European Association for Vision and Eye Research

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Abstract book

21 CME credits


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EVER listed countries travel grants

We are pleased to announce that the following 15 members younger than 40 year in age from listed countries will receive a travel grant for the amount of 400 EUR:

- ACB - Rèka ALBERT - Hungary
  3136 - Mesenchymal-like stem cells from human corneal stroma grown in medium containing human serum as the only supplement
- RV - Adrienne CSUTAK - Hungary
  357 - Diabetic retinopathy screening with computational support
- COS - Dariusz DOBROWOLSKI - Poland
  4374 - Cultivated oral mucosa epithelium transplantation (COMET) in bilateral limbal stem cell deficiency
- LC - Marie KALFERTOVA - Czech Republic
  254 - Evaluation of posterior capsule opacification after cataract surgery using liquifaction method
- MBGE - Gergely LOSONCZY - Hungary
  261 - Identification of novel germline mutations in the VHL gene in Hungarian von Hippel-Lindau patients
- RV - Anna MACHALIŃSKA - Poland
  3216 - AMD and atherosclerosis coincidence: the role of complement system activation and endothelial dysfunction
- MBGE - Ireneusz MAJSTEREK - Poland
  265 - Evaluation of MMP-1 gene expression variants as a risk factor of primary open-angle glaucoma
- MBGE - Dorota NOWAK - Poland
  260 - Analysis of locus 2q13 in Ecuadorian family with keratoconus
- PO - Mykolas PAJAUJIS - Lithuania
  437 - Anterior segment OCT and histopathologic data in conjunctival, limbal and subconjunctival tumours
- VEP - Przemyslaw PAWLOWSKI - Poland
  464 - Electrophysiological assessment of fundus albipunctatus
- G - Donatas PETROSKA - Lithuania
  235 - Digital analysis of the trabecular pigmentation using positive pixel count algorithm
- RV - Simona STECH - Lithuania
  340 - Responce to intravitreal bevacizumab for macular edema following central retinal vein occlusion in patients with pseudoexfoliation syndrome
- RV - Katalin TOTH-KOVACS - Hungary
  3211 - Association of Alzheimer's disease and age-related macular degeneration
- NSPH - Magdalena WASIK - Poland
  309 - Relationship between optical coherence tomography and visual evoked potentials in patients with parasellar tumours without chiasmal compression
- RV - Olesya ZIYATDINOVA - Russia
  3217 - Ranibizumab for the treatment of exudative age-related macular degeneration associated with retinal pigment epithelial detachment

EVER travel grants

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

- ACB - Goran PETROVSKI - Hungary
  2132 - Resveratrol, rapamycin and MG-132 as inducers of autophagy in ARPE-19 cells
- COS - Claudia CURCIO - Italy
  4372 - CREB is involved in growth of pterygia
- G - Omar MAHROO - UK
  4151 - Outcomes of trabeculectomy with transconjunctival application of mitomycin C
- IM - Magdalena BAZEWICZ - Belgium
  429 - Effect of SOCS1 overexpression on RPE cells activated by cytokines
- LC - Marzieh KOHANDANI TAFRESHI - France
  2365 - Semi-automatic 3D reconstruction of the anterior segment from high frequency ultrasound scans
- MBGE - Pete WILLIAMS - UK
  2121 - Changes in retinal neuronal connectivity in a mouse model of dominant optic atrophy
- NSPH - Hafid KHAYI - France
  306 - Association between non-arteritic anterior ischaemic optic neuropathy and sleep apnoea syndrome
- PBP - Sarah VAN DE VELDE - Belgium
  3323 - Topical application of AMA0076, a locally acting rho kinase (ROCK) inhibitor, results in a robust IOP control in a hypertensive rabbit model
- PO - Mieke VERSLUIS - The Netherlands
  3362 - ERK activation and monosomy 3 are associated with Src expression in uveal melanoma and may serve as biomarkers for dasatinib treatment
- RV - Matus REHAK - Germany
  4112 - The effect of anti-VEGF treatment and triamcinolone in experimental retinal vein occlusion
- VEP - Guillermo PEREZ - Spain
  4325 - Assessing the wavelength dependence of intraocular scattering by a new optical approach

Alta Eficacia Tecnología SL, Spain, travel grant

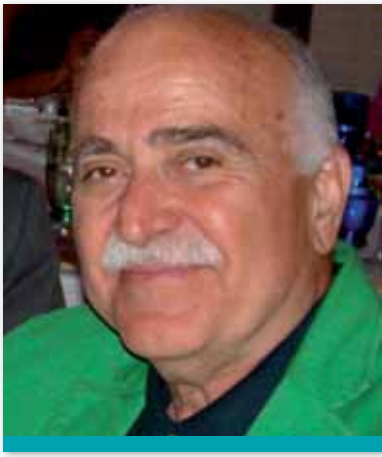
Alta Eficacia Tecnología is pleased to announce a travel grant of 400 EUR for the best paper in the VEP section

