTRACT NOT PROVIDED

To analyse the role of vitreous in a retinal detachment

BERROD JP
Nancy

ABSTRACT NOT PROVIDED

How to localise retinal tears?

KOROBELNIK JF
Bordeaux

ABSTRACT NOT PROVIDED

To analyse the role of vitreous in a retinal detachment

BERROD JP
Nancy

ABSTRACT NOT PROVIDED

To analyse the role of vitreous in a retinal detachment

BERROD JP
Nancy

ABSTRACT NOT PROVIDED
• 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.


**Course 6: Eyelid tumours**

**• 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.
### Course 7: EBO course: Intraocular Inflammation and Infection (Part II)

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<td><strong>B27-associated uveitis</strong></td>
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<td>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.</td>
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**Course 7: EBO course: Intraocular Inflammation and Infection (Part II)**
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 the management of different pediatric uveitis entities. Methods
**Course 8: Experimental models for eye research**

### 1621
**Experimental glaucoma models**

**KALENSKYAS 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**

**BEIERNAN R (1, 2, 3), YHAN ZH (1)**

(1) Singapore Eye Research Institute, Singapore
(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** Intraocular surgery is usually followed in the near term post-operative period 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 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 capsulorhexis 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 intraocular inflammation.

### 1624
**Oxygen induced retinopathy (OIR) mouse model**

**ILISITALO 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.
Femtosecond laser and microkeratome preparation of ultrathin (UT) DSAEK Grafts, the six months clinical results

MIURA 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, disc 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 Cilm 300- microkeratome. The thickness of the first cut was modified for each cornea in order to obtain a final graft thickness of 120 µm. Post-op central graft thickness was performed with corneal laser tomography (Spectra). 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±21.6 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, 0.5 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 surgery, respectively. Significant positive correlation between BCVA (logMAR) and central graft thickness at 1 and 3 months was observed (r=0.74, 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.

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 Femtosecond laser gave rise to a number of irregularities, leading the author to use a posterior cuts endothelial graft. 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) irregularities can be due to the viscoelastic interface or very long-term issues may mostly depend on the endothelial cell (EC) pool brought by the graft, and 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.

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.

Femtolaser assisted preparation and quality of endothelial button

BOURGES JL
Paris

ABSTRACT NOT PROVIDED
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.

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**1643**

**Infectious keratitis in children**

BREMOND DIGNAC D

Ophthalmology, University Hospital, Picardie Jules Verne University (Amiens)

INSERM UMR 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 or fungal pathogens.

**Results**

Clinical forms bacterial, chlamydia, viral, amoebaor 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.

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**1642**

**Herpes and zoster keratitis**

LABETTOULLE M

Ophthalmology, Bicêtre 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 or geographic) to a more severe disease involving the stroma and/or the endothelium. Most of these 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.

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**1644**

**Infectious crystalline keratopathy and its management**

DUA H

Nottingham

**ABSTRACT NOT PROVIDED**
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 into the prescription and 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.

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.

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.
Supranuclear eye movement disorders
BORRIAT 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.
• 1672 Pathology of pigmented fundus lesions
COPLAND 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 characteristics 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 naevi and that they should be observed periodically. The patients should be told to return immediately if they develop new visual symptoms.
Malignant melanoma of the uvea: radiotherapy techniques

DESIARDINS 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 in Europe since 1983. Because of the Bragg peak, 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 emmiting 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 300 grays.

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.

Malignant melanoma of the uvea: surgical techniques

DAAMATO 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

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**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.

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**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.

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**2213**  
**Anterior segment problems with vitreous substitutes**  
HEIMANN H  
Liverpool  

**ABSTRACT NOT PROVIDED**

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**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
SPIEERS 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.

• 2223
Photophobia in neuro-ophtalmological 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 photophobia circuits and examine their application in clinical neuroophthalmology.

• 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.

• 2224
The role of electrophysiology
HOLDER GE (1, 2)
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(2) Institute of Ophthalmology, London
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 DCEV standard techniques for ERG, PERG, 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.

SIS: Doctor, I don’t like bright lights
**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 damaged or damaged corneas. Despite the promising clinical results that we previously reported on corneal cell transplantation, in more robust and elastic materials are required to withstand the adverse host conditions faced for high-risk transplantation in severely damaged or damaged 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 physicochemical properties (e.g. mechanical, optical, water uptake, FTIR, and thermal degradation) and physiological (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.

**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: 10.1±3.4 pmol/g for NA, 48±2.7 pmol/g for AD in the centre; 76.6±15.8 pmol/g for NA, 210±11.1 pmol/g for AD in the intermediate segment; 317.0±55.7 pmol/g for NA and 111±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 77.4±9.8 nmol/L (n=6) and no AD was found. Plasma concentrations (n=4) were 280±25 pmol/L for NA, 36±2.8 S pmol/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.

**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) 10-6M was added to the culture. BMDCs +/- Dexa phenotype, APC function and immunosuppressor activity were examined. A fully allogeneic rat corneal transplantation model (DA to LEW) was used for in-vivo studies. BMDCs +/- Dexa were harvested and 1x10^6 cells injected intraocularly 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<0.004 and n=24 p=0.001 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.

**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 I coated scaffolds. Additionally a cell line of human corneal epithelial cells (HCECs) 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 surface 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. Disperse 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 ECM/scaffolding interaction and cell infiltration studies will be the focus of our research.

**Commercial interest**
Combining innovative imaging: in vivo multilaser confocal microscopy and ex vivo confocal Raman spectroscopy of cornea and skin in nephropathic cystinosis

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(2) Department of Ophthalmology, University Hospital, Saint-Etienne
(3) Department of Biochemistry and Molecular Biology, University of Debrecen, Debrecen
(4) Eye Bank, French Blood Centre, Saint-Etienne

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 woman with advanced nephropathic cystinosis underwent penetrating keratoplasty for severe visual loss and chronic ulceration in her left eye. The only dermatology symptom was skin dryness. Corneas and skin were analysed with IVCM using the innovative multilaser (488, 668 and 785 nm) confocal microscope Visuvscope 1500 and the handheld monolaser Visuvscope 3000 (MAViG GmbH). In order to obtain the chemical composition, ex vivo Raman spectroscopy (LabRAM ARAMIS) (Joelma Yoon, France) was performed on corneal button retrieved during keratoplasty and on a skin sample, both immediately frozen in liquid nitrogen without adhesive.

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 thesaurusinmes like amyloidosis, Wilson disease, Fabry disease or mucopolysaccharidosis.
Mini-pump revisited for ocular drug delivery

HUMAYUN M
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ABSTRACT NOT PROVIDED

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)

New formulations for topical drug administration

GURNY R
Geneva

ABSTRACT NOT PROVIDED

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.
• 2245
Suprachoroidal delivery: new directions and challenges
OLSEN T
Århus
ABSTRACT NOT PROVIDED

• 2246
Electroporation for ocular drug delivery
BEHAR-COHEN F
Paris
ABSTRACT NOT PROVIDED
• **2251**

**Genetic basis of glaucomas**

**TEKELIOYA**

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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**

**KOCAOBRA’S**

Medipol Faculty of Medicine, Ophthalmology Dept., Istanbul

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**

**ENGIN K**

Istanbul

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 retrobulbar 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.
**2262**

**Stem cell culture for limbal deficiency**

**BORDERIE V (1, 2)**

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(2) Centre Hospitalier National d’Ophthalmologie des XV-XX, Paris

**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-derma, 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 culture medium products or feeder cells from animals, 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 animals, and 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**

**FUCHSLUGER T**

Düsseldorf

**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** Films can be created and are successfully applied both on a research and on a clinical level.

**Conclusion** Biomaterials will become a reality in ophthalmosurgery.
**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 microscopy, 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 8.18 mm quartz square. Keratotests, observable with transmitted light or specular microscopes, were sent simultaneously to all volunteer eye banks (n=100). Each participant 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 36 eye banks will be presented. It allowed to identify different methods 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 of 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, DIREC Rhônes-Alpes

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**2266**

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

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(2) Department of Ophthalmology, University Hospital, Saint-Etienne

**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, while in the United States and some other territories, the opposite was true. Europeans use long term organuculture 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), can be severe in most developing countries. Decreasing demand requires: 1) Trachoma fight in endemic zones, 2) Iatrogenic edema prevention. Increasing supply requires: 1) Corneal donation policy 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.

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**2267**

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

HRSOVA K
Prague

**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 polymegathism, 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 PV00UK-P241FL13 of Charles University in Prague.

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**2268**

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

PAREKH M
Zadarino-Venice

**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® (new formulation) or Optisol-GS for 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 improvements: test slides (3rd generation keratotests) were fabricated with technologies employing in microscopy, from images of real human corneas (Optics Letters2012). Diﬀerent mosaics with ECDs covering the usual range observed in eye banks, were created in a 8.18 mm quartz square. Keratotests, observable with transmitted light or specular microscopes, were sent simultaneously to all volunteer eye banks (n=100). Each participant 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 new and quantitative method to evaluate the overall quality of corneal tissues for clinical applications and research testing.

**Conclusion**

The overall quality evaluation of corneas 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**
**Serum-free cornea culture with hydroxyethyl starch as a deswelling agent**

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University Eye Clinic and Aachen Cornea Bank, Aachen

**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 ± 159µm 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 on 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.
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Purpose

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• **2275**
Long term efficacy and tolerability of anti-TNFα therapy in the treatment of non-infectious uveitis – a surveillance study

**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 biologies 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 refractory to standard treatment (ADUR)

**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 accuracy 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 1.5 3 points).

**Conclusion** The results of this trial show clear superiority of ADA over control in the treatment of severe uveitis forms in term of visual accuracy and inflammatory activity.

**Commercial interest**

• **2277 / F089**
Tocilizumab for anterior uveitis and juvenile idiopathic arthritis – a case report

**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 TNFα 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.

• **2278**
Commercial interest
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<th>SIS: Peeling in macular surgery</th>
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<td>TADAYONI R</td>
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<td>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.</td>
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• 2415
What to peel in macular surgery?
GAUDRIC A
Paris

ABSTRACT NOT PROVIDED
Genotype-phenotype correlations in Stargardt disease/ABCA4-related retinopathy

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(3) National Institute of Sensory Organ, Tokyo

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 (PERGs, FERGs) were used to classify 175 patients into three groups (Lois et al. 1999), dysfunction confined to the macula, macular and cone ERG abnormalities; and macular and both cone and rod abnormalities. Patients were also grouped by genotype: G1 - two null variants (N-9); G2 - at least one null variant with or without missense variants (67); G3 - at least two null variants (50); G4 - one missense variant (69).

Results All G1 patients had a group 3 ERG. 26/58 G2 were in group 1; 26/58 in Group 3. 24/47 G3 patients were ERG group 1; 17/47 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 ARCA4 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.

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 ERGs was recorded in normal subjects, containing numbers of prescribed eye movements and blinks. AR models were derived using the Ilkag algorithm over a range of explicit SNR's. The ERG record was recovered as its Fourier implementation User by providing a familiar Excel© spreadsheet interface.
Mechanisms & recovery of vitamin A deficiency

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(2) Ctr for Medical Genetics, Ghent University Hospital & Ghent University, Ghent
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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

**ABSTRACT NOT PROVIDED**

**2433**
Shack-Hartmann aberrometry vs OQAS: the quarrel of the ancients and the moderns?

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(1) Tours
(2) Ophthalmology, Tours
(3) Orsay

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.

**2432**
Spherical aberration and binocularity

**ABSTRACT NOT PROVIDED**

**2434**
Should you decide to perform cataract surgery on your patients, based only on straylight?

**VAN DEN BERG TJTP**
Netherlands Inst. Neuroscience, Royal Academy, Amsterdam

**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**
Quality of vision and 3D

COCHENER B (1, 2), LAMARD M (2), FERRAGUT S (1, 2), IORGAOAN D (3), FATTAKHOVA Y (3), DE BOUGRENET DE LA TOCNAYE JL (3)
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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.
Scleritis and systemic diseases
LEE R
Bristol
ABSTRACT NOT PROVIDED

Infectious scleritis
WATSON P
Cambridge
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 response 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?

Imaging and scleritis
HERBORT CP
Lausanne
ABSTRACT NOT PROVIDED

Scleritis: general concepts
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Moorfields Eye Hospital, London
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.

Scleritis and systemic diseases
LEE R
Bristol
ABSTRACT NOT PROVIDED
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 immunosuppressives and, when necessary, biologics.
Is spectral domain optical coherence tomography useful in improving the contour line with the Heidelberg Retina Tomograph?

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(2) Epidemiology University Hospital, Dijon

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 +0.11 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.

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

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(2) Department of Epidemiology, University Hospital, Dijon

Purpose The aim of our study was to evaluate and compare two Fovoscan stereoscopic measurements of the 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, foveal retinal thickness and average retinal nerve fiber layer thickness (RNFLT) 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=0.003), 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.

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 (GCIP) 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 GCIP and the peripapillary retinal nerve fiber layer (pRNFL) thickness were measured with 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 (GCIP, pRNFL) was sought.

Results Correlations were seen between GCIP, pRNFL and VF sensitivity. In all patients, parameters of both GCIP and pRNFL were moderately correlated with MS. In RGCs with glaucoma, MS correlated more strongly with the VF cluster than with the MS. The highest correlations were observed between superior VF cluster (in dB scale) and inferior GCIP thickness (R2=0.69) or inferior RNFL thickness (R2=0.51). Correlations were slightly greater with dB scale than 1/L scale.

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

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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(2) HUMS, Zaragoza

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 examination 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 0.9 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 intravist and intervisit reproducibility in glaucoma patients. SLP is an imaging technology that may be useful in monitoring glaucoma progression.

Commercial interest
Free papers : Imaging 1 / Treatment in glaucoma

• 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 assessment 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 (RG IPL), were automatically segmented with a custom made software (Mathlab R2009b, The Mathworks Inc.). A normative database for the thickness of the RNFL, the RG IPL, 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, RG IPL and retina within 65 segments.

Results
On average the glaucoma patients showed for RNFL, RG IPL and retina 29.8, 94.9 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 29.65 µm (RNFL), 79.05 µm (GC IPL) and 31.46 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, RG IPL 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.

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

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(2) Eye Clinic - Catania University, Catania
(3) Ophthalmologic Clinic, Foggia

Purpose
To study the effects of palmitoylethanolamide (PEA), a fatty acid ethanoloamide, 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/day 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
Significant 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.

• 2455 / 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 diagnostic. Possible influences of manual center selection on the double hump (DH) shape of RNFLT profile and classification have been evaluated.

Methods
SD-OCT (Spectrals , 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 diverts 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 13 of 159 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

• 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 Recherteru 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 Vcylr ligure).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 hleb revision was performed, leading again to a massive intraocular pressure rise. Meanwhile 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.

Commercial interest

EVER 2012 Abstract book
**2461** Bilateral progressive coats-type exudative retinopathy in Usher syndrome type IIIA from c.528T>G Clarin 1 (CLRN1) mutation

KIVELÄ T, TÄLL M, LINDAHL P, PIMMONEN L, IOUKOVAYRA S, SANKILA EM
Department of Ophthalmology, Helsinki

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 years earlier developed myopia 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 flicked. 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 constructed. Two months later, vision had deteriorated to 20/100 and exudates extended to the macula, OD. He underwent bilateral peripheral cryocauterization. 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 cryocauterization, OS, the exudates remained regressed bilaterally with 20/40 vision, OD, and 20/30 vision, OS.

Conclusion Bilateral Coats-type 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 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 background 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=0.56, 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=26.50, 95%CI: 3.30-203.02, p=0.0034, 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: 1.38-17.25, p=0.01). 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 determine 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 1,997 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 1,997 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 populations 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 microphthalmia 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−/- mice in micro(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 immunohistochemistry, 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. 236 (T368A) creating a new Atb26d restriction site; the mutation converts the Cys at codon 127 to an stop codon (Cys127X). 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 P21 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 Pxdn was dramatically reduced in the dry type 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=26.50, 95%CI: 3.30-203.02, p=0.0034, 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: 1.38-17.25, p=0.01). 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.
**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 ophthalmic 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. Numerous and various daily ophthalmic 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 ophthalmic emergencies. An improvement of the general and emergency practitioners' knowledge in regards to ophthalmic pathologies could allow them to diagnose and treat begin 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.

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**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 allele variant frequency of eNOS gene T786C in patients with normal tension glaucoma and primary open angle glaucoma.

**Methods** The studied group consisted 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 allele frequency was not statistically significant (p=0.9). In women with NTG the allele 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 allele 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 allele form is most frequent in NTG women.

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**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-threatening 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. Assessment of diabetic retinopathy was performed by ophthalmoscopy and fluorescein angiography 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.

SERPNIK2 Statistical significance of the observed linkage disequilibrium:
- rs2070682   rs1658913   rs2227692
- rs2227676   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 r value is 0.573939

SERPINE1 Statistical significance of the observed linkage disequilibrium:
- rs2070682   rs1658913   rs2227692
- rs2227676   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 r 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 physiologic 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 10μm (10-12 cell layers) thickness immediately at the crest of the inner border with a slope towards the subtears 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. Identification and scoring of lid wiper epitheliopathy in dry eye disease 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 occur by the observer and has to be repeated for accurate 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. Then the measurement of the LOT was done in ten blink-intervals. At last the FL-BUT was measured at the slit lamp, three times 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, stddev 1.8) the KG-BUT 3.6 sec average (1.3-4.5sec; stddev 4.3). The LOT was 3.6 sec average (1.7-6.5sec; stddev 1.8). There was no significant correlation between FL-BUT and KG-BUT (R: 0.20, no correlation between LOT and KG BUT (R:8). There was a positive correlation between Fl-BUT and LOT (R: 0.50).

Conclusion This pilot study point at a relation of FL BUT with the Lid opening time LOT. The clinic observation seems 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 translated, 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, immunohistological 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 freeoexene 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. Simon 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.
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 Theaoz 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 Theaoz.

Methods Twenty two patients were included and randomized in 3 groups: 7 patients (4 affected by Sjogren Syndrome -SS) were switched from autologous serum eye drop treatment to Theaoz 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 Theaoz 6-8 times a day (group 3). The OSDI questionnaire, tear film evaluation by BUT, fluorescein 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 group 1, 4 of the 7 patients maintained unmodified their clinical benefit and corneal morphology after switching from autologous serum to Theaoz. 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 T3 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 Theaoz.

Conclusion Theaoz 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 ReGenesing 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
Nottingham

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 reflective 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 hereewith 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 support 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.

• 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 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 99/114 scans (86.8 %). 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.

• 2612
High-resolution spectral domain optical coherence tomography findings in reticular pattern dystrophy

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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 (IZ, 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 layer/outer layer 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. Hypereffe ctive subretinal material accumulation or hyporeffe ctive subretinal lesions, were detected in 11.3% and in 12.5% of scans, respectively. SD-OCT showed hypereffective 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. Hypereffe ctive subretinal material accumulation or hyporeffe ctive subretinal lesions, and hypereffective retinal pseudocysts were also noticed.

• 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 62 patients (40 female and 22 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=0.25).

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.
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 yrs, 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 3A1, one as Stage 3b.

In the 25 patients who had FA, 15 had telangiectatic 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 telangiectasia 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 telangiectatic 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 cryotherapy; 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 telangiectasia and of ischaemic areas in Coats disease. Laser treatment to the telangiectatic 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.

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 0.854 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.

Subfoveal choroidal 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), thinner 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 millimetre. 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.

Subfoveal choroidal thickness: the Beijing Eye Study

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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
Meganeuclase targeting HSV-1 limits viral endothelitis in vivo

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(5) Bichat Hospital, Pr Cocheneau Department, Paris

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

Methods: NZW received intracameral injection of recombinant adenovirus-associated virus equipped with a constitutive expression cassette containing either the meganeuclase gene or a non-coding sequence. After treatment with intravitreal compound 48/80, the treatment group systematically showed a decrease in their average number of contamination plaques evaluated.

Results: In 4 tests with 24 experimental or control corneas, the meganeuclase-treated groups showed a decrease in the number of contamination plaques compared to the control group.

Conclusion: Meganeuclase 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, 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 presented 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 58.8 years (range 22-77 years). Nineteen of the patients were women and 13 were men. Twenty-six patients (81%) had anterior scleritis (17 nodular, 8 diffuse, and 1 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), Bechet'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 spondylitis (n = 1), sarcoidosis (n = 1), Cogan's syndrome (n = 1), ulcerative colitis (n = 2), unspecified inflammatory arthritis (n = 2), unspecific inflammmatory arthritis (n = 2).

Conclusion: The number of systemic disease in our series is similar to 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 corneal microscopy. In addition, lid parallel conjunctival film (LPCOF), tear breakup 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 [45-94.75] 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, LMC and morphology were not affected by disease activity. However, patients on anti-TNF or corticosteroid therapy exhibited LCM 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 [10.00-14.00] seconds and 20.00 [10.93-38.21] vs 9.75 [4.16-28.2], 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.
The effects of autologous serum eye drops in the treatment of ocular surface diseases: a retrospective study

**Purpose** To evaluate the efficiency of autologous serum eye drops 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) +/- 0.9 lines before to 1.69 (20/980) +/- 0.6 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** Cicatrization of PED and improvement of DE symptoms were observed in most eyes under autologous serum.

Comparison of viral vectors for gene transfer to corneal endothelial cells

**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 between 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.

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

**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 biotherapie 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.
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=186) 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=0.019) respectively. Additionally, older patients displayed uveitis anterior (63.2%, p=0.052, n=96) and vitreous involvement (89.5%, p=0.054, n=78) more frequently. Complications during OT (secondary IOP) and (CC=0.32; p=0.009) respectively. Additionally, older patients were more frequently. Complications during OT (secondary IOP, endophthalmitis (6 cases), spondyloarthropathy (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.

Etiologic diversity in patients presenting with atypical and severe anterior uveitis

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Purpose To analyze the etiologic 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 herpetic uveitis were excluded. Patients were divided into three groups: atypical viral uveitis (group 1), typical herpetic uveitis (group 2), and 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), spondyloarthropathy (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.

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% chlorhexidine digluconate (CHL), 0.1% c-desamide (DES), and 1% 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 10^6/ml determined with a hemacytometer and allowed to incubate at 300 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 its positive growth between the drugs.

Results Complete–kill was determined more frequently with PHMB and DESO (p<0.1) 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 separate 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.
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 sensitivity of 25%; associated to first PCR (8/27-1510), this rate increased to 31.7%, and with nested PCR (91E-13BS), we had 34.9% of identifications.

Conclusion
16S rRNA PCR is a rapid alternative to culture, sensitive and reproducible. 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-).

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

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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 3.4×10³±4.5×10³ copies/ml (6×10² 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-dose 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.

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 corneas of rats were infected with Acanthamoeba hatchetti. Cornea infections were graded microscopically. Nine groups were treated with various 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 compared 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 highest 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 safe option for treatment of AK.

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 3.4×10³±4.5×10³ copies/ml (6×10² 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-dose 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.

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 corneas of rats were infected with Acanthamoeba hatchetti. Cornea infections were graded microscopically. Nine groups were treated with various 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 compared 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 highest 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 safe option for treatment of AK.
• 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, -6, -7 and -9 in human glaucoma eyes compared to control normal eyes.

Methods Immunohistochemistry for AQP1, -3, -4, -5, -6, -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 AQP1 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 increased AQP9 expression in the Müller cell endfeet. These results suggest that changes in retinal AQP expression are associated with the development of glaucoma.

• 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 (epidermal vein) pressure and the presence of 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) on Ophthalmic Artery (OA), Posterior Ciliary Arteries (PCA) and Central Retinal Artery (CRA) were performed. Samples were frozen at -70°C 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 (p=0.009, p=0.009, p=0.020). However, there was no significant difference between aqueous ET-1 levels of the three glaucoma groups (p=0.098). The 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.

• 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 is 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 distribution 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 DOPP (diastolic blood pressure replaced by noise with a SD of 10 mmHg) was 1.27 (1.01-1.97) and of the resampled SOPP (systolic blood pressure replaced by noise with a SD of 20 mmHg) 1.09 (0.72-1.53).

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.
**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, supronasal, supertemporal, 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.
Conclusion

With Retinitis Pigmentosa or Cone-Rod Dystrophy, ~6% were found to have ABCA4 mutations found using Sanger sequencing. When NGS was used in a group of patients this technology, particularly the Illumina platform, was highly reliable in detecting mutations but still significant. Evaluation of NGS using ABCA4 as a test system showed that in patients with Stargardt Disease and other ABCA4 retinopathies the detection rate was lower in patients with a clinical diagnosis of STGD disease was ~80%. In patients with inherited retinal degeneration using NGS.

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.

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 inherited 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 chororetinal atrophy, Bull’s 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).

Purpose

Current technologies for delivering gene testing through conventional 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. The presentation will discuss the ability of an NGS protocol to identify likely disease-causing genetic variants.

Results

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

Conclusion

An NGS approach delivers a step change in the diagnosis of inherited retinal 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.

Purpose

Using it: NGS in the inherited retinal degeneration clinic

The introduction of NGS for inherited retinal disease has identified mutations in fewer than one in four of those patients tested. NGS is delivered in the setting of a UK National Health Service accredited diagnostic molecular genetics laboratory. The presentation will discuss 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.
Commercial interest

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 intra cellular metabolism. Residues 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 488 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 3 ns) 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

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.

Commercial interest
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-qPCR) 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.

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 VEGF-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 VEGF-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.

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 to 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 cell 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.

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

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

Results Human genetic studies identify two clusters of mutations which are involved in human high myopia. One involves genes which act 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 scera, 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 dopamine 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 Human 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.
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” МР-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 subarachnoidal 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 subarachnoidal 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.

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 glia-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-specific 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.
• 2711
Foveal changes during ocular movements in normal eyes. A prospective study. Kinetics of posterior pole during ocular movements in various diseases: 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 vertex 2 distance at the CFT1 at the vertex and the straight-forward position and the CFT2 at the vertex 2 and the straight-forward position. The absolute difference between the CFT temp-CFT nasal was compared with the absolute difference between CFT1-CFT2 at the straight-forward 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). Videomorphing 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, non-invasively, 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 volumes 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 fluorescence 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 ref 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±0.12% and a sensitivity of 83±0.4% were obtained. Overall, the accuracy of the automatic classification is 98±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 modelocked 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. Acquisition time of one OCT image is 0.02 second and vertical resolution in the air is 2 μm in the air. Horizontal resolution is less than 1 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 he 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 head forming 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
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 (rtx), Imagine Eyes, France). Cone photoreceptor 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.

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 retrofoveal neovascularization complicating AMD. Atrophic areas were evaluated by autofluorescence imaging Spectralis (in particular with region finder software), OCT (notably choroidal capillarity 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 evaluated.

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 1.15 mm²/year. At OCT, thickness of photoreceptor, pigment epithelium layer diminished about 35% and 35% at the areas edge. Choroidal capillarity 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
HOFFMANN E
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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 (Iribaker RE. 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?
ALIO SANZ J
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 pathways. 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. Cataract 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 immunomodulation 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 dioptric 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, 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 BCVA was 0.41, 0.52, and 0.72 at 0.29, 0.28 and 0.14 LogMAR, respectively, 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 cataract surgery 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 stasis externa and antibiotic use during the peri-operative placement of tympanostomy tubes.
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 oligonucleotide 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.
Compressive lesions

**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 ophthalmic 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 neuropathy. 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**

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Optic neuropathy in Devic’s disease: a diagnostic challenge

**Purpose** To learn about compressive lesions which can mimic optic neuritis

**Methods** Case presentations

**Results** 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 unilateral 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 AQP-4 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.

**Commercial interest**

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Inflammatory optic neuropathies

**Purpose** 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.
Methods has generated a new era for increasing equisitely specific therapy. Improved diagnostics of understanding of immune response during non-infectious uveitis alongside the or the overburdonsome adverse events of immunosuppressive therapy, the advent

Purpose

Bristol risk settings.

Drugs is benefi cial in the perioperative stage, the long-term-use is restricted to high-

reduce the risk of corneal allograft rejection. While the use of systemic immunosuppressive
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 benefi cial in the perioperative stage, the long-term-use is restricted to high-risk settings.

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

Purpose Moving away from the morbidity of steroid therapy for in fl ammatory disease or the overburdensome adverse events of immunosuppressive therapy, the advent of understanding of immune response during non-infectious in fl ammats alongside the explosion in biotechnology has facilitated the development of biologic therapy. This has generated a new era for increasing equisitely specifi c therapy. Improved diagnostics have lead to specifi c targeting for infectious aetologies.

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 ability to predict and therefore target responses. Additionally 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 refractivities 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 in fl ammatory disease.

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

Novel therapeutic strategies for the induction of tolerance in corneal transplantation

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 corneas 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 signifi cantly 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 immunological 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. [Supported by Science Foundation of Ireland (SFI 07/IN.1/B902)]. TR is supported by a Travail Grant from Millennium Research Funds, National University of Ireland, Galway]
Immune modulatory effects of gene therapy to corneal grafts

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Purpose To provide an overview of immune modulatory effects of gene therapeutic approaches to corneal allografting.

Methods The immune reactions caused by corneal allografting will be summarized. Gene therapeutic 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 wipe-out syndrome is well known among glaucoma surgeons. Recent papers have highlighted that this complication may occur but may be at a lower rate than 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 perspective is the grief reactions and sharing information in the role of the clinician and the 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 (AKI), using human AR (AKR1B1) activity as an assay readout. Fractionation of materials in an Amla extract resolved several compounds with AR activity. Structure elucidation by NMR identified the major inhibitor as 1-O-galloyl-beta-D-glucose, also known as beta-glycogallin (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) endotoxin. 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 TNF-a and IL-1β. 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 PEDE, TSP-1 and VEGF-A in the presence of TA were quantified.

**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 PEDE, 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 retina. 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 retina 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.
**2772**

Inventorisation of European education programs

TASSIGNON MJ

Antwerp

ABSTRACT NOT PROVIDED

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**2773**

Surgical skills among European students

CREILZOT C

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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.

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**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.
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 (EBO D) 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 $c ~ 0.33$).

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.

I have passed the exam

MUSELIER A
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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% 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 PRPH2, RPL1, PRPF8, IMPDH1, NRL, PRPF3, NR2E3 and SNRPNP20) 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 15 out of 68 (21.5%) 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%).

### 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 homoygous 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 homoygous for EYS or USH2A markers. We selected 16/30 of the remaining families for SNPs genotyping and homoygosity mapping. We found the causative mutation in 7 families (43%) in a known gene (RPI, RLBP1, NR2E3, CNG1B, IMPG2, PDE6A) while in 6 others sequencing of known genes in homoygous 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 41% 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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**Purpose** Mapping and genome sharing among affected individuals continue to be important for establishing a link between a genetic 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 DOCK8, IPO5 and STK24 at 14q22 loci. 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 identified 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 5q11 were identified. Sequencing of IL1A, IL1B and IL1RN at 2q13-q14.3, SLCA1A1 at 20p13, TGFBI, PITX1 and IIH at 5q11 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 2011/01/N/NSZ/01470

### 2784

**OPA1-related sensorineural hearing loss**


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**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 ADOA and to describe the phenotype associated with these rare mutations.

**Methods** We retrospectively reviewed the files of all the OPA1 patients with documented deafness diagnosed in our laboratory between 2003 and 2011.

**Results** In our series, deafness occurred in 64% 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 sensorineural hearing loss can even be the first event and its association to optic atrophy should prompt molecular genetic analysis, which can lead to an appropriate diagnosis.
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 transition in exon 2 predicting a premature stop codon (Q31X).

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 haplosufficiency. The novel variant broadens the spectrum of the reported OPA1 mutations causing ADOA.

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 screened 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 p.G9230866C-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 NN402597140

• 2785 / T003

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, electroretinogram 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 hyperpigmented 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 24-hue test revealed preserved color vision. Visual field showed a central scotoma. Electroretinogram recordings demonstrated a still preserved rod and cone function. Genetic study revealed a compound heterozygotic mutation for RDH12 in exon 6 (p.Ala206fs 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 stage) 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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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 76±5%, severe non-proliferative DR 75±5%, and proliferative DR 75±5%. 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<0.05) 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 bed, 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±1.7% in the healthy population compared to 93.5±3.1% in early AMD (n=12, p=0.42) and 93.7±3.4% in exudative AMD (n=14, p=0.53). 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 63.6±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. Empirical 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.
2. 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<0.0001) was found for arterioles and venules.
3. Dual ratiometric calculations of retinal oxygen saturation (SO2) demonstrated a significant decrease of arterial SO2 during hypoxia.
4. The order of acquisition of spectral images did not influence the outcome of retinal oximetry results.
5. 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.
6. Other extraneous factors included:
   - Variation in retinal pigmentation.
   - Density of retinal pigmentation.
   - Instrument flash intensity.
   - Lenticular irregularities.
   - 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**

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**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 may permit more targeted therapies to be given.

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**2817**

**Oxygen distribution in the retina**

POURNARAS CJ. Geneva

**Purpose** To evaluate the distribution of the preretinal and transretinal partial pressure of oxygen (PO2) in normal and ischemic retinas.

**Methods** Evaluation of either the preretinal or intraretinal 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 occurring 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.
Novel therapeutic targets in diabetic retinopathy

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The present armamentarium 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 Angiopoietin-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.

Investigator-initiated trials: a corporate perspective

**LAMBOUG**

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.

Perspectives for new treatments at Allergan

**MALTMAN J**

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.

Identifying progression of retinal disease in eyes with NPDR in diabetes type 2 using non-invasive procedures.

**CLINHA-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**  
CS nº 1, Coimbra

**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 (fT-mfERG). Secondary neurodegenerative variables: Retinal Nerve Fiber Layer (RNFL), Ganglion Cell Layer (GCL) and central retinal thickness assessed by SD-OCT. 2) Maculopathy severity 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 Population: Type 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 nº 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 JR
  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
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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(2) Service d’Ophthalmologie, Université Paris Descartes, Faculté de Médecine, Hopital Cochin, Paris

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 uveits 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 imatinib group and 0.36 in the sunitinib group (p=0.02). We furthermore demonstrated 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 proinflammatory cytokines IL-1beta and IL-18 in 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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(1) Ophthalmology, Strasbourg
(2) Parasitology, Strasbourg
(3) Ophthalmology, Dijon
(4) Parasitology, Dijon
(5) Ophthalmology, Grenoble
(6) Parasitology, Grenoble

Purpose Toxoplasmiasis 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-g was neutralized concurrently, the initial parasitic 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-g) 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 conjunctival associated lymphoid tissue
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(2) Institute of Virology, Vaccines and Sera – TORLAK, Belgrade

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 conjunctival-associated lymphoid tissue (CALT) as a mucosal route of immunization.

Methods BALB/c and C57BL/6 mice were immunized conjunctivally with tetanus toxoid (Ttd) as a model antigen. 100 μg/mouse of Ttd was applied onto conjunctiva of one eye, together with mitochondrion-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+, CD23+, and CD38+ cells) occurred in all mice, but mice immunized with Ttd in combination with B. pertussis had the strongest responses.

Conclusion Immunization conjunctivally induced Ttd-specific local and systemic immune responses. The strongest immune responses developed in mice that received Ttd together with B. pertussis.
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 Ophthalmic 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.

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 Ophthalmic 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 (0.93%) with CSC were misdiagnosed as posterior uveitis. Erosionous 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.

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 inflamed 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?
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 pathogenesis of normal (IOP) pressure glaucoma.

Methods The talk will present the results of recent studies which may shed some light on the question whether CSF-P is related to glaucoma.

Autonomic nervous system dysfunction in glaucoma

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Although abnormal intracranial 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.

Quantitative assessment of the visual pathway by DTI-MRI in Glaucoma

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(2) Neuroradiology, University of Erlangen-Nuremberg, Erlangen
(3) Pattern Recognition Lab, University of Erlangen-Nuremberg, Erlangen

Purpose In glaucomatous optic nerve atrophy (gOA) damage of retinal ganglion cells may continue to the linked optic radiations (OR). This study investigated differences between gOA and non-gOA 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 gOA patients, and 35 non-gOA patients (mean age 54±15.9 years, 61±12.4 years, and 49±15.2 years, respectively). The participants underwent 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 SpectraSp 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 gOA patient group the mean defect correlated with FA (r=-0.31; p=0.004) and RD (r=-0.42; p=0.003). In the non-gOA 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 radiations. The damage of the optic nerve was significantly associated with loss of RNFL and aging.

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.
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 hypoxia 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.
Commercial interest

Investigation of such impairment of oxygen supply and vessel diameter change upon flicker light stimulation should be considered for the simultaneous measurements 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.

Combining vessel analysis with Doppler OCT

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 40–60 µm 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

Compared to velocity data as obtained with DVA, the bidirectional Fourier Domain Doppler OCT showed good correlation with LDV data during both normoxic and hypoxic 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 underestimated 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

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 lumincence 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 significantly from 193 ± 20 µm, 228 ± 20 µm, and 60 ± 5.7% at baseline to 202 ± 19 µm, 242 ± 17 µm, and 54 ± 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 (all p < 0.01). 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.

2864

Retinal vessel analysis in animal models

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.
SIS: Metastatic disease from uveal melanoma: prediction, detection and treatment

**• 2871**

**Biology of metastatic disease**

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(2) Liverpool Ocular Oncology Centre, Royal Liverpool University Hospital NHS Trust, Liverpool

**Purpose**

Despite successful treatment of the primary tumour, uveal melanoma (UM) disseminates haematogenously 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 BAP1 associated protein 1 (BAP1), were performed on tissue microarrays of matched primary and metastatic UM. The percentage of tumour 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.

**• 2873**

**Prediction of metastasis**

**DAMATO B (1), COUPLAND SE (2)**

(1) Ocular Oncology Service, Liverpool
(2) Department of Molecular and Clinical Cancer Medicine, Liverpool

**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 histomorphology, mitotic count, extracapsular 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 FSA, 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 enhanced opportunities for basic science research, facilitating the identification of molecular abnormalities influencing the metastatic process.

**• 2872**

**Genetic analyses of uveal melanoma metastases**

**SAHLE S, COULIERIER J, STERN M, MARIANI P DESIARDENS L, ROMAN-ROMAN S, BARILOT ET, PIPERNO-NEUMANN S, LAUBERT C**

Institut Curie, Paris

**Purpose**

To identify genes linked to metastasis development in uveal melanoma (UM), transcriptome analysis linked to comparative genomic hybridization was performed with 63 primary tumours and 115 liver metastasises. 9 primary tumours and their matched metastasises (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 class 2 profile) and the couples were monosomic for chromosome 3 (suggesting a class 2 profile). Examination of the genomic imbalances in couples (all with monosomy 3, suggesting a class 2 profile) indicated that no major alterations occurred at the metastatic step. Very few genes (30) were found differentially expressed between the primary tumour 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.

**• 2874**

**Serum biomarkers of metastatic disease: current practice and future perspectives**

**ANGI M, KALIRAJH H, DAMATO B, COUPLAND SE**

Ocular Oncology Research Group, Liverpool

**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 therapies. As UM disseminates haematogenously, 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 scenario 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 more accurate 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 proteomics technologies.
EVER 2012 Abstract book

2877
Therapeutic options in metastatic uveal melanoma
PIPERNO-NEUIMANN 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
HALL G
Genetic Medicine, St. Mary’s Hospital, Oxford Road, Manchester

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 considerations of 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
BLACK GCM
Royal Eye Hospital, Manchester

Purpose This presentation will provide an overview of recent scientific 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, mitochondrial 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
VOTRIBA M
Institute of Vision, Cardiff University, University Hospital Wales Eye Clinic, Cardiff

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

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 us to make a specific diagnosis. It is important to distinguish between progressive and stationary conditions.
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 retinal pigment 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 the sensory retina, disruption of the RPE, thickening of the outer retinal 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 or subretinal 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 CSCR stages.

Commercial interest

Purpose To evaluate the efficacy of photodynamic therapy (PDT) to treat chronic central serous chorioretinopathy (CSCR) 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 202 µm 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±38.9 μm vs. 172.5±36.6 μm one year after treatment (p=0.004). NR CFT in the untreated eyes was 204.6±30.7 μm vs. 192.5±36.4 μm after self resolution (p=0.01). 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 assess the real role of this treatment in chronic CSCR.
SIS: Central serous chorioretinopathy: what's new?

• 3215
Other therapeutic options
BEHAR-COHEN F
Paris

ABSTRACT NOT PROVIDED
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 patches over time. Various markers of disease progression have been identified including phenotypic characteristics 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 allow discrimination of slow vs. fast progressors. The status of the fellow also has an impact 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 impact for future progression. Identification of prognostic markers is not only important for a better understanding 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 likelihood for the identification of a therapeutic signal.

### 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 choroiderme vascular diseases.

### Gene therapy in rare diseases

**SAHEL JA**

Novartis

**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 AMD 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 (RDVCF) consecutive to degeneration of rod photoreceptors directly affected by causative mutations. Administration of RDVCF, 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 year, 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, 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 improvement and restoration, as well as palliative aids and associated training protocols.

**Conclusion**


### Perspectives for new treatments at Alcon - part 2

**BICK C**

**Head, Clinical Trial Management – Pharmaceuticals, Alcon**

**Fort Wort**

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 vitrectomy, 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.
Sparing of the fovea in geographic atrophy

HOLZ F, SCHMITZ-VALCKENBERG S, FLECKENSTEIN M
CS nº 15, Bonn

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 function occurs. 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.

Stargardt macular dystrophy

HOLZ F, SCHMITZ-VALCKENBERG S, CHARBEL ISSA P
CS nº 15, Bonn

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. All probands will be ARLCA4 genotyped.
Autophagy: a new way to retinal neuroprotection

**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. NMMA 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 a 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 1, show that retinal ischemia alters the dynamics of the autophagic process and suggest a neuroprotective role of autophagy in RGCs exposed to detrimental stimuli.

Neuroprotective factors against retinal injury in response to hypoxia: new perspectives

**Purpose** In the retina, hypoxia is considered one of the key factors to trigger angiogenesis and to promote apoptosis by reducing photoreceptor and other retinal neurons, each of them contributing to vision loss. We recently demonstrated that the beta-adrenergic system interfere 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. VEGF2 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/N0 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.

Retinal neuronal death caused by ocular hypertension

**Purpose** To characterize the anatomical and functional changes that follow ocular hypertension (OHT).

**Methods** In adult albino rats or mice, the episcleral and perilimbic 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 amacrines cells, for periods of up to six months after OHT. There is a protracted and progressive affection of the outer retina which results in a major loss of L M- 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 anatomy or ischemia-induced neuronal death in the innermost retina or in the outer retina, respectively.

RIP Kinases, necroptosis and redundancy in neuronal cell death

**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, Cx3G1-CCL2/rAktC multiple, 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 led 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**
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.
Magnetic resonance imaging revolutionised the diagnosis and management of retinal diseases by providing high resolution imaging and the potential for assessment of novel functional parameters, such as photoacoustic and Doppler and spectral imaging techniques for the assessment of retinal blood flow and oxygenation, and a number of new technologies with comparable resolution. The use of adaptive optics to provide cellular level image resolution, the attempts that are underway to address the shortcomings of current retinal imaging methods, and the complement system. A dysregulated para-inflammation may not be able to maintain tissue homeostasis and functionality. The retina, particularly the macula, is constantly subjected to a low-level of insult mediated by oxidised 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.

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### Imaging and the ageing retina

**KEANE PA**  
NIHR Biomedical Research Centre at Moorfields Eye Hospital, London

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.

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### Macrophages and the ageing and diseased retina

**LIHMANN LI**  
UCL Institute of Ophthalmology, London

Purpose Recruitment and activation of microglia and macrophages are controlled by local cytokine and chemokine signals that also determine neurotrophic 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 monogenic 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.
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.

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.

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.

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.

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.
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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(2) Ana Fakin, University Eye Hospital, University Medical Centre, Ljubljana
(3) Viktorija Kerin, University Eye Hospital, University Medical Centre, Ljubljana

**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 (66%) or bilateral (33%). 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 intracranial ophthalmoplegia. More than half of patients (53%) had visual acuity of counting fingers (1-2 ph) and posterior ischaemic optic neuropathy (PION; 5 unilateral, 5 bilateral). All patients had temporal artery tenderness and reported recent fatigue, headache, jaw claudication, visual symptoms, and signs of systemic vasculitis. Most patients (70%) were treated with corticosteroids within 3 days of diagnosis and clinical symptoms. The median time to corticosteroid treatment was 3 days (range 2-4 days). The median follow-up time was 3 years (range 1-7 years) and 31% of patients had relapse during follow-up. The patient’s visual function was ultimately better than 20/200 in 86% of patients, with 13% having a vision worse than 20/200.

**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. In elderly, all the patients to report amaurosis fugax, sudden loss of vision or diplopia should be suspected to have temporal arteritis.

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**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.

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**3263**

**Atropine use in childhood myopia treatment**

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(2) Dept. of Ophthalmology, University of Warmia and Mazury, Olsztyn

**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 prevalence of myopia in the United States, Europe and Australia is about 30-40%, whereas 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 importance, whereas genetic factors play secondary role. The role of atropine in the lowering 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 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 discontinuation 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 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.

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**3264**

**Is the eye a window to the mind? RNFL thickness measurements by OCT as a biomarker for neurodegenerative diseases**

ASCASOF
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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.
Controversies related to mfVEP use

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Purpose 
To address the usefulness of mfVEP use in clinical research on neuroophthalmology, with a focus on optic neuropathies (Leber and Jôr 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 LHON 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
SCHAFFTEL 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 myopia.

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.

Commercial interest

• 3274
Correction of peripheral refractive errors and its impact on visual performance
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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.
(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 6-12 years old with a history of parental myopia while providing stable and clear vision without adaptation 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 of 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 wereanova 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 metastases. 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 metastases.

### 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. Toxicty 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.
Primary transpupillary thermotherapy for small suspicious choroidal nevi

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(3) Ophthalmology department, Centre hospitalier universitaire de Caen, Caen

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.

Ultrasound features changing during uveal melanoma local treatment

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Purpose The aim of our study was to estimate the echographic sighs (acoustic 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 radiosensitivity 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 installation 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
CHIQUET C
Department of Ophthalmology, University Hospital, Grenoble
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 microorganisms, 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
BRONA Dijon
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. Other questions are not fully answered; what about the use of intrastral 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.
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 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 – (1 * t), for t < 1 year (early phase); ECD = A – (t^2 * 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±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. AKI 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-Sapphire femtosecond laser (FL) pulses. Calcein (622 Da), tagged bovine serum albumin (70 kDa) and one eGFP plasmid (5 MDa) were transfected into two non-adherent cell lines (DU145 prostate-cancer and G5-9, rat glaucoma). Our aim was to adapt the NFT to adherent human corneal endothelial cells (HCEC).

**Methods**
We tested the NFT of calcine in vitro on the HCEC line HCEC-12 seeded at 1500 cells/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 FL beam movements was performed in order to obtain transfection with minimal toxicity. After exposition to FL, 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).

**Results**
Viability was assessed by Trypan blue staining. 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 C. Cyphalum Reu2010;43:63]. 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 (Click-it EdU) incorporation during DNA replication (S phase marker). EC viability was assessed using the triple labeling with Hoechst33342/Ethidium/Calcein-AM with the calculation of the viable EC density by image analysis (Pipparelli IOW/S2011;52:6018) and using an apoptotic marker, pDNA JANED.

**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 below 2000 cells/mm2. For long-term effect, EC 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 arrest 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 bared 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 endothelial loss. Apaf-1 inhibitors not only proved 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**
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 (2008-2009, Group I) versus restricted post-mortem time protocols (2010-11, Group II) were retrospectively analyzed. Data were collected at LIONS Cornea Bank NorthRhine-Westphalia, University Eye Hospital Duesseldorf, Germany.

Results In the years 2008 and 2009 (Group I) 1272 corneal grafts with post-mortem time of 300.0 ± 157.7 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.

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 30 of 8-week-old Lewis rats were investigated. Macrscopic 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-Saffran stained cross sections and ultrastructure, 2/ EC density (IHC) and morphology, 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.
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 effectively 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.

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.

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-dideoxyxyridine (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 (Novartis), Zinag (0.15% Ganciclovir gel), Riaoch + Lombr), and FST-100 (0.4% povidone-iodine-0.1% desametahoxime Fresfight Biotherapeutics). The first antiviral to treat adenovirus ocular infections will hopefully be available in the not too distant future.

Commercial interest

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 resistant, 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 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.

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 this 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. Osborne Fundación de Investigación Oftalmológica, Instituto Oftalmología Fernández-Vega, Oviedo 33012, Spain. Neurons 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-myelinated 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 ‘ischaemic-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
MOZAFFARIEH M
Basel

The classical glaucoma treatment focuses on IOP reduction. Better knowledge of the pathogenesis has opened up new therapeutic 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. Uregulation 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.
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. Coats’ disease is typically diagnosed in male children presenting retinal telangiectasia, complicated by retinal exudates. Choroidal vascular tumors are most frequently circumscripted, 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 proton, 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.

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.2231delC [p.Pro744Leufs7] 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.660C>T [p.Ala227Val] mutation with c.2831delC [p.Pro944Leufs7]. Other Finnish patients with the latter combination 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.
• 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
GAUDRIC A (1), DAMATO B (2), DESJARDINS L (1), ZOGRAFOS L (3)
(1) Paris
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(3) Lausanne
ABSTRACT NOT PROVIDED

SIS: Vascular tumours of the retina and choroid
• 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 deutsans, 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 distribution. 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 (486, 74.4 and 43.8cd/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 infraretinal 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 (1). Opt Soc Am A Opt Image Sci Vis 29(2327-33,2012). This approach makes it possible to separate changes caused by normal aging from the effects of sub-clinical chromatic sensitivity. 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 illumination.

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 Gaugacoma 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 the following referred to as “spc 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 spc plates during a viewing time of 1 s or 3 s. Under unrestricted observation, 3 of 5 daltonian subjects deciphered the red / green spc plates. Blue/green spc plate results in the daltonian subjects matched those of normal observers. 3 of 5 diabetic patients failed in the blue/green spc plate at 1 s, one at 3 s of viewing time. With one exception at 1 s, the diabetic patients passed the red/green spc 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 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 (+2σ) 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 91 years) 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 colour vision using a newly developed, age-corrected system for colour assessment.

Conclusion: The age-corrected 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.
Intracamerular Cefuroxime injection at the end of cataract surgery is a safe procedure to significantly decrease the incidence of endophthalmitis.
**3485**

**Contribution of 3D anterior segment reconstruction by rotative UBM to the sizing of phakic IOL.**

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**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 measures 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
TADAYONI R
Paris
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
Lausanne
ABSTRACT NOT PROVIDED
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 dexamethasone provides visual recovery with excellent safety outcomes.
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 subconjunctivally 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 macular holes. Additional gas injection combined with extended strict posturing can increase the anatomical closure rate without the need of additional surgery.

Clinical and OCT outcomes for full-thickness and lamellar macular hole surgery

STAPPLER T
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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 these 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 heterogeneous 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 of 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.

Myopic foveoschisis: OCT findings, surgical indications and results

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Geneva

Purpose Myofibroblasts play a major role in the production of retractive 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 (α-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.

Conclusion Scanning electron microscopy indicated that active contraction mechanisms are always expressed in epiretinal macular membrane and underlying 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.
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/t-PA/gas/anti-VEGF and to provide definitive outcome comparisons with other management approaches.
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 equity and redness did not differ between the two groups.

Conclusion The results suggest that once a day dorzolamide nanoparticle eye drops have a similar 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

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. Seven healthy volunteers with intraocular pressure (IOP) over 18 mmHg were recruited. IOP was measured with a Tono-Pen VI 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 equity and redness did not differ between the two groups.

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Commercial interest
**3635**

**Synthetic eye prosthesis**


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(7) Erlangen-Nürnberg

**Purpose** Development of synthetic eye prosthesis to provide a long term stable keratoprosthesis

**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 hydrophobic 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.
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 assumption, 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. DMEK) has become an alternative to full thickness keratoplasty and is a promising tool to enhance the outcome. However, there are still challenges for the future. One of these challenges is the management of the immunologic responses to eliminate intraocular tumors. Since inflammation is only one component of most retinal diseases, further investigation of adverse effects and long-term follow-up on the anti-inflammatory medications are warranted.

**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 responses to eliminate intraocular 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 using an IVIS imager. Tumor-specific OT-1 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-dependent tumoricidal activity within intratumoral macrophages. Therefore, restoring tumoricidal activity in intratumoral macrophages is critical for CD8+ T cell mediated elimination of ocular tumors.
• 3651  
**Individual ONH blood flow patterns during changes in perfusion pressure**  
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(2) Center of Medical Physics and Biomedical Engineering, Vienna  

**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**  
STALMANS I  
University Hospitals Leuven, Leuven  

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 vessels 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?**  
PINTO LA  
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**  
JONAS JB  
Mannheim  

The blood pressure in the central retinal win is supposed to be at last as high as the orbital cerebrospinal 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 glaucomatos 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 (LCSA) 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 LCSA.

**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 LCSA would modulate gene expression, including LDLR. Expectedly, we found that increasing the intake in omega 3 LCSA and lowering linoleic acid increased LDLR expression and improved the incorporation of omega 3 LCSA.

**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 LCSA in AMD.

**3662**

Aflibercept in clinical practice: Evaluation of the first 50 patients treated with anti-VEGF 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 a retrospective 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 59-98 years) were evaluated. Mean baseline visual acuity was 0.79 LogMar (STDEV 0.43) at baseline and 0.66 at follow-up (STDEV 0.40) (P < 0.01). Mean follow-up was 1 to 4 months (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. Thirty-nine 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 VA and VA gain rate. Patients who underwent anti-VEGF 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 naive.

**3663**

Lutein decreases complement factor D in age-related macular degeneration

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(2) University of Manchester, Manchester

**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 luten group (p=0.001), resulting in a 6.2% decrease from 2.31 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, rs193555, rs800292, rs1329428, rs1410996 and rs1753194 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 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.
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 today’s most widely spread treatment regimen. The drugs showed similar efficacy and safety in the Austrian population.

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
SIS: Ocular surface disorders in children

**3671**
Diagnosis and treatment of vernal conjunctivitis  
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INSERM UMR 968, Vision Institute, Paris VI University (Paris)

**Purpose**  
Keratoconjunctivitis in children is a rare and severe ocular surface pathology. Two main clinical forms need to be recognized: from mild to severe; however, vernal keratoconjunctivitis is the more common of these severe ocular surface impairments. 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 occur in different populations. 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  
MORTEMOSQUIE B  
Bordeaux

**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  
Nottingham

ABSTRACT NOT PROVIDED
Noninvasive assessment of the tear film stability in children

**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 test 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 valuable method for evaluating both the quality vision and the BUT in children with MGD.
RUNX2 expression in conjunctival melanocytic proliferations

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Purpose
To investigate the distribution and expression of macrophage phenotypes and complement activation in conjunctival melanoma tumors.

Methods
Liberal sections of central and peripheral choroid/conjunctiva from young (<40 years), aged (>70 years, n=4) and AMD (>70 years, n=8) human post-mortem eyes were immunostained with antibodies to leukocyte and macrophage markers. Colony assays showed similar patterns of response, with surviving fractions of 0.2 and 0.5 for CRMM1 (VPA 0.3125 mM) and CRMM2 (VPA 2.5 mM) 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
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.

Macrophage markers and C3d in the central & peripheral choroid of young, aged and AMD

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Purpose
To investigate the differential expression of histone deacetylases (HDACs) in human melanoma cells and primary melanocytes, and to assess the effects of VPA, a broad Class I and II HDAC inhibitor, on cell viability and growth.

Methods
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 inhibited cell proliferation and colony 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.

Results
Compared to young, aged and AMD eyes, localised to Bruch's membrane and choriocapillaris, with 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 eyes showed increased numbers of CD163+ macrophages (M2, proangiogenic) in choroidal and, in central vs peripheral retina. 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 choiocapillaris, 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.

3688 / 5005

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 to 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 immunostained 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 inhibited cell proliferation and colony 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.
**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 protein 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 present in 78% of the cases. Less often, we noted proptosis, or a diminished ocular motility. The radiologic examination (CT-scan, NMR, doppler ultrasound examination) found an inflammation localized to the orbital fat, to the lacrimal 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.  

**Conclusion**  
Treatment lies on surgical excision if it is safely. Corticotherapy is often 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.

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**3687 / S022**  
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 intrabulbar 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.
Role of anti-VEGF

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
Most promising findings can be obtained from trials employing 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

Role of corticosteroids

PURPOSE
Diabetic Macular Edema (DME) management has been revolutionized by the advent of intravitreal approach. Aim 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 employing 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

Role of vitrectomy

ABSTRACT NOT PROVIDED

ABSTRACT NOT PROVIDED

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 vacuuming during vitrectomy.

Methods
Comparative retrospective study of rhegmatogenous complications occurring during and after vitrectomy between two groups of consecutive patients. Group G400 included 1432 eyes vitrectomized with 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 = 0.001). 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 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 result 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, interventionnal case series, we included 49 patients (98 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 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 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=0.564; 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 decrease 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 than 80% of the patients, after ERM surgery. Most of the eyes show persistent macular thickening, but this does not seem to have influence in 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 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.

**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 vitreous 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.
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.

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 highly toxic. We screened a library of 1869 individual genes in cultures of primary murine RGCs. We developed a magnetic protocol for screening, to animal models, and hopefully to the clinic

Changes in retinal ganglion cell morphology after optic nerve crush and experimental glaucoma

KALENSKYAS G
Kaapio

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 laser 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.

Results After 6 weeks of glaucoma, 31% of axons died, but there was no loss of YFP-RGC bodies. 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 < 0.001), 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 tuberculous 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-TB 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 principles 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 choroidal 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 cases where angiographic work-up is deemed necessary.

• 3844
How a benign granulomatous uveitis can become a killer case

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Purpose: How a benign granulomatous uveitis can become a killer case

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.
TB or not TB...or what else?!
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(1) Torrette-Ancona
(2) The Eye Clinic, Politecnico 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. In fact, 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.

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
CHAUVES 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 patient’s 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 patients. There are special anatomical features that predisposed this group of patients 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 hypotonic maculopathy. Therefore, pre-operative assessment must include axial length measurement and careful 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.
**SIS: The blue light photoreceptor and ipRGCs: Review and update of their role in human health**

- **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
  KARDON RANDY (1, 2)
  (1) Department of Ophthalmology and Visual Science, University of Iowa College of Medicine, Iowa
  (2) Department of Veterans Affairs, Iowa
  **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 stimuli were 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.

- **3864**
  The importance of blue light exposure to circadian integrity and general health
  LUCAS R
  Faculty of Life Sciences, Manchester
  Melanopsin-expressing retinal ganglion cells are capable of supporting an array of accessory 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.
Melanopsin and its role in photophobia

KARDON RANDY (1, 2)
(1) Department of Ophthalmology and Visual Science, University of Iowa College of Medicine, Iowa
(2) Department of Veterans Affairs, Iowa

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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(2) Laboratoire Hubert Curien (UMR CNRS 5516), University Jean Monnet, Saint-Etienne
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(4) Impulsion S&S, File Optique Vision, Saint-Etienne

**Purpose**

Anterior and posterior stroma of human cornea present different biophysical characteristics, the latter 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: 90µm 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, 1506FL (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±0.9µm/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 identified as a limiting factor.

**3872**

**Large optico-reconstructive corneal grafts in complicated cases**

BARRAQUER J

Instituto Barraquer, Barcelona

**Purpose**

Demonstration of different procedures for eye surface reconstruction and visual rehabilitation in complicated conditions.

**Methods**

Case 1: LASIK photokeratomeulosis 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 meticulous surgical technique, adequate postoperative medication (local and systemic corticosteroids, cyclosporine A eye-drops 2%), immunosuppressors, topical cycloplegics, etc. and vigorous postoperative follow-up control.

**3873**

**Spectral domain OCT-assisted “big bubble” deep anterior lamellar keratoplasty in keratoconus patients**

WYLEGALA E (1, 2), TARNAWSKA D (2, 1), WROBLEWSKA CZAJKA E (1, 2), JANISZEWSKA D (1), WOWRO B (1), DOBROWOLSKI D (1)

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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 (The iVue from Optovue Fremont California USA). Corneal thickness was measured preoperatively, after manual pre-cutting and after the big-bubble creation. Manual pre-cutting of corneal stroma revealed residual bed thickness of 240-270 µm (mean 256 µm). When residual corneal bed 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 Anatomy, Children’s Hospital Boston, Harvard Medical School, Boston
(3) Scheepens Eye Research Institute, Harvard Medical School, Boston

**Purpose**

To 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 rods (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=0.6745).

**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 lamellar 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 bacteria 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-sac conjonctivae (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%) and 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.

**Patch grafts 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 stable 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.
Initiating a glaucoma interest group in Belgium

STALMANS I
University Hospitals Leuven, Leuven

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.
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 3.2% 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 Unions 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  
CREUZOT C  
Department of Ophthalmology, Dijon  

**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.

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**4212**  
Geographic atrophy  
STAURENGHI G  
Ponte Lambro  

**ABSTRACT NOT PROVIDED**

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**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 choroideremia.

**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.

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**4214**  
Reccurrence 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 most of the cases and decrease the rate of complications. Long-term remission may be achieved in specific entities, after treatment discontinuation.
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
• 4221
Clinical study results with new wireless electronic subretinal implant alpha-ims

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SACHS E.1, STENGEL K (1), WILHELM B (5)
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(3) Mobility Training, Tübingen
(4) Klinikum Friedrichshafen, Dresden
(5) Steinsens Center Ophthalmal., Tübingen

Purpose
Restoration 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 TTN electrodes (Zrenner et al. Proc. R. Soc. B 2011, 278: 1489). 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 paracentral. All patients were able to perform the function tests except one. Two had decreased retinal function after surgery. Results in all other patients were: light perception 9/9; light localization 8/8; motion recognition 5/9; grating resolution 8/9 (up to 3.3 cycle/degree); Landolt C rings 3/9 (up to 6.0/6); 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 discrimination 6/9; improved outdoor mobility 5/9. Patients’ experiences: recognition of unknown objects, faces, colors, characters, touching objects, 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 development, immunity, neurodevelopment and arteriosclerosis

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(2) Embryo Genomeppic, CHU Paris Nord, Hopital Jean Verdier, Bondy
(3) INSERM U676, Hopital Robert Debre, Paris

Purpose
Identify cause of congenital syndrome with macular dystrophy, absent fovea in consanguineous family 6 yo girl with congenital nystagmus, slow vision after informed consent.

Methods
Family had complete ophthalmologic, neurologic, examination, brain MRI, genetic tests, array CGH, lipid profiles, vascular Doppler UP, Mouse,human fetal ISH

Results
Proband had congenital nystagmus and corpus callous 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 hippocamp hypoplasia. ABC4A testing was negative as 18 ARR genes. Parents have normal vision,ERG/VEOCT, angio and brain MRI. Array CGH showed 1148 homoygenous 3q23 deletion up to 6th introns of SGEF gene in 3 sibs. Sister had absent fovea on OCT; few vision and macular dystrophy; brother had decreased retinal function on multifocal ERG with normal vision. Girls have repeated infections. EHB hepatitis,dental abscesses. Well parents harbor same heterogenous deletion. Mouse antibody In situ hybridisation mapped to retina! Human Fetal brain cortex ISH was positive: SGEF controls leukocyte trans-endothelial migration, 1st phase of arteriosclerosis. Mother with high cholesterol 212mg/dl and hype-triglyceridemia had normal cerebral arteries doppler US normal examination w/o arteriosclerosis 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-hre65 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-hre65 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.

Results
Ten patients were included in an ongoing study. All patients were able to perform the function tests except one who had decreased retinal function after surgery. Results in all other patients were: light perception 9/9; light localization 8/8; motion recognition 5/9; grating resolution 8/9 (up to 3.3 cycle/degree); Landolt C rings 3/9 (up to 6.0/6); 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 discrimination 6/9; improved outdoor mobility 5/9. Patients’ experiences: recognition of unknown objects, faces, clothing, characteristics, touching objects, 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

• 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 114 cases (66.7%). Viral distribution determined 55 CMV retinitis, 48 VZV retinitis, 34 HSV 1 or 2 retinitis and 9 EBV panuveitis. Non viral 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 (39%) followed by a primary intracocular lymphoma (12,1%), a bacterial aetiology (7,5%), Behcet’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
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 newborns 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 retinocochloidal 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.

Circadian 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 study 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 disturbances were applied. After a follow up of 3 months, the patients with persistent 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 treatment 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.

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. Plasmalogens 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 plasmalogens in the control of retinal vessel development through PUFA release from their sn-2 position.
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.

**4231**
Genetics of keratoconus

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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

**4233**
Inflammation in the pathogenesis of keratoconus

JUN A
Baltimore

**4234**
Oxidative stress in keratoconus

MENEZO ROZALEN JL, PERIS-MARTINEZ C
Fundacion Oftalmologica del Mediterraneo, Valencia
Endocrinology and keratoconus

GATZIOFAS 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 binoocular chromatic pupillometer (Bino L, 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 characterization 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 the 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 ophthalmic centre in Poland – the Department of Ophthalmology at the Jagellonian 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 ocudolastic surgery (epicanthus, lid coloboma, exotropia and exotropia, trichiasis, distichiasis, lid replacement, free skin transplantation), cornea transplants (first in Poland), glaucoma surgery (sclerotomy cricotica posterior superficialis), cataract surgery (cataract iridectomy technique), clear lens surgery in myopia (before Fukada).

**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 department of 4243 patients was performed. Diﬀerent forms of pituitary tumors were found: the classic tumor pituitary apoplexy, accidental during MRI analyses and during treatment for an pituitary adenoma. Of the 82 macroadenomas, found in the notes over 5 years, 10 cases had posterior pituitary apoplexy, which is a higher incidence than described in the literature. In 17 cases an apoplexy was found, which is a higher incidence than described in the literature.

**Results**
In 17 cases an apoplexy was found, which is a higher incidence than described in the literature. In 17 cases an apoplexy was found, which is a higher incidence than described in the literature.

**Conclusion**
The differential diagnosis is important in neuro-ophthalmological clinical practice. The different MRI patterns will demonstrated during the presentation.
**4245**

**Strabismus and visual acuity in children with ocular coloboma**

**ARNAUD M, NADEAU S, AZIZ A, HAMDAN J, DENIS D**

**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 microphthalmia. There was no significant difference between children in group I and II. 29 Colobomatous anomalies were found in group I and 17 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.

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**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 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.
Combined approach: practical tips

MCNAUGHT A
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(2) Cranfield University, Bedford

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 adjustable suture techniques
3) 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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(2) Center for Nano and Biophotonics (NB Photonics), Ghent

**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 analyses the intravitreal mobility of both model polymeric beads with different sizes and surface groups, as well as gene nanomedicines composed of poly(amide amine)s and plasmid DNA.

**Results**

Cationic nanoparticles were readily immobilized in the vitreous humour, while anionic polymeric beads remained mobile. Surface modification with the hydrophobic polymer polyethylene glycol (PEG) resulted in the best mobility of the polymeric 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.

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**4263**

Ghrelin's expression in the eye and its implication in the reduction of intraocular pressure

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**Purpose**

To investigate ghrelin 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-acetyl ghrelin was subconjunctivally 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 lecin, 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 a smooth muscle actin. Ghrelin, but not des-acetyl 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**

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**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 diabetes 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 analyses showed significant reduced levels of omega-3 PUFAs including docosahexaenonic 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 PDR. 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.

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**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® TrueEye hydrogel SCL, saturated with moxifloxacin solution 0.5% (Avelox) and levofloxacin solution 0.5% (Tavaicin), 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. Aquous 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 humour 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 humour.3. Ophthalmic drug delivery through contact lenses increases bioavailability.
Circulating 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 show 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.

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 Nfr2, 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.
Course 14: MGD - Pathophysiology, diagnosis and clinical treatment

**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 widespread dry eye disease that affects millions of patients worldwide.

**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 endogenous and exogenous 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 hyperpermeatization 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.

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**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 overt 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 hyperpermeatization of the ducts and hardened secretion. 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 secretion 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 atrophic 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 and receive not enough attention. In patients with ocular discomfort it is important to investigate the blinking action, the lid margins (crusts, vascularity, 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.
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 illumination. The extent to which reduction of target contrast and changes in retinal sensitivity caused by the presence of a glare source affects both thresholds remains to be established. We investigate how CA is affected by glare source intensity, surround luminance and 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 (Optical & 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/m² in the pupil plane), three eccentricities (5, 10 and 15 degrees), and three background luminances (1, 2.6 and 26 cd/m²) 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(6):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 illumination, a more pertinent parameter in studies of DG. DG thresholds were estimated with a staircase procedure: the retinal illumination 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 illumination is approximately constant and independent of source size. On the other hand, pupil plane illumination increases as source size increases.

**Conclusion** These findings suggest that DG depends mostly on localised retinal illumination, 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 stronger 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, corneas 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 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 (1/380,000) 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-/- mice. 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 Brl/ia 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 evoked potentials showed progressive decrease of N1+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. Brl/ia 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 reflexes 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.

• 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 of a 12 months 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.

• 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-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 bioclectrical 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.
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 immunoneurofluorescence 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.

Purpose 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 intravitreal ranibizumab injections combined with laser photocoagulation on 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 neovascularisation ( retina and/or anterior segment) were analyzed in 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.

Purpose 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 intraocular 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 intraocular 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.

Purpose Vasomotor reaction of retinal arterioles in hypoxic and ischemic conditions

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Purpose Retinal blood flow is autoregulated by the adaptation of the vascular tone of resistance vessels (arterioles, capillaries) to changes in 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 hemodynamics 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 V/flow 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 insulins-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.
Treatment of macular oedema due to branch retinal vein occlusion with laser induced arterial constriction. Twenty years results of retrospective interventional study

REHAK J

Olomouc

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.
**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 reluctance 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 reluctance 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.

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**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 choriocapillaritis as for MEWDS or APMPE.

**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 process 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.
• 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 well 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.

• 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 neovascularization (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 injections. 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 56.9±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±54.7 µm vs 281±161.3 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=0.06; 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.
• 4431
Keratoconus and keratectasia

COLIN J
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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 descemet (d) and preDescemet (p/d) 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 (p/dDALK), whereas 21 (22.1%) eyes underwent manual lamellar dissection (pDALK) 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-correlated visual acuity was significantly better in p/dDALK group than in pDALK group at years 1 and 2. But, at the final examinations, there was no significant difference between the study groups (0.25 ± 0.02 logarithm of the minimum angle of resolution in p/dDALK group and 0.32 ± 0.15 logarithm of the minimum angle of resolution in pDALK 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 ≤30º 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. Symmetrical-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 & corneal curvature.

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.

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 ≤ 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 V, 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 1 (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 < 0.02). Corneal higher order aberrations did not change after the procedure (p > 0.05).

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.

SIS: Current management 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 months 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, Ovay, 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  
H-S 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 hydroxypropylguar 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 Non, Lipids, cornea vital coloring tests, cornea thickness (μm), 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 peroxiredoxin 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 in 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 reactivity. 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 was 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 computer-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 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 neovascularization area.  
**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 Sytane 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**
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 consecutively and prospectively selected. Participants were classified depending on the results of standard automated perimetry (SAP) and intracocular 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<0.005) 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). AUCs were observed for the rim area of Cirrus (0.954; 95% confidence interval [CI]: -5.9±6.1 dB (p<0.001) for the normal and glaucoma groups, respectively.

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.

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 21-37 mm). 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±1.55mm) was associated with axial length (P=0.001; OR=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.
**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.

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**Marginal 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 pseudophakic 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 surgeons preference and experience.
**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 proton therapy between June 1993 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 22 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 39.0% at 15 years and the specific survival rate was 89.9% 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.

**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 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 follow-up time was 5.8 years (range, 6 months–16.8 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 the irradiated area in 9 patients.

**Results** The 5-year cumulative rate of local recurrence after the second treatment was 7.69% (7 patients among 26 reirradiations); 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=0.002).

**Conclusion** A second course of PBT for recurrent uveal melanoma was associated with a relatively good probability of local control and a low enucleation rate. This retrospective analysis suggests that survival in reirradiated patients is not compromised by administration of a second course of PBT for recurrent uveal melanoma.

**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 recurrences? 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 criteria were a minimum of two echographic eight measurements after treatment and a follow up of a minimum of 6 months, exams were made by the same specialist (PC).

**Results** Over the 1155 patients treated, 779 encountered the inclusion criteria. The mean decrease is 6% 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 encountered 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 significant difference for local control if the tumor increases (p<0.0003).

**Conclusion** Analysis of the 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.
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 (8.3%), aged between 13 and 24 years at diagnosis, treated in our hospital in 1965-2006. 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 1994, 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 4.4-11.7 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 8, 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.

Fine needle aspiration biopsy in uveal melanoma: the Curie experience

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Purpose
In order to possibly 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 tumour with 25 or 23 gauge needles. Histoacryl glue was used after transcleral biopsies and cryotherapy for transvitreal biopsies. Patients signed an informed consent.

Results
188 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 UNA for CGH array was present in 76% 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 and 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.

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 young female of 19 years of age, with no hepatic metastatic disease.

Methods
A young Algerian girl was sent 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. Ruberosis 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. One chest drain was created. Care was turned to the right lung. The left lung was not involved 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 oculomotor pathologist diagnosis was an epithelioid ciliary body melanoma of 10x10 mm. On April 3rd a pleurodesis was created with pleural biopsies of the Thoracic Surgery Unit. Mesothelial pleural hyperplasia without malignancy sign was diagnosed. A chemotherapy with Muphoran has been advised by oncologists but 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 mechanisms of responsible mesenteric lesions for death in the hepatic vicinity has to be explained.

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, epitheloid 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 (CGH, NimbleGen 72K microarrays) monosomy 3 or partial deletion of 3p associated with low 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, quality, 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 D1/DD5/D15 (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 PI 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.

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**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 eyelashes. 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 infrared 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 strabismus 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**

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**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 periphery. 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.

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**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 temporal inferior RNFL thicknesses (133.18 in controls vs 125.63 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 r=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:10ng/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<0.0003), and P<0.0004, and P=0.0008, respectively. In NT-4 supplemented media, the numbers of regenerating neurites (P<0.0001) and the numbers of TUNEL-positive 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.

**4477 / T142**
The use of propranolol in the treatment of periorbital 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 periorbital 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 series 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.

**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.
**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 major 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 (50µM) for 24h hours. Autophagy gene activation was studied by cDNA PCR array.

**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.

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**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 (50µM) 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.

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**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 (anokia). Phagocytic clearance assays of the engulfment of anokic 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 anokic 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 anokic 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 TSHB-1 (phagocytosis bridging molecule). Similar expression patterns were also observed in the anokic 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.

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**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 characteristics 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 exhibit 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. Ca2+ dynamics of APRE-19 cells were recorded using fluorescent microscopy after mechanical stimulation. Various Ca2+ 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 sarcoplasmic 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 Ca2+ kinetics model of RPE was able to reproduce the Ca2+ dynamics of APRE cells with high accuracy with above 0.97 cross-correlation. Further, including stretch-sensitive ion channels explained the Ca2+ 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  
Vertau

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 (MIRROR).


**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 velocimetry (LDV), while breathing ambient air and pure oxygen.

**Methods**
30 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, InSedos, 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<0.001 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 intraocular 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 triamcinolone 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 significant 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.
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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(10) Allergan, Marlow
(11) Klinikum Ludwigshafen, Ludwigshafen

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 14.1 days (503.1 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). Reductions in central retinal thickness were also observed. Intraocular pressure measurements over 25 mmHg 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.

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 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 14.1 days (503.1 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). Reductions in central retinal thickness were also observed. Intraocular pressure measurements over 25 mmHg 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.

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 volunteers (mean age 30.6 years) underwent digital retinal vessel analysis using the retinal vessel analyser Imedos Systems (Germany), (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.
\section*{• 4631 Infection and inflammation in Boston Type 1 KPro}

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\textbf{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 1 surgery.

\textbf{Methods} Review of clinical experience through the last 6½ years dealing with Boston KPro type 1 surgeries and subsequent possible complications such as melting, thinning, extrusion and endophthalmitis.

\textbf{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 metalloproteinasises 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.

\textbf{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.

\section*{• 4632 Boston Keratoprosthesis in 2012: preventing complications and optimizing outcomes}

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\textbf{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.

\textbf{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 KPros 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.

\textbf{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 appositions. Primary Boston KPro surgery provides good outcomes and device retention in situation such as limbal stem cell deficiency where traditional keratoplasty does poorly.

\textbf{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.

\section*{• 4633 Advances in imaging of the OOKP lamina}

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\textit{Brighton}

\textbf{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 corneoscleral envelope initially through suturing. Later on, the overlying bucual 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 is aided by periodic radiological imaging.

\textbf{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.

\textbf{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.

\textbf{Conclusion} Much work remains to be done to improve imaging of the OOKP lamina. Considerations include image resolution, speed of acquisition, radiation dosage, costs, and repeatability.

\section*{• 4634 Oculoplastic complications of OOKP surgery}

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\textbf{Purpose} To report the incidence, types and management of oculoplastic complications following OOKP surgery.

\textbf{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.

\textbf{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.

\textbf{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 Metropia Visual Stimulus Generation software (Cambridge Research System) at $0.7, 2.20, 3.50, 10.4$ 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 ($\log$MAR) with increasing glare settings was observed from 0.12 without BAT to 0.27 with BAT at High. Mean visual acuities ($\log$MAR) 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 successful 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 Image software, the tear meniscus height (TMH) was measured and the x-y-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±0.08mm. 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 with a handheld dermatological CM.
Methods Using the handheld dermatological reflectance laser-scanning microscope (Vivascopc 3000, MAVIG GmbH) equipped with a 830nm laser, we observed cornea, bulbar and tarsal conjunctiva, eyelid margin, lacrimal puncta and palpebral 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 Vivascopc3000 made it possible to easily access ocular and periorcular tissue that remained challenging to observe with ophthalmological CM. With a definition of 1µm, the Vivascopc3000 could allow non-invasive optical biopsy of all normal and pathologic ocular surface as well as periorcular 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 Vivascopc 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 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 a supplementary dimension by allowing the use of fluorescent markers liable to add a new structural information relevant to the diagnosis.
Methods Ex vivo animal and human corneas, healthy volunteers and patients were successively examined using the multi-laser vivascopc 1300 (MAVIG GmbH, Germany) equipped with 4 lasers (488, 635, 785nm) and the corresponding emission (Em) filters. For each excitation (Ex) wavelength (488, 635, 785nm), 3 observation modes were available: pure reflectance (λEx = λEm), mixed reflectance (λEx = λEm) and fluorescence (Ex ≠ Em). 200–400µm skin and periocular tissues were examined using 200x magnification.
Results Using excitation and reflectance, the 3 Ex-λ showed complementary structural informations of the corneal surface. The whole corneal examination could be performed in 15 minutes. Among the 5000+ images, we have observed corneal structures, Descemet membrane, whole corneal thickness, superficial keratitis, stromal corneal layers, keratoconus, blood vessels, corneal ulcer, limbal area, limbal capillaries, limbal vessels, Meibomian glands, tarsal glands, conjunctiva, lid margins, lacrimal puncta, palpebral skin, lid margin and lid margin glands.
Conclusion IVCM is proposed as a new era for clinical exam of cornea and ocular adnexa, allowing high resolution images of tissues, providing critical informations otherwise difficult to obtain. Future investigations will be needed to compare these results with histopathological samples.

• 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 corneas 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 microkeratome 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 Sawadis theory. The new presentation of the dielectric spectra, of δε (delta epsilon) = δε(ln f ) was used. The presented method and the Sawadis 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 different relaxation regions with two structural distance parameters δ, 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. HOA variations 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 aberrometer can be used in our daily practice for an objective and reproducible assessment of the BUT.

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**4647 / T032**

Corneal respiratory function by FAD autofluorescence lifetime

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**Purpose**
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 b-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.

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**4646 / T030**

Tear film break-up time evaluation by real-time wavefront aberrometry in adult patients with meibomian gland dysfunction

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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=0.006) in all patients in Group 2 compared to the normal tests subjects (Group 1).

**Conclusion**
Studying the HOA variation is a valuable method for evaluating both the quality vision and 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 patients with severe MGD.

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**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 (T0) and one month postoperatively (T1-M). The anterior chamber depth (ACD), the angle-opening distance at 500μm (AAD500), the trabecular-iris space area at 500μm (TISA) and the scleral spur angle (SSA) in the temporal and nasal quadrants were measured. Patients were classified based on their surgery: the surgery was penetrating keratoplasty (PK group), it was descementer’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 increased from 3.13mm (SD 0.69) to 3.55mm (SD 0.341) after PK (p<1) , and from 3.22mm (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 0.20mm (SD 0.126) to 0.23mm (SD 0.100) (p=0.03) in the TISA and after PK, mean anterior chamber angle width decreased from 0.27mm (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 0.25mm (SD 0.089) to 0.26mm (SD 0.083) (p=0.207) in the TISA and after PK, from 0.269mm (SD 0.114) to 0.321mm (SD 0.068) (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.
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). Visual 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 veins 65% ± 6% and the arteriovenous (AV) difference was 33% ± 6%. The oxygen saturation in the venules correlated with the visual field mean defects (r = 0.39; p < 0.008 and r = 0.26, p = 0.015 respectively, n = 56). The AV difference decreased significantly as the visual field defect worsened (r = 0.38, n = 3000); 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 veins 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.

Oximetry in glaucoma: correlation of metabolic changes with structural and functional

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Purpose: To elucidate the effect of benzalkonium chloride (BAC) on the intraocular pressure (IOP) lowering efficacy of a local ROCK-inhibitor (AMA0076).

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% BAC. 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: 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% BAC was 38%, 45% and 53%, which was significantly stronger compared to their BAC-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% BAC.

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 episceral vein catarization in order to induce stable elevation in intraocular pressure (IOP). CXCR3 antagonist or the vehicle only were subconjunctivally injected in glaucomatous eyes (n = 10 in each), which were assessed for IOP weekly during two months. Aqueous humor outflow and trabecular filtering 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 filtering 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 filtering function and subsequent aqueous humor outflow, further protecting the retina against IOP-related degeneration.

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 immunohistochemical 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 was a trend (p = 0.09) could be distinguished. Topical treatment with 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 ROCKs 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.
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 C57Bl/6 mice. Immediately after surgery SD1D4 (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 ng/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 (SD1D4) 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=0.03). A trend towards an increased bleb area after SD1D4 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.

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 intraocular 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, 8th 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 dependent and sustained manner after a single topical dose in Dutch Belted rabbits. This new class of ROCK inhibitors has potential therapeutic value for the IOP lowering treatment of glaucoma.

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.
**4663**

**Natural history of an early diagnosed retinocytoma: case report and literature review**

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**Purpose**

To study the ophthalmoscopic 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 and ecorgraphic evaluation. Monthly ophthalmoscopic and ecographic evaluation were recommended. Detailed fundus drawings and fundus photographs and descriptions of the retinocytoma were collected.

**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 chorooretinal 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.

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**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 naive 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 eye was also treated with cryotherapy while all eyes underwent transfundal 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.

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**4664**

**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 melphalan 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 juxtapapillary 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.
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-Fluoracil (1%5-FU), followed by extensive surgery and adjuvant (post-surgical) 1%5-FU topical chemotherapy in the management of corneo-conjunctival 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 conjointal 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 local irritation. No-one patient discontinued therapy because of 5-FU side effects. No surgical amniotic membrane repositioning due to early sutures dehiscence. 1%5FU, and aesthetic results were obtained by surgery. Two patients (5%) needed short-term.

Conclusion Combined neo-adjuvant topical chemotherapy with 1%5FU, extensive surgery and adjuvant 1%5-FU topical chemotherapy appear a safe and effective combined treatment in the management of conjunctival SCC.

Ocular lymphoblastic leukemia in the eye region

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Purpose Manifestations of acute lymphoblastic leukemia (ALL) in the eye are rare and mainly occur in children. The purpose of this study was to investigate clinical, histopathological and genetic characteristics of Danish cases with ophthalmologic 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 A 51-year-old woman was evaluated for decreased vision in her right eye. On examination, her visual acuity was 20/20 in the right eye (RE) and counting fingers in the left eye. Abnormalities were confined to the RE. Slit lamp examination revealed a lacrimal gland mass. Cytogenetic analysis of the specimen was formed by 32% of lymphocytes and 68% of normal cells. The mass was aspirated and had small new vessels in the stroma. An anterior chamber aspirate was performed, and a pink pseudohypopyon occupying 40% of the AC. The iris was corrugated and small new vessels in the stroma. A band-like infiltrate was observed in the surrounding tissues. The mass was aspirated and had small new vessels in the stroma. A band-like infiltrate was observed in the surrounding tissues.

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. One patient responded well to therapy.
**Schwannoma of the ciliary 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 ciliary 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.

Histologically the tumor was determined as Verocay schwannoma (cellular solid component or Antoni A type). Immunohistochemical study revealed a positive reaction for vimentin, protein S-100 and neuron-specific 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-Quart. Moreover, the test serves to assess whether a patient 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 field 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, affect 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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Antwerp

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 biomeetry, 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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Brest

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 (DQAS) 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-Quart. 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
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 r(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**

MOURTOUKOS S

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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**

TSERVAKIS I.

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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**

ANASTASAKIS A

Department of Ophthalmology, University Hospital of Heraklion, Heraklion

There is a basic question. Is it necessary to drain? Because if it is not necessary then it is better to avoid drainage because 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 anaesthesia.

**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.
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 for 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 polyethylene terephthalate painted with six matt colour sprays: red, white, brown, ochre, yellow, purple 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 five following colour spaces were favourable: the L*a*b* colour space ([1.5,3.5],[8.0,1.9] and [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*a*b* colour space is highly sensitive; therefore, it is most effective in distinguishing small retinal 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*a*b* and HSV for automatic distinction.

A shift in the balance of vascular endothelial growth factor and connective tissue growth factor by bevacizumab causes the angioblastic switch in proliferative diabetic retinopathy

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(4) Pathology, University Medical Center Utrecht, Utrecht

Purpose In proliferative diabetic retinopathy (PDR), vascular endothelial growth factor (VEGF) and connective tissue growth factor (CTGF) may cause blindness by neovascularization followed by fibrosis of the retina. It has previously been shown that a shift in the balance between CTGF and VEGF in the eye is associated with this angioblastic 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, and CTGF correlated positively, and VEGF correlated negatively with the degree of neovascularisation. It has previously been shown that intravitreal bevacizumab causes 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 angioblastic switch, and identifies CTGF as a possible therapeutic target in the clinical management of PDR.

Severeity 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 (-0.0004) or YB thresholds (r2=0.0022). Patients with no DR often exhibited normal visual acuity (~1.0 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 diabetes 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.
**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 (BRCPCs) and rat glial cells.

**Results**

Co-cultures of BRECs with BRCPCs 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 MDRI 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 the in vivo VEGER-dependent changes occurring in DME.

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**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 (SFT) 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. SFT 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, 30 days after surgery.

**Results**

Eighty-four eyes of 67 patients who had cataract surgery were included. Mean SFT of SD was 215.9 ± 69.4 µm before surgery, 211.3 ± 67.3 µm at Day 7, 226.5 ± 68.9 µm at 1 month and 230 ± 62.2 µm at 3 months. Mean SFT increased significantly between before and 3 months after surgery (p<0.004). For diabetic patients mean SFT increased in the same proportion as in general population but later (Day 7 versus Day 30). No significant difference was observed between group with Diabetic Retinopathy (DR) and group without. For the only patient who developed an Irvine Gass Syndrome, SFT increased.

**Conclusion**

Mean SFT 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.

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**Subthreshold micropulse photocoagulation with true yellow 577nm diode laser for macular oedema**

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**Purpose**

Subthreshold, or tissue sparing, Diode Micropulse Photocoagulation (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 significant macular edema (CSME) due to diabetic retinopathy, venous branch retinal occlusion and central serous retinopathy.

**Results**

Controls performed 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 intraocular damage.

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**Peripheral capillary network enlargement in diabetic maculopathy**

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Ophthalmologie, Reims

**Purpose**

Diabetic macular edema has been associated with increased intraretinal levels of VEGF. Therefore, ischemia is probably part of the pathophysiology. 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 November 2011 and March 2012. 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?
FUCHSLUGER T
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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 requiring 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 successfully developed biomaterial

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Purpose
Development of an biomimetic artificial cornea to provide a long term stable keratoprosthesis 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, keratoprosthesis 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

GRiffith M
Ottawa

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 arteriolar 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 arteriolar 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 arteriolar 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.

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**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 urine 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 (means standard error: 1.35±24μm vs. 1.42±18μm, P=0.035), whereas adjusted mean CRVE was similar in all participants. CRAE and CRVE were positively correlated to GFR (r²=0.09, P=0.005 and r²=0.09, P=0.006, respectively). In addition, CRAE was negatively correlated to UACR (r²=0.12, P=0.02) and no significant relationship between CRVE and UACR was found (r²=0.01, P=0.31). The observed relations between retinal vascular calibers (CRAE and CRVE) with renal function parameters (GFR and UACR) remained significant after adjusting for age, gender, mean blood pressure, smoking, glycaemia, 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.

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**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=51,28female:age-64.80yrs) and HE (n=51,28female:age-21.30y). The OAs 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 flow measurement of OA. Accuracy of MRI measures was studied using a vessel phantom ([3]-14mm). Six constant flow rates (5.54-34.41ml/min) were used as reference.

**Results** Phantom investigation showed good agreement between the reference and MRI measures with a percentage error:<7%. The mean and SD of RI (HE:0.68±0.08; HY:0.63±0.09), ΔV (HE:2.63±1.03; HY:1.85±1.23), and SI (HE:58.6±1.01, HY:66.3±0.03) of OAs volume flow rate curve were significantly higher in the elderly group compared to the young group (RLP: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±4.96ml/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.

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**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 administration of L-NMMA and phenylephrine signifi cantly increased resting ONHBF compared to phenylephrine (p=0.04). The relative decrease in OPP during suction cup application was comparable with all drugs administered.

**Results** Administration of L-NMMA and phenylephrine signifi cantly increased resting ONHBF 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 49% and 72%, p<0.05). In all three groups, the decrease in ONHBF was less pronounced than the decrease in OPP, but not signifi cantly 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.
**Quantitative and qualitative label free imaging using mass spectrometry in the context of an ophthalmic application**

**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.

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**Eye motion increases temporal visual field extent**

**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 = 1.2.10^-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 128.5° (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.
How to get your work published?

**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**
Course 15: Surgery of inflammatory eyes

• 4771
Surgery of the inflammatory cornea or sclera
BORUSES JR
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 management 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 fibrosis 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

• Posters T001 - T143, exhibited on Thursday ................................................................. 214
• Posters F001 - F123, exhibited on Friday ................................................................. 250
• Posters S001 - S137, exhibited on Saturday ............................................................. 281
• **T001**

**Relationships between estradiol, progesterone, and plasminogen activator inhibitor longitudinally during normal human pregnancy**

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(2) Applied Physics Laboratory, Johns Hopkins University, Laurel, MD USA, Laurel
(3) University of Debrecen Medical and Health Science Center Faculty of Medicine, Departments of Biochemistry & Molecular Biology, Debrecen

**Purpose**

To investigate the hypothesis that the plasminogen activator protein (PAI) rise in the eye is controlled locally instead of systemically. During pregnancy, systemic blood levels of estradiol (E2), progesterone (P4) and plasminogen activator inhibitor (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 Immulon 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 concomitant elevated systemic blood E2 and P4 hormone and PAI-2 levels, indicating the possibility of local control of proteinolytic 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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(2) Chronic inflammatory disease research center, Suwon

**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 proteoglycan E2 (PGE2) production in orbital fibroblast was also evaluated.

**Results**

Pirfenidone attenuated the IL-1β-induced COX-2 mRNA and protein increase. In electrophoretic 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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(1) Department of Histology and Embryology, Medical University of Warsaw, Warsaw
(2) Department of Ophthalmology, Medical University of Warsaw, Warsaw
(3) Department of Ophthalmology, Military Health Service Institute, Warsaw
(4) Department of Medical Genetics, Medical University of Warsaw, Warsaw

**Purpose**

Autosomal dominant optic atrophy (ADOA) is a genetically heterogeneous disease, with OPA1, OPA4, and OPA6 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 electrodiagnostic 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 transition in exon 2 predicting a premature stop codon (Q11X). The mutation co-segregated 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 haplosufficiency. 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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(1) Institute of Human Genetics, Polish Academy of Sciences, Poznan
(2) Hospital Metropolitano, Quito
(3) Bresner Systems, Spokane
(4) Department of Pharmaceutical Bacteriology, Poznan University of Medical Sciences, Poznan

**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**

Sequence analysis of lincRNA localized ~1kb from 5' end of STK24.

**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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(2) Department of Ophthalmology at Tishah University, Madinah
(3) Department of Ophthalmology at Eye and Ear Infirmary, Chicago

Purpose
To define the natural history, genotype-phenotype correlation and differential diagnosis of the Brittle Cornea Syndrome (BCS). Or Ehlers Danlos Syndrome (EDS) type VIII 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 retractive 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 300 μm 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 corneas is not a feature of the latter condition. A 14 bp insertion was found in exon 2 of ZNF469.

Conclusion
EDS VIA 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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(2) Department of Histology and Embryology Medical University of Warsaw, Warsaw
(3) Department of Medical Genetics Medical University of Warsaw, Warsaw

Purpose
To report on a Polish family with unusual corneal changes associated with the arginine 124 mutation.

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 strands.

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 high reflective deposits characteristic for granular corneal dystrophy. Genetic testing identified a heterozygous missense (IGC 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 in 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 mechanisms of the disease.

T007
NHS gene mutations in non syndromic cataract
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(2) INSERM U930, Equipe 2, TOURS
(3) Service d’Ophthalmologie, Nouvel Hôpital Civil, Strasbourg
(4) Service de Génétique, CHU Brestonnaou, TOURS

Purpose
Many genes can be involved in congenital cataracts according to different inheritance patterns. NHS (Nance-Horan Syndrome) gene is involved in a rare X-linked sydromic cataract associated with some mental abnormalities. 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 sydromic 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=16). The exons of NHS gene were amplified from genomic DNA by PCR, and the amplicons were directly sequenced. NHS gene copy number was determined by PCR, and the amplicon were directly sequenced. NHS gene copy number was determined by PCR.

Results
We identified 6 punctual mutations of NHS gene in different patients: 2 missenses mutations, 3 frameshift mutations and one intronic mutation. The analysis of NHS gene 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 had a relative low expression.

Conclusion
We found 2% mutations of NHS gene in our cohort study. For some patients we can’t yet absolutely eliminate a Nance Horan Syndrome 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 sydromic cataracts.

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 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, electoretinogram 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 hypopigmented 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-photorceptors. Farnsworth Munsell 24-hue test revealed preserved color vision. Visual field showed a central scotoma. Electoretinogram recordings demonstrated a still preserved rod and cone function. Genetic study revealed a compound heterozygote mutation for RDH12 in exon 6 (p.Ala269fs and p.Arg234His). Two years later VA decreased to 1/100 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, BE, C3, FHR 1-3, FRH3 and ARMS2/HTRA in Age-Related Macular Degeneration**

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(2) Ophthalmology Clinic Universidad de Navarra, Pamplona

(3) Multicenter group, Pamplona

**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, BE, 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 Innovacion.

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**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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(2) Larissa neurology university hospital, Larissa

**Purpose**

Diabetic retinopathy is a sight-threatening 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 hypo-fibrinolysis.

**Methods**

A case control study was carried out Assessment of diabetic retinopathy was performed by ophthalmoscopy and fluoroscopy 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 & 332 cases observed

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<th>rs1050813</th>
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<td>Pearson’s p value is 0.575255</td>
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</tr>
</tbody>
</table>

**Conclusion**

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

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**T011**

**Non-syndromic retinitis pigmentosa: Phenotype-genotype correlation in twelve Tunisian families**

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(2) Jules-Gonin Eye Hospital, Lausanne, Lausanne

**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 characterized by preserved para-arteriolar retinal pigment epithelium and yellow round deposits in the posterior pole and there was no hemerolacia.

**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.

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**T012**

**Vascular endothelial growth factor A genetic polymorphisms and AMD in Tunisians**

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(2) Immunology Research Laboratory of Visceral Transplantation and Immunopathology, Tunis

**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 polymorphisms (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 = 0.002). Furthermore, the mean of VEGF plasma level is significantly higher (170.97 pg/ml) in patients with enhanced VA compared to those with loss of 3 or more lines in visual acuity.

**Conclusion**

In addition to the higher risk for exudative AMD in Tunisian patients with the -2578 A VEGF, our results show that this allele 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.
• **TO13 / 2466**

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

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(2) **Medical University, Lublin**
(3) **Dep. Clinical Genetics, Lublin**

**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=0.09). 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=0.75). In group of women with POAG the allelic frequency was also similar to men (respectively, in women: TT-41.2%, TC-50%, CC-4.8% 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%), compared 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 allele form is most frequent in NTG women.

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**• TO14**

Nailfold capillaroscopic examination and T786C endothelial nitric oxide synthase polymorphism in normal tension glaucoma patients


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(2) **Dep. Clinical Dermatology, Venereology and Paediatric Dermatology, Lublin**
(3) **Dep. Clinical Genetics, Lublin**

**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 capillaroscopic 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: megalocapillaries or dilated capillaries (44.4%), ruffled/bushy (18.9%), coiled (17.1%). Assessing the T786C polymorphism of eNOS gene in NTG patients, TT genotype was present in 36.3% patients, TC in 52.6% and CC in 11.3%. There were no correlation between SNP variants and capillaroscopic results nor cold provocation test (p=0.09 and 0.2, respectively).

**Conclusion**
The T786C polymorphism of eNOS gene does not influence the capillaroscopic results. The high incidence of sclerodermia-like changes in capillaroscopy in NTG needs further studies.

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**• TO15 / 2465**

Activity and epidemiology of a recently-opened ophthalmic emergency center in an University Hospital

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(1) service d'ophtalmologie, CHU Nancy, Nancy
(2) **Epidémiologie et Évaluation Cliniques, CHU Nancy, Nancy**

**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 ophthalmic 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 hours. 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 examination or treatment. Number of various daily ophthalmic 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 ophthalmic emergencies. An improvement of the general and emergency practitioners knowledge in regards to ophthalmic pathologies could allow them to diagnose and treat begin 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.

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**• TO16**

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 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%, 11.8% 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 university 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 visual, 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 blindness were defined as vision worse than 20/60, 20/60 to 20/100 and worse than 20/100 in the better eye, respectively.

**Results** In this study, 857 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 99%), 3.7% (2.5-5.0 CI 99%), and 7.4% (5.7-9.1 CI 99%), respectively. These findings were 3.7% (2.3-5.1 CI 95%), 1% (0.2-1.7 CI 95%), 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.

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**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 (74.3%), 77 ulcerative colitis (25.2%) and 1 macroscopic 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%), mydriasis (23.3%), eyelid secretion (12.2%), dry eye (9.5%), watering (6.8%), diplopia (5.4%), metamorphopsia (4.4%), 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 14% scleritis (n=1). No events was reported. Methotrexate was associated with dry eye (p<0.05).

**Conclusion** Ocular symptoms are frequent in IBD patients, but are nonspecific and rarely associated with ocular inflammation. Systematic oculomotor symptoms assessment is of poor value for diagnosing ocular inflammation in clinical practice in IBD patients.

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**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, arachnoida, 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 crural, 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 VISTAT 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 subarachnoidal 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 subarachnoidal 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 allele 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.

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**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.

**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**

**Purpose**
Different studies indicate that the presence of retinal microaneurisms, 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 microaneurysms.

**Methods**
Human retinas were obtained from 17 donors: 14 old donors and 3 middle-aged donors. Basement membrane proteins (collagen IV, laminin, fibronectin, nidogen), perlecans, 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 middle-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 diminished in Type II microaneurysms. In addition, MMP-9 was strongly expressed in microaneurysms producing basement membrane disorganization.

**Conclusion**
Collagen IV, laminin, fibronectin, nidogen and perlecan were increased, 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 diminished in Type II microaneurysms. In addition, MMP-9 was strongly expressed in microaneurysms producing basement membrane disorganization.

**T022**

**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 involved 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 operator 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 and 11 years, and 222.83 ± 3.53 (219, 226) for subjects aged 12-14 years. There was no significant difference with age 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.

**T024**

**Purpose**
To study the changes in choroidal development in normal children with no refractive error.

**Methods**
Fiftytwo children aged from 3 to 14 years with refractive error from 0-1.5 spherical 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 obtained in 96% of eyes examined. Mean (SD) choroidal subfoveal thickness was 287.17 (70.85) for children aged 3-6, 297.14 (66.92) 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.
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Conclusion continued until the proliferative period. After the HRF treatment, a decrease in the morphology of dermal collagen fibrils showed more prominent with the passage of day after treatment. Although an increase in inflammatory responses with inflammatory cell ingrowth compared to the control as well as a well-aligned collagen network structure at the nanostructural level. 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.

Methods Fifty nine samples of ocular pterygium and twenty samples of normal conjunctiva, surgically removed, were tested with immunohistochemistry, immunofluorescence and western blot analysis.

Results Between pterygium specimens and normal conjunctiva specimens, significant differences were observed in the expressions of proteins HSP90 (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 Hpyoxia-Inducible Factor-1a and HSP90 may have a role to play in pterygium pathogenesis.

Purpose Research has shown that HSPs participates in preserving HIF-1a function. In this study, HIF-1a, and HSP90, 70, expression and immunofocalization 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, immunofluorescence and western blot analysis.

Results Between pterygium specimens and normal conjunctiva 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 Hpyoxia-Inducible Factor-1a and HSP90 may have a role to play in pterygium pathogenesis.

Purpose The development of endonasal dacryocystorhinostomy is associated with the advent of nasal video endoscopy which enables a perfect visualization of the surgical site. As the inferior turbinate bones are close to the lacrimal duct orifice at the level of Hasner’s valve, anatomical variations of endonasal structures could be associated with the occurrence of epiphora.

Methods The results of nasal endoscopy 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 fossa 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 lacrimal duct stenosis (avec p >0.05). It appeared that there are major anatomical 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 anatomical 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 lacrimal duct stenosis was found. However it remains essential to perform preoperative nasal endoscopy in order to detect a possible cause of lacrimal duct stenosis and thus evaluate the feasibility of surgery.

Purpose The purpose of this study was to investigate the long-term effects of high radiofrequency (HRF) tissue-tightening treatment 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 groups 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.

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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.

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 surgical site. As the inferior turbinate bones are close to the lacrimal duct orifice at the level of Hasner’s valve, anatomical variations of endonasal structures could be associated with the occurrence of epiphora.

Methods The results of nasal endoscopy 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 fossa 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 lacrimal duct stenosis (avec p >0.05). It appeared that there are major anatomical 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 anatomical 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 lacrimal duct stenosis was found. However it remains essential to perform preoperative nasal endoscopy in order to detect a possible cause of lacrimal duct stenosis and thus evaluate the feasibility of surgery.
**T029**

**Blood-retinal barrier serum ferritin transport in mouse retina**

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(2) Centro de Bioclinica Animal e Tecnologia Gênica (CBATEG), Universidade Autónoma de Barcelona, Barcelona

**Goal**
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 Scar2 receptors were measured 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 cells/eyelid zones that significantly 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 accumulation. Recently, ferritin was found in the cytoplasm of iron-delivery protein. TIM2 and Scar2 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 retina parenchyma. HSF was intravenously injected and as expected, ferritin crossed the BRB, probably through TIM2 and Scar2 receptor binding, and accumulated in perivascular cells. In the presence of BRB breakdown injected ferritin was also found accumulated in TIM2 and Scar2-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.

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**T031 / 4645**

**Tear film break-up time evaluation by real-time wavefront aberrometry in normal subjects**

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(2) Bretonneau University Hospital, Tours

**Goal**
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, Ovacy, France) Hartmann-Shack (HS) aberrometer. The aberrometry was performed once every second for up to 20 seconds. HOA measurements were performed 3 times in a row. BUT variations 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 and BUT. BUT was significantly decreased (P=0.0065) in all patients in Group 2 compared to the normal tests subjects (Group 1).

**Conclusion**
Studying the HOA variation is a valuable method for evaluating both the quality vision and the BUT in patients with MGD and evaporative Dry Eye. The IRX3 HOA aberrometer can be used for an objective and reproducible assessment of the BUT in the follow-up of patients with severe MGD.

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**T032 / 4646**

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**Goal**
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 Scar2 receptors were measured 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 cells/eyelid zones that significantly 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 accumulation. Recently, ferritin was found in the cytoplasm of iron-delivery protein. TIM2 and Scar2 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 retina parenchyma. HSF was intravenously injected and as expected, ferritin crossed the BRB, probably through TIM2 and Scar2 receptor binding, and accumulated in perivascular cells. In the presence of BRB breakdown injected ferritin was also found accumulated in TIM2 and Scar2-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.

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**T033 / 4646**

**Tear film break-up time evaluation by real-time wavefront aberrometry in adult patients with meibomian gland dysfunction**

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**Goal**
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.

**Methods**
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 lentivector, 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 reporter protein. Moreover, we detected significant differences in transduction rates between human and murine EC lines as well as between 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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(4) Department of Pathology, University Hospital, Saint-Étienne

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 woman with advanced nephropathic cystinosis underwent generating 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, 638 and 785 nm) confocal microscopy ViaScope 1500 and the handeld monolaser ViaScope 3000 (MAVI 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 thiazaurines like amyloidosis, Wilson disease, Fabry disease or mucopolysaccharidoses

• 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 etiologies 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 66% 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 (Cationom®, Vismed®, Optive® and Systane Balance®) on the recovery process of the debrided cornea. 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 (Cationom®). Interestingly, inflammatory cells infiltration in the stroma was at its lowest following Cationom® 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 (Cationom®) is well tolerated by debrided cornea and allow for a safe healing of the cornea. The findings suggest that Cationom® have the potential to benefit patients with corneal epithelial 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) drops reduce instillation 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 prostaglandins (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 infiltrates when compared to BAK-free timolol/P-timolol combination. In contrast, BAK-preserved PG/timolol FC presented elevated IVCM staining and goblet cell count demonstrated that BAK-free Catioprost/P-timolol is the best tolerated combination.

**Conclusion**
BAK-free Catioprost/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**

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**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 28 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 (1%), 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.

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**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 concentrations in basal tear samples collected from KC (n=10) and control patients (n=10). The percentage SFRP1 of total tear protein concentration (SSFRP1) 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 SFR5 showed unique patterns of immunolabelling. SFRPS was localised to epithelial cell membranes and lamellar vessels in control corneas; cell membrane and cytoplasmic immunolabelling, and increased expression centrally, was seen in KC. SFR5 was expressed strongly in the corneal stroma (KC and control). SFR2 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
**TO41**

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.

**TO42**

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 corneal or limbal tissue was excised at different time intervals after injury. The expression of genes for a number of growth and differentiating 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-1) 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-1 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-1 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.

**TO43**

Gene transfer of HSV1-specific meganuclease to the murine cornea

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**Purpose** Recombinant Aden-associated virus (rAAV) encoding meganuclease was specifically designed to address Herpes simplex virus type 1 (HSV1) which causes a specific meganuclease to the murine cornea

**Methods** Recombinant adenovirus (rAAV) encoding meganuclease was specifically designed to address Herpes simplex virus type 1 (HSV1) which causes a specific and efficient method to induce a specific meganuclease into cells expressing corneal epithelial cell markers. The proliferation of these cells was supported by FGF and EGF.

**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-1) 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-1 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-1 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.

**TO44**

Noricandil: 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 persistent 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 anger 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 vasodilator effects, may erode 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 a week. 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 was observed 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=0.018, p=0.031, p=0.022). Also, in the fluorescence immunostain, the reduced expression of VEGF 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.

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**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 – (43), 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 mofloxacin 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.

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**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 – (43), 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 - mofloxacin 0.5% and hydroxypropylguar and sorbitol in group A, and mofloxacin 0.5% and hydroxypropylguar in group B provide medium compliance. Using only hydroxypropylguar and sorbitol in Group C and hydroxypropylguar in Group D demonstrated a high compliance.

**Conclusion**
First pathogenetically substantiated the choice of therapy based compliance in patients after two-step LASIK.
**T049**

**Lacrimal 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 unilateral herpetic 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’s), tear break-up-time (TBUUT), tear reflex (Schirmer 1 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 TBUUT was strongly reduced in the affected side (4.8/µg/mm2 vs. 2.0; 4.6 sec ± 1.1 respectively) compared to the non-affected side (0.57/µg/mm2 ± 0.13; 7.7 sec ± 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 ± 0.13 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 (5.7 vs. 7 ± 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 (Proflkon A 525/WC) for 30 minutes per test. Wetability and deposits accumulation on anterior surface were evaluated according to the International Organization for Standardization IS011980 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 installation.

**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 lenses that showed very significant deposits accumulation (visible after drying tear film) were 25%, 34%, 20% and 27%, respectively and the percentage of lenses 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 range 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 subgroup (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 demographics and lenses wear history.

**Conclusion** With the increasing availability 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 hyperreflective 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.

**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 separated on two-dimensional polyacrylamide gels that were silver stained.

**Methods**
Soft CLSs 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, polymorphic 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 2-D 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 underestimated. 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 were 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 spumvik).

**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 cases. Among the 508 included patients, an infection was diagnosed in 185 cases (36.4%): 54% of cases were due to bacteria, 36% were due to virus, 6% were due to fungi and 4% were due to amoeba.

**Conclusions**
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 TearLab® 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 TearLab® 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 tetrastig (p=0.004 and 0.02, respectively). In addition, The modulation transfer function (area under the curve) and the Strehl ratio were significantly lower in the affected eyes compared to the non affected eyes (p<0.012 and 0.002).

**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 Meibopatch® (eyelid-warming device) in patient with mild and severe Meibomian gland dysfunction.

**Results**
The root mean square was significantly increased for high order aberrations (p=0.0007) when compared to untreated eyes. Meibopatch® improved the quality of vision evaluated by OQAS and Hartmann-Shack aberrometry before, 15 days after, 1 month after treatment.

**Conclusion**
We have observed a significant improvement of the BUT, OSI, Meibomian gland secretion quality, MTF and OSI after treatment.

**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 opacity with dyskeratosis, and circumferential corneal neovascularization. Cutaneous features of palmpoplantar 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 HiSeq and whole exome capture processing were performed. CNV and insertions/deletions analysis and comparisons with public databases were performed. In-house pipeline filtering and exome capture processing was performed. Sequence reads were aligned, and screened for single nucleotide variant and insertion/deletion calls. In-house pipeline filtering and exome capture processing was performed. CNV and insertions/deletions were identified 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 heparin sulphates, for management of severe neurotrophic keratopathy.

**Methods** Eight patients with severe neurotrophic keratopathy were treated with RGTA. The patients were followed up for 12 weeks.

**Results** Seven patients showed a significant improvement in visual acuity. One patient did not show any improvement.

**Conclusion** RGTA may be a promising, non-invasive, alternative therapy in severe neurotrophic keratopathy.

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**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** We developed hydrogel scaffolds made of chitosan and structural proteins. The scaffolds were used to culture corneal epithelial cells.

**Results** The scaffolds supported the growth of corneal epithelial cells.

**Conclusion** Chitosan hydrogels may be a promising material for further clinical tests directed towards the development of implantable corneal epithelial cells.
**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) clinical 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 1° 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 dipters (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 Moorhen Ulcers: management with Rituximab and peripheral graft

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**Purpose**
Moorhen ulcer is a rapidly progressing, painful, ulcerative keratitis which affects the peripheral cornea. We report 6 severe cases of Moorhen Ulcers (4 patients) with corticoresistant 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 Moorhen’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 Moorhen 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: 57 men 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 stable 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 (PKin keratoconus patients.

Methods 62 keratoconus patients were divided into 2 groups. FLPK group contained 32 patients, PK group 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±0.3D 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±8.3% and 34.1±7.8% respectively.

Conclusion Femtosecondlaser-assisted surgery results in lower 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 (T1) and one month postoperatively (T2). The anterior chamber depth (ACD), the angle-opening distance at 500µm (TISA), the trabecular-iris space area at 500µm (TISA) and the sceral 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 descemeter's stripping automated endothelial keratoplasty (DSEA group). Preoperative and postoperative measurements were compared using signed rank test of Wilcoxon.

Results Twenty patients were evaluated: fifteen (75%) in the DSEA group, five (25%) in the PK. Mean anterior chamber depth width increased from 3.31mm (SD: 0.699) to 3.35mm (SD: 0.341) after PK (p<0.1), and from 3.22mm (SD: 0.466) to 3.44mm (SD: 0.591) after DSEA (p=0.679). In the temporal quadrant, after DSEA, 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 DSEA, mean anterior chamber angle width increased from 0.253mm (SD: 0.089) to 0.286mm (SD: 0.089) (p=0.027) 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 performed to confirm the angle changes.

**T071 / 2326**
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 (Whitehart.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 retainer EC were identified by EdU incorporation during long-term culture: 30 days for organ cultured human corneas: a new clue for the existence of endothelial stem cells.

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 biosynthetic 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 experimental devices used until now for ICMD assessment.

Results None of the usual animal models of ICMD assessment seemed acceptable for various reasons: primates for ethical reasons (presbyopia is not a disease), rabbit, rhesus and cats for biological reasons especially because of their spontaneous endothelial regeneration, or financial reason especially for long-term monitoring after implantation in primates, pig, calf or others. 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 preclinical 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. The 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 (Alliborn, 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 mm Hg was 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 (SP000 Tomey). Endothelial viability was determined with the triple Hoechst/Ethidium/Calsein labeling coupled with image analysis of the whole endothelial surface immediately after the cut (JOVS 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% fetal 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 ECM morphology were measured by image analysis (Cell-P, Olympus, and SambaCorneaTriBin) after alizarin red staining and flattening. On the other half of the cornea, ECM differentiation was studied with NAK AT-Pase, ZO-1, JAM-1 and proliferative capacity (Ki67, Click-it EdU) were studied by immunostaining in flattened corneas. Endothelial cells and stroma were observed by histology on cross sections stained with Herematin/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 cells/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 cornea 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**

50 corneas of 6 month-old Large White pig, 20 of 10 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). Macroscopic data: 1/ histology on Herematin-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 keratoplaty. It has been reported that BBT may produce two types of bubble outlines: clear or white margin. It seems that the components of the posterior lamella obtained with each bubble rim 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 handed 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.
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/Hams culture medium supplemented with 10% FCS. Keratocytes underwent illumination (670 nm) for 13 minutes following exposure to 100 nM concentration of photosensitizer chlorin e6 (C6e) in the culture medium. One day after treatment, bFGF, HGF, KGF, TGFß1 and VEGF secretion 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 0.95, of TGFß1 2.83 and of VEGF 9.01 pg/ml 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 C6e 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.

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 catalyze 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 (266 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.
Purpose To compare the central corneal thickness parameters and central corneal thickness (CCT) in four different groups of patients, to find the correlation between the central 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 divided into four 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 17 males, 87 females. Average age was 59 (± 23.8) years. In the POAG group average CCT was 553 (± 32) µm, ECD 2548 (± 345) cell/mm², hexagonal cells 66% (± 10%). In younger subjects average CCT was 525 (± 43) µm, ECD 2940 (± 345) cell/mm², hexagonal cells 66% (± 10%). In the older healthy patients group average CCT was 546 (± 39) µm, ECD 2394 (± 416) cell/mm², hexagonal cells 64% (± 16%).

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.

Abstract

Purpose To determine the distribution of the central corneal thickness in adult residents of Lithuania.

Methods Lithuanian residents in the age of 18 and senior, who were registered with 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.

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 57.3 (± 0.6) years, and among women - 63.6 (± 1.4). The average CCT of individuals by age groups equalled to 18-29 (508 ± 28 µm), 30-39 (576 ± 19 µm), 40-49 (513 ± 18 µm), 50-59 (544 ± 21 µm), 60-69 (544 ± 21 µm), 70-79 (535 ± 19 µm), and 80+ (536 ± 11 µm). 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 µm, 545.0 ± 0.8 µm of men, and 544.4 ± 1.1 µm of women. The thickest corneas among Lithuanian residents was measured in individuals under 40. In senior persons it becomes thinner by each decade from 2 to 8 µm. The central corneal thickness has no relevance to gender.

Purpose Three 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 (100µm vs 166 µm, 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=−0.49; p= 0.063) or at 3 year (Spearman=−0.60; p= 0.014). 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.

Purpose To determine the effect of cryopreserved amniotic membrane transplantation (AMT) on 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 a temporary, 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) (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 CASA-1000 (Tomey Inc., Japan).

**Methods**

From the Casia 1000 we exported the following raw data: anterior and posterior surface dioptic 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 discrimination level between normal and suspect/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 discrimination 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, TM5 and Pentacam.

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**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 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 (LAI, 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 VFQ-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±10 to 70.5±18 (p=0.045), respectively. Best corrected visual acuity improved by 3.2±4.3 Snellen lines. Mean follow-up was 1.26±1.3 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.

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**T087**

Boston Keratoprosthesis (Type 1): visual prognosis and complications

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**Purpose**

To describe the functional results and sight threatening post-operative complications of Type 1 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**

59.5% retention rate with overall improvement in visual acuity demonstrates that Type 1 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.

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**T088**

Ukraine implantation results of collagen-based bioengineered substitutes of donor corneal allografts in rabbits

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**Purpose**

Ukraine Implementation Results of Collagen-Based Bioengineered Substitutes of Donor Corneal Allografts in Rabbits.

**Methods**

Bioengineered corneal substitutes (BCS) were fabricated by cross-linking porcine type 1 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. Non-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 epithelisation.
**T089**

Laser subepithelial keratomileusis (LASIK) versus femtosecond sub-Bowman keratomileusis (FSBK) to correct myopic astigmatism

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**Purpose**

To compare the safety and efficacy of LASIK versus FSBK to correct myopic astigmatism.

**Methods**

A retrospective pilot study of 846 consecutive eyes (427 FSBK and 419 LASIK) was performed. The inclusion criteria were astigmatism of 0.7 ± 0.2 and in FSBK group was 0.8 ± 0.2, p = 0.3. Safety in LASIK group was 1.0 ± 0.1 and in FSBK group was 1.02 ± 0.1, p = 0.01. Three months after surgery, astigmatism was similar in both groups: -0.52 ± 0.6 in LASIK group and -0.54 ± 0.6 in FSBK group (p = 0.6). The sphere was higher in the LASIK group than in FSBK group (0.24 ± 0.7 D, LASIK group and 0.12 ± 0.5 D, FSBK group) p = 0.05. BCVA and UCVA were slightly better in FSBK group (BCVA in FSBK group 1.02 ± 0.1, BCVA in LASIK group: 0.9 ± 0.2, p = 0.001). UCVA in FSBK group was 0.9 ± 0.2. UCVA in LASIK group was 0.86 ± 0.2. Enhancement rates were higher in FSBK group. 97 eyes (22.62%), than in LASIK group, 66 eyes (15.21%), p = 0.01.

**Conclusion**

LASIK and FSBK show similar safety and efficacy when used to correct myopic astigmatism ≥ 1.50 D. Postoperative ISCVA 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.

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**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 rings 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.
• 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 (ISS), 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, ISS insertion; first ISS insertion and afterwards, CXL.

Results After the numerical simulation, the following effects are observed: the CXL causes 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 ISS achieves a higher effect after the CXL treatment is previously performed.

Conclusion The combination of the two treatments, collagen CXL and ISS 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 ISS 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 superfice under slit lamp and later with the OCT Anterior Segment Module. The Spectralis SD-OCT offers a 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, full-thickness keratectomy and amnion 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, MAVIC 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, its dermatological arm support and an ophthalmology examination table comprising a 5 degrees of freedom stand (Zesis, 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 arm 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 these adaptations, the first multiflaser 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 continuously slows medium renewal in order to improve corneal storage.

Methods The BR (patented) comprised sterile endothelial and epithelial chambers closed with transparent window 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 adapt 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.

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 anesthesia. 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 rim zone. The flap was then replaced and the interface was irrigated. Minimum residual pachymetric value was estimated not inferior to 400µm.

**Results** Postoperative controls at 1 and 3 months showed a reduction of anisometropia up to 70% with residual spherical 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 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”, keratometry with “Pentacam”, “Atlas”, confocal microscopy with Confocan 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 stroma 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.
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, orthokeratology 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. 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.

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. The variations found in the CH and CRF are not significant in the descriptive level with any of the designs (p>0.05). At baseline -6 months, the improvement in ISCVA (LogMAR) is 0.13 in 5mm diameter respect to 0.07 in 6mm diameter Among the changes in CH and ISCVA (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 ISCVA.

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.

Cis-urocnic 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-urocnic 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, at 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

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 microkeratome (Moria France). Grafts are inserted by the Endosaver® (Ocular System Inc; USA) by a 4 mm incision and applied by a bufferring of a air bubble in the anterior segment after a peripheral iridectomy. 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 (30-120 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.

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, orthokeratology 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 back 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 back 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.
**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 refractionmeter 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 sportmen 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 than -2.00 D. Aberrometry has given more myopic results than refractometry. Cylinder 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 corneas do not depend on the cycloplegic status. Low order Zernike aberrations strictly correspond to the refraction error.

**T107**

Comparison of decellularization methods for human corneal lenticules

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**Purpose**

Human or animal thin corneal lenticules (1) 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 I. were prepared with a Mioria microkeratome on human organ cultured corneas mounted on an artificial anterior chamber. After desepithelialization, an anterior I. was obtained with a 90 µm head and a posterior I. with a 110 µm head. Four physical methods (sonification at 37 kHz for 45 minutes, 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, 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-Elubium-Calcine 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 (Dow 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 l1 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 (eECD) 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 eECD 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 eECD 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 eECD (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 eECD (P<0.05). They corresponded to apparent EC loss of respectively 28%, 36% and 36% compared to eECD.

**Conclusion**

ECD at D5 is dramatically lower than eECD but subsequent decrease seems slow. 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.
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;52:6008) 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 SF2000P).

Results Both grafts were uneventful. For the allograft, ebECD 48h before graft was 3787 cells/mm^2 and postop ECD decreased of 56%, 60%, 40% and 43% at D5, D15, D20 and D30. For the autograft, pregraft specular ECD was 17072 cells/mm^2 and postop ECD were 1941, 1934, 1924, 1909 and 1900 cells/mm^2 respectively at D1, D5, 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 peris operative events, since almost no early cell loss is observed during autograft.

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 immunocytochemistry 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, and 38.4/0.76, 34.2/0.38, and 45.7/0.72 (p<0.0001). The average percentage of p63+ small cells was, respectively 2.65, 4.76, and 1.3% in clones obtained from 11-, 14-, and 18-day primary cultures. (p=0.0082). 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, 34.2/0.38, and 45.7/0.72 (p<0.0001).

Conclusion In the explant culture system, limbal epithelial progenitors are better preserved after 2 versus 3 weeks of culture.

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 Chk2 in facilitating productive HSV infection in corneal epithelium.

Methods We used human corneal epithelial cell lines – HTEpiC 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 corneal 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 molecular 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 choroida. 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 cornneas of 9 Chinchilla rabbits. The superficial cornneas of the right eye of the rabbits were excised with a 6 mm punch. AHCM lamellae (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 levofloxacine 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.

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**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 Deficieny (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±14 µm in successful cases, 88±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.

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**T115**

Treatment of ligneous conjunctivitis 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 homogenous and heterogenous 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.

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**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 conjunctival pannus and stromal involvement underwent autologous cultivated oral mucosa epithelial transplantation. Cellular material was obtained from buccal mucosa, tripinized, 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 recurrent 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 (IOC) and the axial length of the globe (AL). Intraobserver and interobserver reproducibility were evaluated, using intraclasis 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 0.95. Intraobserver and interobserver reproducibilities were high, particularly for Mourits’ exophthalmometer, concerning EPBCS and IOC 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.

• T119
Lyman borreiosis with ocularse manifestations during childhood period

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Purpose Lyme borreiosis (LB) is the most common human tick-borne disease in the Northern hemisphere. The various ophthalmologic manifestations of Lyme borreiosis (LB) during childhood period are discussed in this study.

Methods Six children with LB-associated oculars 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 otitis, Two abducens palsies, one optic 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 otitis 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.

• 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% oxybuprocaine drops were used prior image acquisition. A Mefaroot 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 grade atrophy of the choioed and retina after reduction of plasma ornithine with diet, 1 Pedder’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.

• T118
Vincristine-induced unilateral ptosis

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Purpose To report the occurrence 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 thorax-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 Neutrocytosis is a well-known complication of vincristine. 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 aetologies 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.
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. Presuming risk factors, both though 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.

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 +/- 90.9 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/disc area ratio (cases: 0.45 +/- 0.31, controls: 0.26 +/- 0.27, p=0.002, Mann-Whitney U test), cup/disc horizontal ratio (cases: 0.67 +/- 0.22, controls: 0.48 +/- 0.23 p=0.003, Student t test), cup/disc 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 +/- 0.482 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 eye.

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 hepatosplenomegaly, 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.
• T125
Relationship between retinal nerve fiber layer thickness and the duration and severity of Parkinson's disease

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Purpose To determine in patients with Parkinson's 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 182 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=0.007 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=0.000, 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 supranormal 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 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 analysis 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 ± 0.002 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 0.962 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 fibers

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Purpose The main purpose of this work was to study the retinal nerve fiber 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 to 7 groups: MS eyes with a history of acute optic neuritis (MS+ON eyes, n=39) and MS eyes without history of optic neuritis (MS-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) perimeter (Metrovision France). Retinal nerve fiber thickness were measured by Optical coherence tomography (OCT, fast RNFL thickness protocol).

Results The rate of MS-ON eyes and MS+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 127.3 um for inferior RNFL thickness, p=0.05). An increased P100 latency and decreased P50 and N95 amplitude were noted in MS+ON eyes compared to MS-ON eyes (respectively p=0.01, 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.
Purpose:

Background: 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 retrolubar 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) who 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±36 years; range: 19-55 years, SD: 10.88). No patients in the active stage of the disease. The peak systolic (PSV) and diastolic (EDV) blood flow velocities, indicators of peripheral vascular resistance such as Gosling Index (PI) and Poaceot 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 (Unianova). Additionally, we analyzed the obtained values of blood flow in patients who received immunomodulation therapy and in patients who passed neuritis optic 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 exist of retrolubar hemodynamics impairment.

### 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 funduscopy 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 (BP) then at 1 month (M1) and 3 months intervals (M3). 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 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.
Aicardi syndrome is rarely associated with macrocrania. We reviewed the literature to describe an interesting rare case of Mohr-Tranebjærg Syndrome, a X-linked 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 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.

**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 spasms.

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 callosum. 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 reviewed 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: 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 at while fixating 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 dyslexia.
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 26 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.

Neurotrophic keratopathy associated with congenital agenesis of the corpus callosum

Ophthalmology, Zaragoza

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 exotropia, bilateral optic nerve hypoplasia, delayed visual evoked potential flash type and altered corneal sensitivity 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 sensitivity is a fact that will be suspected to perform early diagnosis and appropriate treatment and follow up.

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 66.2±11.55 microns (51.0 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 mm3 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 fibers, increase in optic disc cupping, retinal vascular tortuosity and thinning, and visual functional impairment.

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 gyrus 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 66 with cytomegaly (CM), 59 with myelomeningocele (MM), 69 with puretious meningocele (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.

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**T144**

**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.
EVER 2012 Abstract book

**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 usefulness 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±3.7 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±4.9 mmHg. Mean CCT measured with UHS ST was 543.7±75.2 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 techniques 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.

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**F002** Comparison of intraocular pressure measurements with the reichert pt100, the keeler pulsair intertypull soft 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 intertypull® 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.

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**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 pneumotonometer Diaglab Modular OméR 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 means 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 chronomorphological lower IOP therapies could be powerfully studied using paired intra-subject 24H nyctohemeral rhythm data comparison, during repeated sessions overtime before and after treatment.

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**F004** Relationship between IOP and biomechanical corneal values measured 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** Fifty-five eyes from 65 healthy subjects were prospectively and consecutively selected. All of them underwent a full ophthalmic 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 were calculated between IOP values and corneal biomechanics parameters obtained by ORA and were also calculated.

**Results** IOP parameters, evaluated by Pearson correlation coefficients were significantly correlated with r=0.001; r=0.826 for IOPg vs. IOPcc and IOPg was linearly associated with r=0.826 for IOPcc-IOPg. IOPg had a linear relationship with CH (r=-0.802) and with CH and CCT (r=-0.678). IOPcc had a linear relationship with CH (r=-0.802), CRF and CCT (r=-0.466).

**Conclusion** IOPg and IOPcc have a positive linear correlation. ORA biomechanics parameters COR, CH and CCT show also a linear positive relation between them.
• F005
Comparison between Keeler and ORA IOP measurements

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Purpose To evaluate the relationship between intraocular pressure (IOP) measurements obtained with Pulstar 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 IOPk, IOPcc, and IOPg-IOPcc were 1.8 mmHg and 0.01±1.54 mmHg respectively. Pearson correlation coefficients showed that IOPk, IOPcc and IOPg were significantly correlated (p<0.001): r=0.816 for IOPk-IOPg, r=0.826 for IOPk-IOPcc and r=0.587 IOPcc-IOPg.

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-corrected 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 kare tonometry, optic disc assessment and automated perimetry IOP post injection at 5, 15, 30 and 60min. Standard injection technique.

Results Mean baseline IOP was 16.92 mmHg (SD 4.98, 95% CI 14.95 to 18.88). Thirty minutes post Apraclonidine 1% administration, mean IOP was 13.71 mmHg (SD 4.58, 95% CI 13.74 to 17.67). Paired Student’s t test giving a P value of 0.068 indicated that administration of Apraclonidine 1% prior to intravitreal treatment did not cause a statistically significant IOP reduction in patients with ocular hypertension and glaucoma. Immediately postinjection, mean IOP was 41.54 mmHg (SD 14.1, 95% CI 37.20 to 45.88). Paired T test results showing a p value < 0.0001 confirmed a statistically significant difference between baseline and immediate post injection IOP 13 out of 24 (58%) of the study patients required anterior paracentesis post intravitreal injection according to our devised protocol.

Conclusion The authors propose the use of the formulated paracentesis protocol for intraocular management in patients with ocular hypertension 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 higher rates of OHT were compared to patients without pre-existing glaucoma (21.7 mmHg +/- 12.4 versus 17.2 mmHg +/- 4.5, p = 0.06). No significant difference was found in diabetes subgroup (n=46, p = 0.32), nor in YAG capsulotomy subgroup (n=12, p = 0.8) compared to the control group. The peak of IOP was significantly correlated with the total number of IVI (p = 0.01, R = 0.19). The mean highest IOP was 17.2 mmHg in ranibizumab group, 18.8 mmHg in bevacizumab group and 19.9 mmHg 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.
Poster session 2 : Glaucma - Electrophysiology/ physiological Optics/ Vision Sciences - Immunology / Microbiology - Physiology / Biochemistry / Pharmacology

• **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 to 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 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. Myopic NTG 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 < 0.007). VF defect location was significantly different between the two groups, with superior defects more prevalent in the myopic NTG group (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 and standard maculogram analysis.
  
  **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 7x7 mm, Optovue Inc.). We analyse: MD, PSD and FLV 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 ± 3.5%) results report: MD: -0.25 ± 1.46 dB, PSD: 5.9 ± 1.4 dB, FLV: 18.4 ± 1.26% and GLV 19.2 ± 2.72%. Controls (61.6 ± 4.9) results were: MD: 0.0 ± 0.22 dB, PSD: 1.6 ± 0.1 dB, FLV: 19 ± 0.1% and GLV: 9.8 ± 2.3%.
  
  **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 pigment epithelium (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 pigment epithelium (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.
  
  **Methods**
  Peripapillary RNFL thickness was quantified by optical coherence tomography (OCT). The six corresponding retinal areas were defined by a standardized grid of 7x7 mm. RNFL intensity/irregularities were assessed and correlated to RNFL measurements.
  
  **Results**
  84 glaucomatous eyes were investigated. A correlation between RNFL thickness and RPE alterations as detected by widefield fundus autofluorescence (FAF) was found. RNFL was significantly thinner in the superotemporal (ST) quadrant, followed by the inferonasal (IN) quadrant. The inferior nasal (IN) quadrant showed the least amount of RNFL thinning.
  
  **Conclusion**
  This study provides early evidence that in glaucoma RNFL degeneration with the location of visual field (VF) defect.

• **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 algorithm 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 WDX 3D, Korea 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 provided 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 (F1), whereas the interobserver agreement of the DDLS evaluated clinically by slit lamp was substantial (0.80). The DDLS evaluated by the integrated algorithm of 3D non-mydriatic retinal camera was not itself satisfactory in the diagnosis of glaucoma. ROC curve showed that DDLS evaluated using 3D monitor had the best predictive power (F93).
  
  **Conclusion**
  ONHP obtained by 3D non-mydriatic retinal camera are useful in evaluating patients with glaucoma, however, the integrated algorithm of the device to calculate the DDLS needs to be improved.
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 (0.56 – 0.83) and Rmax 0.092 – 0.902; 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 between cRNFL and cRVT and cRAT profiles (Rmax 0.35 and 0.68 (0.96 – 0.03) and Rmean 0.65 (0.92 – 0.02). 26 and 24 of 64 plots showed significant correlation 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.

**F015 / 4453**

**Biomechanical response of lamina cribrosa and prelaminal tissue to an acute induced IOP elevat**

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Purpose  We decided to investigate the effects of an acute induced IOP elevation on the prelaminal tissue and on the lamina cribrosa in glaucomatous eyes and in healthy eyes by means of a 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 prelaminal tissue displacement (PTD) and the lamina 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±1.7 vs. 20.8±17.5 μm (P<0.0039), whereas LD was similar in the two groups: 4.5±3.7 vs. 0.2±0.20 μm (P<0.36), and not statistically different from 0 (P>0.36).

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 prelaminal tissue is lower in patients with POAG than in controls.

**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 nerve 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 820.8±8.2 to 273.3±7.4 μm and cRNFL decreased from 20.8±3.4 to 7.6±3.8 μm. 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.

**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 interobserver reproducibility in normal, ocular hypertensive (OHT) and glaucomatous eyes.

Methods  A total of 138 eyes were enrolled in 3 groups: 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 observers, and the ganglion cell analysis (GCC) 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 92.27±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 0.53-1.67 %, and TRTSD ranges were 0.61-2.64 μm and 0.83-2.22 μm, for respectively the intraobserver and interobserver reproducibility analysis.

Conclusion  To our knowledge this is the first study of GCC 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 (dH) 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.

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**F018**

**Glucoma 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 RT Vue 3D-optic disc plus ONH map then macular map RNFL parameters and macular complex (retinal nerve fiber plus retinal ganglion cell plus inner plexiform ie GCC). Statistical analysis: normal and glaucomatous population were compared with a Mann-Whitney test. Area under curve (AUC), sensitivity 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 0.762 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 RT Vue 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 bias 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 peripapillary parameters.

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**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 based on the basis of lens conditions.

**Results**

IOI group was significantly older, with lower IOP and higher MD as compared to VCC. IOI/VCC outcomes were significantly different and concordance was poor to moderate but slightly better with transparent lens than with cataract (NO/NC 1, 2 or 3). Morphometric parameters as TSNIT average, superior, inferior, rim area, horizontal integrated rim width, and rim area positively correlated with cup area (vertical cross section), average nerve width, 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 (dH) 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.

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**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. TSITN average, superior average, inferior average, TSITN 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 TSITN average had the highest ICC (0.967), while the TSITN standard deviation showed the lowest ICC (0.928). The COVs ranged from 2.4% (TSITN average) to 21.8% (NFI). Test-retest variability was 6.5% for the NFI and 2.51 for the TSITN 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 (reference 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 parameters.

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 >30 µm 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<0.53). 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, 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 variability 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 analyses by stereometric parameters 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.

• F024 / 2456
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, 23 and 29. The average thickness values for healthy subjects were 32.95 µm (RNFL), 79.02 µm (GCIPL) and 121.46 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 diverts 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 segments: 10 borderline (BL), 5 outside normal limits (ONL). Shifting C further on the temporal rim changed 33 segments: 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

Poster session 2 : Glaucoma - Electrophysiology/ physiological Optics/ Vision Sciences - Immunology / Microbiology - Physiology / Biochemistry / Pharmacology

EVER 2012 Abstract book
• **FO25**

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 0.5 mg/ml (BTFC; Gembrot®) in patients with primary open-angle glaucoma (POAG) or ocular hypertension (OHT).

**Methods** This was a combined analysis of five prospective, observational studies involving 5,596 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 = 5,164) 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 mm Hg 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 66% 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**

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• **FO27**

Effectiveness 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 brimonidine and dorsolamid effects of 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 computerized 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 4.2 mmHg in the first and 3.0 mmHg in the second, that presents high statistical significance. From 15.6% patients (11 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.

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• **FO26**

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 trial 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 RNFL 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.

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• **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 palmitoyl ethanolamide (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 (PSTD). 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 ± 3.44 mm Hg P < 0.001). A statistically significant difference in the MD was found between the two groups (PEA treated, 2.9 dB ± 2.9; Placebo treated, 8.55 dB ± 6.51 P < 0.001). Furthermore, the change in PSTD 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
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 (OHT).

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 OHT. AIC were conducted using Bucher’s method. The main endpoints was intraocular pressure (IOP) measured at 3 months and hyperemia 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 0.04% [-0.13;1.10]), bimatoprost 0.01% [-0.19;1.09;0.06]), travoprost [-0.45;0.033] and latanoprost 0.04% [-0.12;0.00]. T2345 was found statistically significantly superior to latanoprost 0.04% [-1.52;0.28] for ocular hypertension or ocular redness. T2345 was found statistically significantly superior to BAK-free travoprost and bimatoprost (odds ratio 95% Cl 0.10; 0.40; 0.10; 0.83), bimatoprost 0.01% [0.27; 0.31; 0.36], latanoprost 0.04% [0.14; 0.40] and latanoprost 0.01% [0.14; 0.31].

Conclusion In terms of efficacy on IOP indirect comparisons never found T2345 statistically significantly inferior to the others. T2345 was found superior to latanoprost 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

• 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 24± 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 900 am both 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 mHg) and 38% with Xalatan™ (9.0 ± 2.4 mHg). These results meet the limits set for non-inferiority of T2345 to Xalatan™. Concomitant hyperemia 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, 12pm, 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.

Commercial interest

• F031
Prostaglandin drug partitioning into contact lens material

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Purpose Patients who take topical ocular hypertensive 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 pharmacokinetics 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 high performance liquid chromatography (RP-HPLC).

Results Tafluprost and bimatoprost partition from product solution into contact lens material rapidly (within 15 min). At 37°C, for all solution volumes tested, Fisol for bimatoprost was approximately 2X higher than Fisol for tafluprost.

Conclusion Both tafluprost and bimatoprost partition rapidly from product formulation into soft contact lens material. Tafluprost (log P = 4.2) is more hydrophobic than bimatoprost (log P = 3.2) and partitions more strongly than bimatoprost into contact lens material. This study demonstrates that contact lens wearers should remove lenses prior to instilling the product formulations. Lenses may be reinserted after drop instillation.

Commercial interest
• 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 febrile 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 ligation). 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. Meanwhile 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.

• 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 (CAGC).

Methods Patients with medically controlled end-stage CAGC (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 CAGC eyes with cataracts.
Marginaly 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 pseudophakic 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.

Ex-press glaucoma shunt for the treatment of complex glaucoma

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Purpose To assess the safety and efficacy of Ex-PRESS Mini glaucoma (EMG) shunt for the surgical treatment of 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, vitreoretinal surgery, OSD). Surgical procedure was in accordance with published methods. 10 cases of complex glaucoma were reviewed retrospectively over a period at least 6 months following surgery. The end points were: intraocular pressure (IOP)/number of glaucoma drops used/visual acuity. Unqualified success was defined as IOP < 19 mmHg without glaucoma drops, and qualified success was IOP < 19 mmHg with 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 11.6 mmHg (sd 1.4 mmHg). 3 cases required drops to achieve the target IOP. The mean IOP being 18.7 mmHg (sd 0.8 mmHg) with a mean of 1.3 glaucoma medications required at 6 months post-operatively, (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 glaucoma. EMG shunt was relatively easy to insert with a minimum of post-operative manipulations. The 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 success. Although 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.

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 (ILE) and mid twenties in the right eye (IRE). Despite anti glaucoma medications and surgery, systemic examination was negative for carotid cavernous fistula, low-grade dural arteriovenous fistula, dextrthyroid 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 intrakrallary cavity, the collagen drainages completely reabsorb. 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 subconjunctival or subchoroidal space.

**Conclusion** Thus, the drainages do not provide enhanced outflow of aqueous humor from the eye through the anastomosis in the late postoperative period. The reason of this is a fibrous intraocular or subconjunctival 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 shallow anterior chamber were studied. Spectral domain OCT (Heidelberg, Germany) was performed before and seven days after laser peripheral iridotomy treatment in all cases. Spectral attention was taken to evaluate angle changes. Main measures were: anterior chamber volume, central anterior chamber depth and temporal angle width.

**Results** Thirty 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 somoted to iridotomy with Nd: Yag laser. The procedure is effective to increase anterior chamber volume, 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. Patton 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 stage 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 in narrow angle someted to iridotomy with Nd: Yag laser.

**Results** Histological studies of eyes in the late postoperative period showed that the polymer drainages from digel exist in the intrakrallary cavity, the collagen drainages completely reabsorb. 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 subconjunctival or subchoroidal space.

**Conclusion** Thus, the drainages do not provide enhanced outflow of aqueous humor from the eye through the anastomosis in the late postoperative period. The reason of this is a fibrous intraocular or subconjunctival level.

**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 Cycloagulation (UC3) procedure in patients with primary open-angle glaucoma (POAG).

**Methods** Prospective multicenter clinical trial. 39 eyes of 39 patients with POAG, intracocular pressure (IOP) ≥ 21 mmHg, an average of 1.65 failed previous surgeries and an average of 3.2 hypotensive medications were monitored 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<0.005), for a mean preoperative value of 28.9 ± 6.8 mmHg in group 1 and 29.2 ± 6.9 mmHg in group 2. In the case of 18.1 ± 4.4 mmHg in group 1 and 16.1 ± 8.2 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 intracocular 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 performed at day 0, 7, 45, 90 and 180 including visual acuity, IOP by goldmann tonometer, slit lamp examination and optic disc evaluation. Safety was assessed 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 occurred at all visits: at day 7, 45, 90, and 180, IOP was 19.92 +/- 5.05, 19.12 +/- 5.22, 18.89 +/- 5.08, 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 hyperemia, subconjunctival hemorrhage and corneal epithelium disorder occurred. 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.

• 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 suffers iris disinsertion 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 traumaism. He referred 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 cornea, transparent cornea, severe iridodonesis, 360° iris desinsertion, afaquia, and 22 mmHg of intraocular pressure.

Results A +14 dioptr lens provided the best corrected visual performance achievable of 0.65 with LE. Non-invasive treatment was selected in order to avoid surgery complications.

Conclusion Ophthalmologists should to monitor intrasacular 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
Glucomatous 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 a 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 Magnetric 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 left eye than in the left eye as well; the visual quality continues to deteriorate possibly due to surgical intraocular 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 (poly(methylmethacrylate) (PMMA, 7 and 15 µm), polyurethane (PU, 7 and 17 µm), Silica (13 µm)) on IOP elevation was compared. It was found that IOP of examined group with the use of Silica (13 µm) was the highest, while IOP of control group was the lowest.

**Results**
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 lower than in control group.

**Conclusion**
This model could be used to create rat model of glaucoma with stable increased IOP. The different size microbeads could provide the IOP with the desired values.

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**FO51**

Experimental glaucoma model in two lines of rats using polystyrene 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.

**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 mum 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 lower than in control group.

**Conclusion**
"Bead model" method could be used to create rat model of glaucoma with stable increased IOP. The different size microspheres could provide the IOP with the desired values.

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**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 untreated 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=0.080) at 3 days after microbeads injection. These the IOPs were decreased by 39.47 % and 9.68 % at 1 day after a single sonication.

**Conclusion**
Our results show 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.
Conclusion
VA20=0.09±0.14logMAR (p=0.3), and CS=1.08±0.16 (p=0.6) of the mentioned system showed the following values: VA100=0.01±0.09logMAR (p=0.9), 0.1±0.11logMAR, VA20=0.13±0.19logMAR, and CS=1.06±0.2, whereas the interposition of diaphragm to improve mesopic visual function was exhibit. Baseline visual acuity and contrast sensitivity scores and without the interposition of the diaphragm were: VA100=0.01±0.09logMAR (p=0.9), 0.1±0.11logMAR, VA20=0.13±0.19logMAR, and CS=1.06±0.2, whereas the interposition of the diaphragm to improve mesopic visual function was exhibit. Baseline visual acuity and contrast sensitivity scores

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±0.26logMAR, and CS=0.62±0.32, whereas values for the interposition of diffuse illumination device were: VA100=0.03±0.14logMAR, VA20=0.19±0.17logMAR, and CS=0.76±0.33 (p<0.0001). On the other hand, in drivers aged under 40, statistically significant differences were not found. In this condition, baseline visual function was: VA100=0.1±0.11logMAR, VA20=0.13±0.19logMAR, and CS=1.0±0.2, whereas the interposition of the mentioned system showed the following values: VA100=0.01±0.09logMAR (p<0.9), VA20=0.09±0.11logMAR (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.
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, autorefractometer WAM-5500 and aberrometer iTrace. Monocular measurements were made under natural accommodation and pupil size. Results 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 < -0.50D and low-hyperopic/emmetropic group (22 eyes) if their subjective refraction was > -0.50D. 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 spherical 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 spherical values (0.21 and 0.26D comparing 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.
**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**

Sixty-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 (-0.5:0.0 D or -1.0:0.0 D), 2) fluctuation of accommodation (±0.1 D or -0.1 D), 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±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 (0.14 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.

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**F062**

### The effect of simplified and traditional chinese character on accommodative reponses in myopes and emmetropes

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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=0.037). NITM was larger for traditional chinese character 0.61±0.34 D than for simplified chinese character 0.53±0.33 Dg=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 NITM 0.61±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 was 1.58±1.93 seconds while the emmetropes 0.90±1.26 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.

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**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 was 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**

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**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 corresponds to the recommended standard viewing distance. At a viewing angle of 33.4° the plates were recognized by 4 of 7 Daltons. At a viewing angle of 1.8° the plates were recognized by 3 of 7 Daltons. 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**

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**F065**

### 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 was 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**
• 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 chromatophic sensitivity. We have compared immunohistochemical photoreceptor’s stain with arrestin, redopsin, 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 redaction on the cone responses (p<0.01). Because we used chromatic stimuli 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 electroretinogram 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 stimuli 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 contractions 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 children

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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 (59-70 years) with a full-thickness MH (3rd stage by Gass, 6-8 months duration) were examined. Coherence optical topography (Stratus3000 OCT, Carl Zeiss) was 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 micropquipment (macula 12’, MP1, Nideck). The cone ERG, photopic flicker ERGs (FERG) at 8.3, 10, 12, 30 Hz were recorded (REItport/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±12°C, TMV: 7.3±1.0 mm², 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 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%), indicating to a drastic violation of the bipolar cell activity. 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.

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=-0.66; p<0.0001, for both of them). These scores varied linearly with eccentricity. The DE was inversely correlated with the PPWS (r=-0.56; p=0.0001) and positively with the collision score on the indoor mobility course (r=-0.56; 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. Colour thresholds measured in dynamic luminance contrast (LC) noise when a spatially structured object is defined only by colour signals. 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); 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 interocular scores were 2.29±0.223, 2.34±0.228 and 3.09±2.490.0, respectively. Multiple linear regression showed that CS significantly correlated with age (β=-1.1, P=0.0011), gender (β=-40.1, P=0.001), LogMAR BCVA (β=165.4, P=0.001) and SE(β=-165.4, P<0.001).

**Conclusion** Once our study is 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 mean CS 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 range 0.12 to 32 cd/m²) 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 (KOSA, 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 86% 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.

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**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 electrophysiological 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 and after 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 eye 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.

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**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/6 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 biocellular 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.

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**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 factors 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. Retina and posterior poles were collected to analyze gene expression by RT-PCR. We specifically focused on 65 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 sensitivity 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.
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

Autoimmune TL, obtained from the lymph node of C57BL/6 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

Autoimmune 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 naive 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 of uveitis in the adoptive transfer model.
The dynamics of molecular markers expression of blood lymphocytes activating at patients with an uveal melanoma at the different types of treatment

**FO81**

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±4-57 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 combined 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 estimations 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 combined 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.

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 intraorbitally 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**

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 unaected eyes (59±25 cells/mm2, n=10-14) than patients with FUS, who had an average DC density of 46±18.4 cells/mm2 (n=2) in their affected and 21±6 cells/mm2 (n=15) in their unaected 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. Much lower numbers of DCs were present in FUS, a clinical similar uveitis.
**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 data and aqueous humor of patients with endophthalmitis and control (cataract surgery) were collected. Multiples immunosassay 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 humor 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.

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**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 gutrat, 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, goscott 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 cornel ulceration and there was never evidence of infection elsewhere. Unfortunately 2nd 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.

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**F088**
Syphilitic uveitis: Vilnius region perspective: 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. Veneral Disease Research Laboratory (VDRL) and/or Treponema Pallidum Heamaglutination Assay (TPHA) and/or reactive Rapid Plasma Reagin (RPR) were obtained in all 6 patients. Posterior uveitis was the commonly present 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 rosales of the iris. Five patients were treated with intravenous benzylpenicillin and one – oral ceftriaxone.

**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.
Tocilizumab for anterior uveitis and juvenile idiopathic 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, biomicroscopy, intraocular pressure, 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 20/80–20/150(OD) and 20/200(OS). In 2007 VA decreased to 20/200(OD) as ME developed. Additional systemic therapy included between 2008 and 2009: Calcipotriol, 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.

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: 0.03–0.66, 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 EYES 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.

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 additional identifications. The Streptococcus-specific PCR was positive in 13 cases. The Streptococcus-specific PCR provided no additional diagnostic 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.

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.

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±4.45×10⁷ copies/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.
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 seemed 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.

Conclusion IB has a greater sensitivity than GWC when sample of aqueous humor (AH) was taken the 3rd week. 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.

Successful management of recurrent Acanthamoeba keratitis using topical and systemic miltefosine

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Purpose Acanthamoeba 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, dexamethasone, and ciprofloxacin 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, McBrude et al. 2007, Walochnik et al. 2009, Polat et al. 2012].

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.

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 inflamed 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 a real co-infection, or false positive?
Castleman disease may reflect poor general condition in patients with Castleman disease. Although it is extremely rare, uveitis accompanied with Castleman disease was introduced for refractory uveitis in a 58-year-old man. 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), Goldmann perimetry, and OCT.

**Results**

After tocilizumab treatment, large cells in the anterior chamber were undetectable and vascular permeability was improved in FA. 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.

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## F099

Ocular granuloma, uveitis and X-linked chronic granulomatous disease

**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 pine wood. Two hours later, she developed maculo-papular rash on her limbs. On examination, left visual acuity was 1/10. The affected eye showed a thin, translucent, linear scar in the upper part of the cornea. Inspection of the place where the girl was playing revealed the presence of numerous processionary pine caterpillars.

**Results**

The affected eye showed a thin, translucent, linear scar in the upper part of the cornea. The findings were consistent with an ocular foreign body. The diagnosis of iritis was confirmed with slit-lamp examination. The patient was treated with topical corticosteroids, antibiotics, cycloplegics, hypotensive eyedrops, and intravenous mannitol.

**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 0.25 logMar or worse, and 3 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: treatment with 12 receiving methotrexate +/- mycophenolate mofetil and 5(29%) receiving anti-TNF a therapy (infliximab or adalimumab) in addition to methotrexate +/- mycophenolate mofetil. 13/16 patients with JIA (81%) had iritis associated with their joint flares 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. Epithelial 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 resumed. 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 Crepidiastium denticulatum on oxidative stress-induced retinal degeneration
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Purpose This study was to determine whether Crepidiastium denticulatum, is effective at blunting the negative influence of 1-histidine (SR): salolamine (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 was 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 was tested in vitro was by hematoxylin-eosin staining and terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (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 HO2, OH and 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 retina 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, electoretinograms 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 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 composed 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 in and in many cases severely aggravate macular degeneration. We have reported previously low-intensity ultrasound (LIUS) of less than 1 mW/cm² shows cytoprotective and anti-inflammatory effects on chondrocytes and cartilage tissue under pathological 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 PFG (α-agonist of VEGF receptor), NaCN and H2O2. Then, they were untreated or treated with varying intensities of LIUS with a maximum of 200 mW/cm² once for 20 min a day. Viability of cells was examined with Trypan blue and Annexin V/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 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 Natriuretic 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 intravascular 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% timol) 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 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 inner 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 peri-papillary retina of healthy individuals.
Methods
Twelve otherwise healthy individuals (mean age 36.5 (SD 10.5) years) underwent dual wavelength retinal oximetry (ImedosSystems, Germany), non-contact tonometry (Keeler Pulsair, UK) and manual sphygmomanometry 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 vessel autoregulation 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 homozygous for the CC allele, 50 were homozygous for the TT allele and 31 subjects were heterozygous. 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 sphygmomanometry, non-contact tonometry (Keeler Pulsair, UK) and dynamic retinal diameter measurements using the retinal vessel analyser (ImedosSystems, Germany). 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 dilatation (~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 dilatation (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 analyze 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, DBP73 (11)mmHg) and intraocular pressure (12 (3)mmHg) upon arterial and venous oxygen saturation measurements (p=0.05). Superior and inferior MF, PD and MD were comparable (MF 97 (9)% and 97 (8)%, p=0.955, PD 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=0.6001).
Conclusion
Regional variations in oxygen saturations of retinal arterioles and venules are independent of age, blood pressure and intraocular pressure.
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 rhgomonometry and continuous retinal vessel diameter measurements using flicker light provocation (Iiva, limedosystems, 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 30 sec baseline diameter recording followed by 3 cycles of 20 sec flicker and 80 sec recovery.

Results
Immediately after smoking systemic, 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 = 0.0009). However, intra ocular pressure as well as arteriolar and venular diameter were unchanged (IOP: 15.2 (5) mmHg to 15.3 (3) mmHg, p = 0.633, arteriolar diameter: 12 (5) au to 125 (15) au, p = 0.416; venular diameter: 163 (16) au to 167 (15) au, p = 0.0329). 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 54 (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.
**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 30cm 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 eyes 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.

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**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 asthenia, decreasing of visual acuity, headache. The aim of the study was to conduct investigation of direct and consensual pupillary reactions on the flashlight, accommodative-convergent 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, autoradiotmetry, 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 both eyes during one month.

**Results**

Irifrin 2.25% 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, asthenia 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.
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 cupula 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 = 1.2.10^-9). This increase was highest (46%; p-value = 1.2.10^-24) in the temporal quadrant. Median maximal visual field temporal excursion 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.

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 Nrf2.

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.

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 or angiotensin converting enzyme inhibitor or angiotensin II receptor blocker, prior references were found in serum levels of EPO among controls, BRVO, and CRVO.

Results Aqueous level of EPO was higher in RVO (27 eyes; BRVO 16 eyes/CRVO 11 eyes) than in control subjects (RVO, 681.198-190) mU/ml vs. control, 129.5.4-24.4) mU/ml P=0.001). More specifically, aqueous EPO was higher in CRVO than in BRVO (CRVO, 118.318-190) mU/ml vs. control, 33.3198.62.5) mU/ml P=0.001). However, no differences were found in serum levels of EPO among controls, BRVO, and CRVO groups (CRVO, 111.1mU/ml[5.4-16.4] vs. BRVO, 100mU/ml[5.7-16] vs. control, 9.2mU/ml[5.7-11.2], P=0.09). 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, 816[563-1425] mU/ml P=0.002).

Conclusion In RVO, aqueous levels of EPO are elevated and could be associated with retinal ischemia and ME.
**POSTER SESSION 3**

**Pathology / Oncology - Retina / Vitreous - Lens and Cataract**

**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, vacuolated keratocytes of “honeycomb-like” structure and a very sparse amount of stromal matrix. Posterior stroma appeared non-characteristic bazes, 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 features, it can be used for confirming the diagnosis.

**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 invade the eyelid and the conjunctiva 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 we must perform large eyelid reconstruction. Through our small case series, we describe the clinical features and our management of this tumour.

**Methods**
We report six patients presenting with eyelid sebaceous carcinomas: three nodular sebaceous carcinomas, 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. To the high grade of malignity, Moreover, the biological behavior of this kind of tumour requires long-term oncologic following.

**S002**

**Digital analysis of the changes in carcinomatous conjunctiva using Aperio nuclear v9 algorithm**

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**Purpose**
To evaluate and analyze biologic 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 tumours specimens from 6 patients (6 eyes). The average age of the patients was 64 years. There were two males and four females. In 3 patients (3 eyes) conjunctival tumor was excised, cryoapplication 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 1568 till 5000 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 ≤15.5% (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.

**S004**

**Amelanotic conjunctival melanoma: diagnosis and therapeutic difficulties**

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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, CT scan, Ultrasound...) 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.
• **5005 / 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 (50-72hrs) was 3.73±M, 5.42μM and 8.33μM for CRMM1, 2 and CM2005.1 cells, respectively. Colony assays showed similar patterns of response, with surviving fractions of 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 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.

• **5006**

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 ophthalmic and neuroradiologic findings. Pathology following biopsy revealed a tuberculous granulomatous lesion.

**Conclusion** A complete systemic investigation confirmed tuberculous etiology of this granulomatous lesion.

• **5007 / 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 mimicking 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 and had small new vessels in the stroma. An anterior chamber aspirate was performed, leading to the diagnosis of diffuse large B-cell lymphoma. This high-grade lymphoma was treated with chemotherapy associated with radiotherapy.

**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.

• **5008**

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. 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 choroidal 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 23-gauge 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-histochemical 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 vitreous biopsies by a 23-g 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=1.10. 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 intracocular lesion forming extrascleral 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 2.89mm (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 dexamethasone 700 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.
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 tumors 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 a 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 siRNA 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 (NON) as typical of melanoma transformation and of a small pattern of proteins as selectively modulated in ocular melanoma.

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 patients' tumors [Nemat 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: 8/12/22/26/29-33) was administered i.p 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 M466), 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 M466). 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.

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 metastases 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 serious macular detachment in RE. Optical coherence tomography confirmed the macular neurosensory detachment in the RE. Since clinical suspicion of choroidal metastases, we referred the patient to the Ophthalmology 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 recovery 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.

Retinoblastoma – risk factors and quality of life

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Methods: Retrospective study for 84 eyes treated for retinoblastoma (RB) in Ophthalmological Department, Hospital "Prof. Dr. Nicolae Obălu" Iasi. Clinical parameters studied: age of diagnosis, adjuvant factors (hyposia, pregnancy, hemorrhage, congenital rubella, ionizing radiation, endocrinological disease of mother) and hereditary factors. Statistical analysis: program SPSS 16.0, test Mann-Whitney, Kruskal-Wallis were used.

Results: Between 1953 and 2010 in Ophthalmological Clinic were treated 702 eyes and 77 were diagnosed with RB. Unilateral cases were 70 cases and 7 cases bilateral RB. Hyposia were at 24.7% RB versus 4.8% children without RB (χ²RB = risk factor 13.4). Hemorrhages during pregnancy were 27% in mother with children with RB versus mothers with cWBr – risk factor 1.735. Mother inflammations were registered at 39% children with RB versus 17% cWBr – risk factor 2.205. Congenital rubella was at 15.6% children with RB versus 5.6% cWBr – risk factor 1.943. Endocrinological diseases of mothers were 20% versus 7.9% – risk factor 2.222. Ionizing radiations were found in 81.8% children with RB versus cWBr – risk factor 3.112. 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 diagnosed and treatment was for all cases enucleation. Quality of life is poor because of radical treatment and esthetic reasons.

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 patients’ tumors [Nemat 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: 8/12/22/26/29-33) was administered i.p 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 M466), 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 M466). 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.
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 pseudohypopyon, 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.

Acute dacroyoadenitis as atypical presentation in Sjögren Syndrome

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Purpose To present a case report of a patient with acute dacroyoadenitis as an atypical clinical presentation of Sjögren Syndrome.

Methods A 57-year-old female developed acute left dacroyoadenitis 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 dacroyoadenitis 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. Topical cyclosporine and pilocarpine have reported benefits for severe xerophthalmia in recent medical trials.
**SO21** / **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 erythematous 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 intraocular with a lot of eosinophilic cell in the pathological material; where the patient already was known with a pulmonary myeloblastic hypereosinophilic disease and treated with hydroxy 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

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**SO22** / **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 protoposis 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, gland, bone, cartilage, epithelium and neuronal-brain tissue. On follow-up examination there was no protoposis 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.

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**SO23**

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 ophthalmological 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), episceral venous congestion (n=31), ocular motor 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; ocular motor palsy in most cases (n=8). Ophthalmological sequelae were more frequent in patients with treatment visual impairment (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 ophthalmological sequelae after specific additional medical treatment.

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**SO24**

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 HFL 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 stills 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 central retina relative to the 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.

• **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 pathophysiological theory formulated about macular holes formation concerns vitreous 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 antero-posterior 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 serious foveolar detachment and is a consequence of tangential tractions of the pre-foveal 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 implication of 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, 223.6±70.1 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: 286.6±114.5 µm, 279.1±112.7 µm, and 283.1±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: 21.65–25.47 mm). 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 B·: 0.39, P<0.001) and older age (B: 0.02, B·: 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: To examine the normal thickness of the subfoveal choroid 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: 21.65–25.47 mm). In multivariate analysis, mean choroidal thickness (253±103 µm) decreased significantly with longer axial length (non-standardized correlation coefficient B·: 0.46, standardized correlation coefficient B·: 0.39, P<0.001) and older age (B·: 0.02, P<0.01).

Conclusion: Mean subfoveal choroidal thickness in elderly Caucasians was 253±103 µm. For each mm increase in axial length, and for each increase in year of age, subfoveal choroidal thickness decreased by 46 µm and 4.1 µm for each mm increase in axial length and each year increase in year of age, respectively.

• 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 (Ozurdex®) 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: 28.3% had a CRVO and 71.6% 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 retreatment 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 323 (91.2%) subjects. Mean SFCT was 253.8 ± 107.4 μm (range: 83 to 854 μm). In multivariate analysis, SFCT was associated with younger age (P < 0.001; correlation coefficient: 0.12; beta coefficient: 0.37; shorter axial length (P = 0.001; r = 0.28; 5.1; 0.13), deeper anterior chamber depth (P = 0.001; r = 0.39; 5.0; 13), thicker lens (P = 0.001; r = 0.26; 0.08; flatter cornea (P = 0.001; r = 0.46; 0.3; 11) and better best corrected visual acuity (logMAR = 0.00; r = 0.48; 4.6; 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 15 μm (95% CI: 11.9, 18.5) for every increase in axial length of one millimeter. For each year increase in age, the SFCT decreased by 4.1 μm (95% CI: 4.6, 3.7) (multivariate analysis).

**Conclusion**
SFCT with a mean of 254 ± 107 μm in elderly subjects with a mean age of 65 years decreased with age (4 μm 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 andBVCA 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 intrasession 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 512 x 128 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 0.82 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 = 0.800; 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’ (RIM0, RIM1) 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 wks. Time between screening encounter and first laser treatment (OBJECTIVE 12). Urgent: Minimum standard 70% of patients/5 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 notes. 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) and Objective 12 (screening to laser time) The attendance 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 aqueous 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 ± 0.4 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 ± 220 μm in the STTA group and 534.4 ± 157 μm in the PPV group. One, 3 and 6 months postop CMT were 392.1 ± 193 μm, 284.8 ± 101.7 μm and 354.2 ± 156.4 μm 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 (Zener AVR ratio). Seventy seven age- and sex-matched healthy subjects were included in the study as a control.

Results The mean AVR was 0.80 ± 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 = 0.016). 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 0.4mg 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 < 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 TRiBR (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 TRiBR 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 RPE.
• **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 28.2±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 0.17±0.17 (mean±SD), and the mean CMT was 353±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=0.001), 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: results 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 macula edema following retinal vein occlusion to 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-up. 220 patients with retinal vein occlusion (53.9% 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. Eight 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 ± 230.1 µm 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. 308% of patients at M1, 55.9% at M3, and 35% at M6 had an improvement ≥ 15 letters in BCVA from baseline. An IOP ≥ 21 mmHg 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 transients. At 6 months, one third of the patients required a second injection. The mean time for re-injection 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 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 macula 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 sphygmomanometer) 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 97.52% ± 9.80% (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 97.57% ± 9.90% (paired t-test, p = 0.028) immediately following exercise, and 97.26% ± 8.90% (p = 0.04) at 15 minutes following exercise.

**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 affected arterioles was performed 30 minutes later. The expression of Vegf, Vegfa, 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 Aqp1, Aqp4 and Kir4.1 channels was 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 glotic alterations of Müller cells and the redistribution of Kir4.1 protein.

Conclusion The constriction of the artenary 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 might be 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 detected in 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=0.04) 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 our initial clinical outcomes of dexamethasone 0.7 mg intraocular 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 (CME) 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 204.2µm) at 2/12 post-injection. BCVA was also significantly improved at 1/12 post-injection and further to 2/12 post-injection in nine of the patients especially in the nonischemic subgroups. Complication rate was relatively low with only four patients having a moderate raise in intraocular pressure managed with topical therapy and one patient suffered 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 large subconjuctival haemorrhage.

• 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 known 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 (SFT) and smaller choroidal neovascularization (p=0.043) as predictive factor for responder: SFT was 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.

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**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 monzygotic 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 monzygotic twins was 0.85 (95% CI 0.75-0.95) compared to 0.43 in dizygotic twins (95% CI 0.23-0.66), (p for diff<0.001).

**Conclusion**
The finding that the monzygotic 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.

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**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 chorioscleral 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.

**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 prefered nasal side, confluence in 63% when multiple area. At OCT, thickness of photoreceptor, pigment epithelium layer diminished at area and edge. Choriocapillar depth values, FA and ICG data were mainly significant 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, it’s 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.

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**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 examinations.

**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±0.40 logarithm of the minimum angle of resolution (logMAR), and the final BCVA at 60-month follow-up was 0.66±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 (0.1 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 67.3±5.2 years were included in the study. Progressive, exudative AMD was diagnosed in 33 eyes. 75 eyes had drusen or were degenerated. Laser radiation was applied transsclerally 6 times for 3 min once in two days to the macula. 20 patients with AMD (30 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.

**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 time.

**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-1β, IL-6, IL-10, TNF alpha and IL-12/p70. Finally, the level of the major angiogenic factor VEGF-A was measured in these media by ELISA.

**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 concentrations (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-p56S6K 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-p56S6K 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-butylhydroperoxide (t-BHP). We found that exposing cells to t-BHP (400µM) showed complete inhibition of Akt and p70/p56S6K active forms. However in cells enriched with DHA (20µM) and co-treated during 24 hours with Resveratrol (50,30,10 or 1µM) or the Resvega formula, Akt and p70-p56S6K active forms were restored. In the experiment with t-BHP, we observed that human ARPE-19 cells 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-1β, IL-6, IL-10, TNF alpha and IL-12/p70. Finally, the level of the major angiogenic factor VEGF-A was measured in these media by ELISA.

**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 concentrations (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.

**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-IVB 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 (641 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±3.5 years. A vascularized PED was present in 7 of 9 eyes that developed an RPE tear. 44.44% 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 -1.0 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=0.003). 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.

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**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 extramacular 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 to and after surgery.

**Results** BCVA prior surgery was 10/100 in the three patients. Funduscopy and OCT examination showed one SFCL bubble localized under the fovea. Four months after surgery, it was achieved anatomic restoration, without rest 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 had functional outcomes, probably due to a previous damage of pigment retinal epithelium and PR, aggravated by SFCL toxicity.

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**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 (98%) 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 ARM (OR: 4.48, significant for ARM 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 risk factors already described, including the most risk factors already described, including the most risk factors already described, including the most risk factors already described, including the most risk factors already described, including the most risk factors already described, including the most risk factors already described, including the most risk factors already described, including the most risk factors already described, including the most risk factors already described.
**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.

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**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 hypothesised 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 ciliary 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 intravenous 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 supine position before (t+2 min) and after the administration of acetazolamide (t+2 min) at 6 min, t+10 min and t+30 min. The mean variation of the intraocular pressure was compared between the two groups.

**Results** Consecutively to the intravenous injection of acetazolamide, a reduction of the intraocular pressure was observed in both groups (both p<0.05). 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.

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**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% intraperitoneally 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.

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**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 C57BL/6j 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: Resvega (NA). C-VEGF group: vehicle and intravitreal anti-VEGF. Oral treatments (100 µL) were administered 10 days before 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 CNVSupported in part by GARCIA-GARCIA J, IVANESCU A, GARCIA-GARCIA J, GARCIA-LAYANA A, SÁNCHEZ-DEL-ROMERO M, GARCIA-LAYANA A, IVANESCU A, GARCIA-GARCIA J, GARCIA-LAYANA A, SÁNCHEZ-DEL-ROMERO M, GARCIA-GARCIA J, GARCIA-LAYANA A, SÁNCHEZ-DEL-ROMERO M.
Purpose: To study macular involvement in non infectious intermediate, posterior and panuveitis.

Methods: The data of 201 eyes 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 (11.0%), 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 in 32 eyes (15.9%), macular oedema due to choroidal neovascularization in 2 eyes (1%), 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.

目的: 以比较分析法评估在 HIV 患者中的 CMV 感染 (CMVR) 与无额外眼外感染 (EO-CMV) 感染

方法: 这是一项回顾性队列研究。所研究的所有 CMVR 患者中, 有 24 眼 (11.9%) 与 EO-CMV 感染。在 CMVR 组中, 24% 发展了 EO-CMV, 而这些患者中 60% 有 CMVR 感染。在 CMVR 组中, 24% 发展了 EO-CMV, 其中 50% 有 CMVR 感染。

结论: CMVR 感染与无额外眼外感染 (EO-CMV) 感染相关性显著增加, 但没有显著差异在两个组群。(OR 0.7; CI 0.5-1.4), 尽管死亡率较高 (24% 对 15%, p=0.002)。多变量逻辑回归分析显示, 长时间的抗 CMV 治疗前有较高风险的 CMV 感染, 但无显著差异在两个组群。(OR 1.27; p=0.037) CMVR 感染, 但无显著差异在两个组群。(OR 0.7; CI 0.5-1.4)。死亡率较高 (24% 对 15%, p=0.002)。多变量逻辑回归分析显示, 长时间的抗 CMV 治疗前有较高风险的 CMV 感染, 但无显著差异在两个组群。
**S069**

Acute worsening of retinal lesions during oral steroid treatment in a case of intracocular 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 treatment.

**Methods**
A 49-year-old woman complaining of progressive 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. Further 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 occurred, taking the appearance of a very severe retinal necrosis. Another vitrectomy was thus performed to exclude again infectious causes but was negative for virus and toxins. 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 lymphoma may lead to dramatic lesion extension preceded by temporal clinical stabilisation or improvement.

**S070**

Ocular effects of combined therapy with pegylated interferon (PegIFN) 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 PI 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 PegIFN-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-ribavirin 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 tuberculous uveitis.

**Methods**
It is a retrospective study at the Saint Roch University Hospital in Nice. We followed eight patients (13 eyes) between September 1997 to March 2011, who presented with unilateral or bilateral tuberculous uveitis.

**Results**
A slit lamp examination revealed an anterior uveitis in twelve eyes. Six eyes presented granulomatous keratoprecipitates, five had posterior synchiae. 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 exudative 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 analyses of aqueous humor were negative. One vitreous sample was negative. All the patients were treated with anti-tuberculous therapy as well as systemic steroids with a favorable clinical outcome without any recurrences observed.

**Conclusion**
Our case series shows that tuberculous 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 helpful.

**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 three, 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 thickness 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 immediately before and after HD. The relationships between the systemic hemodynamic changes and the ophthalmologic findings during a single HD session were evaluated.

**Results**
The mean intravascular 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±3.4 μm. After HD, the ocular surface changed significantly; the tear-break up-time and basal tear secretion (Schirmer’s test) decreased, whereas the keratopathy 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.

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**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 1063 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 caucasian 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 extraretinal 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. Thermal or blast effect can cause 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 irradiates, 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.

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**S075**

**Pathologic findings for patients with acute and symptomatic floater**

CHO MJ

Retina, Seoul

**Purpose**
To evaluate and establish the rate of pathologic findings for patients with acute and symptomatic floater.

**Methods**
Retrospectively records of 3377 eyes (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 ophthalmoscope.

**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 (94%). The incidence of retinal tear was 0.8%/28 eyes) and 2/eyes of them were undergone barrier laser. The incidence of lattice degeneration was 1.8%/63 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) and 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.
• **S077**

Drumastic effect of bolus cyclophosphamide in a severe case of lupus retinopathy

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CHU Braivou, Ophthalmology, Nancy

**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 asymptomatic, rapidly progressive decreased visual acuity (8/10 P2 OD, 1/20 P14 OS). Fundus examination disclosed bilateral macular oedema, numerous petrupapillary 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 cyclophosphamide 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 GASNERUBRUM 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 EVEREST ascent (8000m) and complaining of left eye central scotoma and visual acuity defect. 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 symptoms 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**

A source of laser radiation we used Ti: sapphire laser oscillator «Coherent», which allow to obtain a sequence of pulses of duration 1.30 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 1.30 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 and sclera with marked destruction of pigments and collagen fibers in the sclera, 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 effect on retinal and scleral structures.

• **S080**

Unilateral Terson syndrome. Outcome after early vitrectomy


Ophthalmology, Zaragoza

**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 intraretinal 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 had 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 improve 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.

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• **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 (PECHR) 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 subretinal/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** PECHR 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.

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• **S083**

**Subretinal injection of recombinant tissue 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 thromolytic agents. We aimed to assess subretinal injection of rt-PA associated with anti-VEGF in the humatoma as a complication of AMD and to establish predictors of efficacy in order to identify target patients.

**Methods** Inclusion criteria were patients with subretinal hematomas 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 subretinal hematomas were included. 62% patients showed significant improvement at 6 months (p<0.04) contrary to the one-year results. Displacement of haemorrhage was observed in all patients and no complication during the surgery was noted. The mean dose of rt-PA was 50 µg/ml. All patients received locoregional anesthesia. Postoperative complications were cataract (25%), recurrent hemorrhage (25%), and ocular hypertension (12%). No cases of endophthalmitis or retinal detachment is observed.

**Conclusion** The extensive recent hemorrhage with underlying healthy macula appears to correspond to treatment contrary to the old hematoma with pigment epithelium rupture and the hematoma after anti-VEGF injections responsible of large pigment epithelium detachment.

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• **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 resistance increases with the reduction of the inner diameter of the extrusion canula. This increases the duration of silicone oil extraction. The purpose of this study was to compare 2 surgical procedures for silicone oil extraction: 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 sclerotomy after conjunctival dissection whereas a 25-Gauge transconjunctival sclerotomy enabled saline infusion. In the second group both infusion and silicone oil extraction was performed through 21-Gauge transconjunctival sclerotomies. The duration of each procedure was the main outcome measure.

**Results** The mean duration of the 21-Gauge procedure was 42 minutes compared with 22 minutes in the combined 20/25 Gauge procedure. Transitory intraoperative hypotony was encountered in two patients, one in each group. During the postoperative follow up, a vitreous hemorrhage occurred in one patient of the 23 Gauge 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 enucleated for longstanding RD and PVR. The CE strongly expressed EGFR. We have hypothesised that the disease RD and PVR stimulate a dormant population of RPCs in the CE in presence of a niche constituted by EGE. 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 four porcine eyes, one non-operated porcine eye, and one human eye enucleated for orbital tumor served as controls.

**Results**Were 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. Ki67, 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 fundoscopy showed a cystoid macular edema and optic nerve palor (RE). Many pigment deposits were present in retinal mid-periphery of both eyes. Optic 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 isionic 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, 180 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 validated by general practice doctors and/or neurologists.

**Results** 20 patients in group A, 25% in group B, 30% in group C, have early stage AD. 20% in group C have mild cognitive impairment (MCI). 25% in group B, 35% in group C, have early stage AD. 20% in group B, 30% 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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Ophthalmology, HUCA, Osco do

**Purpose** To show the long-term evolution of two cases of Combined Hamartoma of Retina and Retinal Pigment Epithelium (CHRPE), one managed by vitrectomy, and other managed conservatively.

**Methods** A 46-year-old male and a 35-year-old female, diagnosed as having a CHRPE, were observed during four years. One of them underwent pars plana vitrectomy due to an extensive associated epiretinal membrane (ERM), and the other patient declined surgery. Full clinical examination, including Best Corrected Visual Acuity (BCVA), fundus examination and Optical Coherence Tomography (OCT) was performed.

**Results** For the patient who underwent vitreoretinal surgery, the evolution was initially satisfactory, with anatomic improvement (assessed by funduscopy and OCT examination) and visual acuity stabilization. However, four years later he presented with a complaint of visual loss, and severe macular distortion was confirmed by OCT. The patient who asked for a conservative management, showed no visual nor funduscopy changes during the follow-up.

**Conclusion** Vitreoretinal surgery for CHRPE 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.
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 intravitreal injection have been fully reported.

Methods We describe the case of a seventy-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 inner retinal layers as aftereffect. Visual acuity reached 9/10 Pa 2 months 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.

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 FEERG), 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 spike 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 choioid, 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 electroretinographic and no relevant family history, may be indicative of a developmental retinal abnormality.

Primarily 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, interventionnal, 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 electroretinography were performed to assess safety and efficacy.

Results Treatment was well-tolerated in all cases. Mean BCVA improved from 40 /1.20 letters to 51 /1.7. Mean sensitivity improved from 20.6 / -3.2 dB to 22.5 / -3.7 dB.

Conclusion Ramipril demonstrated a good local and systemic safety profile as well as efficacy 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.

Recurrent retinal detachment secondary to hereditary congenital collagen disease

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Purpose Hereditary progressive arthro-ophthalmopathy, also called Sticker 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 20 G 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 determine 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 intrapenetronal transmitter. Electroretinograms (ERG) were used to evaluate retinal function and retina 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, 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 associated with retinoschisis 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 Retinoschisis 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 (anxiety, autoimmunity and serology tests).

**Results** Patient was treated with oral 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: 27µm and 219µm in foveolar region, 275µm and 302µm in temporal parafoveolar region, 201µm and 265µm 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: 246µm and 261µm in foveolar region, 232µm and 261µm in temporal perifoveolar region vs 276µm and 308µm in nasal perifoveolar region, 199µm and 230µm in temporal parafoveolar region vs 262µm 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 angiotenisin 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 sarcoidosis while 23 patients were considered as having either indeterminate or presumed sarcoidosis, according to the criteria of Abad et al. A raised ACE (p=0.013) 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 (18.7%) 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.


**5097 / 2717**

Atrophic areas and/or 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 not 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 refractive atrophic neovascularisation complicating AMD. Atrophic areas were evaluated by autofluorescence imaging Spectralis (in particular with region finder software), OCT (notably choroidocapillary 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 evaluate.

**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 areas edge. Choriocapillary depth values, FA and ICG data were mainly significative in the large atrophic areas and less 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.

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**5099 / 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 360º 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 996 µm in pre-surgery visit and 1024 µm in post-surgery visit using Glaucoma Application; and 942 and 947 µm, respectively, with Axonal Application. Reproducibility showed 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.

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**5098 / 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 centring for the red, green and blue channels of the image respectively.

**Results** Results 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 (48.5 microns) and the user-selected foveal centre (406 microns). Convolution with a Gaussian to identify the fovea produced the worst results with mean SD of 69.9-64.8 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.

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**5100 / 2617**

Subfoveal choroidal thickness: the Beijing Eye Study

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**Purpose** To study subfoveal choroidal thickness (SFT) 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 SFT.

**Results** Mean SFT was 251.8 ± 107.4µm (range: 86.9-254.1µm). In multivariate analysis, SFT 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, SFT 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, SFT 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 SFT decreased by 4.1µm (95%CI: 4.6, 3.7) (multivariate analysis).

**Conclusion** SFT with a mean of 251.8±107.4µm in elderly subjects with a mean age of 62 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 SFT and best corrected visual acuity strongly points towards a functional aspect of SFT.
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 1988, 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 386 months. 28.2% of 78 infected children were treated in utero upon detection of a maternal infection. 66.1% of 71 alive newborns 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 retinchoroidal lesion, 5 strains were analysed: 4 were genotype II (2 peripheral lesions, 1 macular, 1 peripapilae) 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.

Ocular circulation 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 were noted. Two questionnaires (PSQI and Epworth) regarding sleeping disturbances 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 PST (73%). A history of corticosteroid treatment 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.

Circadian cycle and chronic central serous chorioretinopathy
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Ophthalmologie, Reims

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 were noted. Two questionnaires (PSQI and Epworth) regarding sleeping disturbances 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 PST (73%). A history of corticosteroid treatment 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.

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 (5.6 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 10.6 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 (ETDRS), 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 months.

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 30.56µm 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 28µm. The mean IOP slightly increased to 17.83 mmHg (we had 1 case at 24 µm). 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 63.41 letters (+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; 56% 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.

• 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 phgymognosymania (UA-767, A&ED 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.

• 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 two 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.

• 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 (BRECAs). 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 different co-culture BRB models, based on BRECAs bovine retinal pericytes (BRPcCs) and rat glial cells.

Results
Co-cultures of BRECAS 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 BRECAs with VEGF, which downregulated MDRI and GLUT1 mRNA levels, transiently reduced expression levels of endothelial junctional proteins and altered their organization, increased the number of intercellular gaps in BRECAs monolayers and increased 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 months after cataract surgery. Choroidal thicknesses were independently 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 213.3 ± 67.3 μm at day 0, 213.3 ± 67.3 μm at day 7, 226.5 ± 68.9 μm at 1 month and 220 ± 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 significant differences were observed between group with diabetic retinopathy (DR) and group without. For the only patient who developed a maculopathy and 78 served as non diabetic controls.

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 577 nm diode laser for macular oedema

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Purpose Subthreshold, or tissue sparing, Diode Micropulse Photocoagulation (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 choriotetinopathy (CSR), macular edema secondary to branch retinal vein occlusion (BRVO), and even glaucoma.

Methods We used micropulse technology with 577 nm 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 significant macular edema (CSME) due to diabetic retinopathy, venous branch retinal vein occlusion and central serous retinopathy.

Results Controls performed 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 DME, due to PDR, BRVO and CSR, SDM photocoagulation is at least as effective as conventional photocoagulation without any clinically discernible evidence of laser-induced intraretinal 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 November 2011 and March 2012. 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.

Results A total of 45 patients were excluded because of previous 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 (cLECs). 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-independent 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 cLECs. 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 cLECs. 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 cLECs and primary culture of lens epithelial cells.

Conclusion Lens epithelial cells possess CAT1, and CAT1 may provide substrates for synthesis of B-defensin-1.
The lipids of lens in the aging and in cataractogenesis

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Purpose to study influence of lens lipids on its optical properties

Methods 80 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 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 final 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 linolic. The content of saturated and polyunsaturated fatty acids was approximately identical. When the 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.

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 (80 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 Selenium resulted in significant cataract formation compared to control group, p<0.001. In the CS groups, 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.

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 tricarbonyl 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 chemiluminescence 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.

Effect of Crocus sativus stigmas (saffron) extract on sodium selenite induced cataract formation

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Results Selenium resulted in significant cataract formation compared to control group, p<0.001. In the CS groups, 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.

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 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.
**Poster session 3 : Pathology / Oncology - Retina / Vitreous - Lens and Cataract**

### 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 child with congenital cataract. Systemic and ophthalmic examinations were performed.

**Results** The two affected patients, a 3 month old boy and a 7 years old girl with cataract and mystigmas were studied. Lenscopy was performed on both patients with IOL implantation in the older patient. A homozygous region of 12 Mb on chromosome 3 was identified. This region contained the previously reported FYCO1 gene. Molecular analysis revealed a homozygous c.2206G>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. (AHG 2011).

**Conclusion** Mutations in FYCO1 are also present in the Egyptian population. We have shown that it is developed de novo in this family thus indicating that this nucleotide is a hotspot for mutation and does not represent a founder effect.

### 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 minimincision coaxial phacoemulsification (2.2 mm) combined with the bimanual irrigation/aspiration (I/A) on the corneal optical quality characterized in terms of corneal aberrations.

**Methods** One hundred and eight 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 I/A. An aberrometry (OPD scan II, 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 : 0.09/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 ± 0.87 (p=0.74). At 1 month, we observed a mean reduction of : 0.25/D ± 0.21D at Day 15, and 0.23/D ± 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 29.92 ± 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.

### Sunflower cataract in Wilson’s disease : transmission electron microscopic study

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**Purpose** To report ultrastructures 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. He has bilateral sunflower cataract & Kaye-Fletchcr ring.Her right eye underwent phacoemulsification with a CCC and intracocular 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.

### 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 polishing using the silicone sleeve of the irrigation/aspiration (I/A) cannula. It is also possible to do safer polishing aspiration of cortical masses.

**Methods** We used Bausch & Lomb® single use I/A cannula 8910ST 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.

**Results** We use this method for years with different types of phacoemulsification devices. It gives a very clean scraping of posterior capsule 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 silicone 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 108 patients in which visual acuity was assessed before and after surgery, complications, pre-, intra- and postoperative, the reasons 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 ≤ 0.1 or worse in the better eye
2. Severe glare, diplopia or anisometropia ≥ 1.5 D
3. Impaired lifestyle due to cataract:
- OR
- Co-management of other pathology: 23
- Glaucoma (15), Diabetic Retinopathy (7), AMD (1)

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), ARM (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 91.23±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, third month, 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 (77.66%), 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 (92%) 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 3.2 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 IOL Master 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 unit. 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 angiography, 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 borderline and the margin of limbs. We measured the position of the 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 +/- 0.26 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, 15% have obtained the same level of accuracy. In the laser group, the three circles have the same center, and then are concentric, cell-to-cell of a rhexis good centration, unlike the manual rhexis. The femtosecond laser rhexis was circular 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.

• 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'Ophthalmologie 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 Artiiles were implanted. Three eyes underwent further keratorefractive surgery (biopptic). 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.

• 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 endothium in patients with and without pseudoexfoliation syndrome (PES). 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 PES (mean age 77.1 years [range 61-87]) and control group - 25 patients without clinical signs of PES (mean age 76.8 years [range 62-86]). SPSS 21 statistical package was used for statistical analysis.

Results: In the group of patients with PES 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] (± 351.73), hexagonal cells – 95.94 % [range 45-75] (± 5.92 %), CV - 31.92 [range 25-39] ± 4.26. The mean difference between two groups with and without PES 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 95.94%, 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. PES had no impact to hexagonality and coefficient of variation in cell-size.
**S129**

Visual acuity and contrast sensitivity function between spherical 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 spherical (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±0.01 logMAR units, and 0.01±0.02 logMAR for aIOL without differences (p=0.13). The aIOL CSF was better than the sIOL, but we did not find significant differences at any spatial frequency (p=0.01 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 did not find a great improvement of aIOL. According literature, differences are significant at 6mm pupil diameter.

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**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 (Acismart 36A, Carl Zeiss Meditec) whereas the aspheric customized group (12 eyes, 6 patients) received on the dominant eye an Acissmart 36A and on the other eye a zero spherical IOL (Acis smart 46 LC, Carl Zeiss Meditec). Inclusion criteria were a -0.25 to -0.3µm preoperative corneal SA and a monocular postoperative visual acuity (VA) ≥ 2/20. Reported visual outcomes were best corrected monocular and binocular distance Snellen VA and uncorrected monocular and binocular near VA. A binocular defocus curve was performed from +0.1 to -4.0 Diopters (D) by 0.25D step. A corneal and total higher-order aberrations (KRI, 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 -4.03 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 spherical 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.

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**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 (IOL) in an optomechanical eye model.

**Methods**
Freshly enucleated porcine eyes with an implanted AIOL and removed cornea were placed in a cuvette with R5 (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-date 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 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.

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**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 reflectance 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 (Tropecco, 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 a RMS deviation of some µm for spherical surfaces and corresponding 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 cefoxime in reducing early-phase adherence of staphylococcus epidermidis to hydrophobic intracocular lenses

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Purpose: To evaluate the bacterial anti-adhesive effect of cefoxime and moxifloxacin on the primary-attachment phase of S.epidermidis to acrylic intracocular 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 cefoxime 1mg/0.1ml, 15 min before incubation in a S.epidermidis suspension 108 CFU/ml. All groups were incubated in the bacterial suspension for 15 min before being added with antibiotics. 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:41(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-T2:1,25.103[SE:1.18 ; SD: 9.72] and Cef-T2:1.103[SE: 26.9 ; SD: 107.6]. There was no significant difference in antibiotic time introduction concerning ceftazidime (p=0.132). Moxifloxacin was more effective when used before incubation (p=0.001). Overall, moxifloxacin was more effective than cefoxime (p=0.001).

Conclusion: Both moxifloxacin and cefoxime significantly reduced S.epidermidis adherence on IOLs. The anti-adhesive effect was superior with moxifloxacin. 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, 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 irrigation 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 intracocular 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 Lens Opacities Classification System III (LOCS III). Half of the eyes were assigned to phacoemulsification with low fluidics (300mNmm vacuum and 20cc/min maximum aspiration flow), and the other half to high fluidics (500mNmm 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 Neodynium 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, 3.84 ± 3.43, 8.89 ± 7.35, 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: The 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.

Poster session 3: Pathology/Oncology - Retina/ Vitreous - Lens and Cataract
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 capsulotomy 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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