- Christian CASANOVA - Montreal
  4321 - Spatio-temporal responses in the visual cortex evoked from first and higher order thalamic nuclei in tree shrews: a voltage sensitive dyes study

Spot the difference! The electrophysiological differentiation of retinal fleck and spot disorders

HOLDER GE
Moorfields Eye Hospital (London)
Institute of Ophthalmology, University College London (London)

The lecture will discuss some of the causes of fleck or spot lesions in the retina, and use a case based approach to demonstrate the value of electrophysiological testing in their differential diagnosis.



The development of microkeratomes from the very early ages, with handmade and mechanical systems, until the fempto - laser technology today

PALLIKARIS I
University Heraklion

Ocular surface and refractive surgery

COCHENER B
University department of Ophthalmology (Brest)

Purpose

Dry eye represents nowadays the most common complication after PRK and even more frequent after LASIK. Preoperative dry eye constitutes a risk factor for postoperative severe dryness; that it why it appears crucial to detect and treat surface disorder before surgery.

Methods

We will remind the list and hierarchy of tests available for the assessment of ocular surface. Unfortunately, values of the defined criteria are variable and there are a lot of variations in the methods. Moreover, the correlation between clinical symptoms and tests results is very poor. The access to tear osmolarity (TearLab©) could be an interesting new biomarker. A study will be presented showing that 44% of patients, candidates to LASIK have an asymptomatic dryness before surgery (mild to moderate stage).

Results

Related to the principle of these two procedures, the cause of ocular surface deregulation lies on neurotrophic disturbances (secondary to nerves section) and inflammation (wound healing process). In addition, changes in corneal shape can affect the tear dynamics with an increase in ocular surface dessiccation. All these phenomena are systematically observed after photoablation for a transitory period of 1 to 3 months. But, sometimes, they do persist beyond one year (20%), becoming chronic and a source of a great discomfort and dissatisfaction (10%). The strategy of treatment will be discussed, in grading the medications according to the growing severity.

Conclusions

Is there a difference between surface PRK and LASIK? Hinged flap induced transection of a large number of afferent sensory nerve fibers during lamellar cut, which impacts the integrated lacrimal gland OS functional unit. Finally, LASIK is responsible for more dry eye syndromes than PRK, should be prefered in case of a preoperative ocular surface disorder.

Clinical and molecular genetic aspects of optic nerve hypoplasia

TRABOULSI E

Optic nerve hypoplasia is one of the leading causes of childhood blindness in the USA, with estimated incidence of 1/10,000 live births. It is characterized by a subnormal number of optic nerve axons with preserved blood vessels and glial tissue support. It is congenital and non-progressive. The speaker will present clinical data on more than 100 patients from a pediatric clinic and will review the associated neurological and systemic problems in these patients. A review of underlying molecular genetic, pathogenetic mechanisms and environmental factors will also be given. Optic nerve hypoplasia is an important cause of irreversible blindness. It is undoubtedly a heterogeneous group of conditions. Environmental causes play an important role in its etiology and associated conditions are numerous. Endocrinologic complications are treatable and neurological problems need to be identified and addressed. Studies are underway to identify genetic causes and to provide guidelines for prevention and management.

From comfort to pain: neural basis of ocular surface sensations

BELMONTE C
Instituto de Neurociencias, UMH-CSIC (San Juan de Alicante)
Fundación de Investigaciones Oculares, Instituto Fernandez-Vega (Oviedo)

The exposed surface of the eye is richly innervated by sensory nerve fibers originating from trigeminal ganglion neurons. They reach the cornea and bulbar conjunctiva as thin myelinated or unmyelinated nerve fibers lacking morphological terminal specialization. However, electrophysiological studies have shown that sensory neurons innervating the eye are functionally heterogeneous. Based upon their response to specific stimuli, different functional types of sensory nerve fibers have been identified in the cornea and bulbar conjunctiva. Mechanonociceptor fibers (~20% of the total) react only to mechanical forces; polymodal nociceptor fibers (~70%) respond to mechanical forces but also to heat, exogenous chemical irritants and endogenous inflammatory mediators. Cold-sensitive fibers (~10-15%) display an ongoing impulse activity at basal corneal temperatures and increase markedly their firing frequency with moderate cooling. Differences in transduction capacity among ocular sensory fibers are attributable to the variable expression of different types of transduction channels (members of the TRP superfamily, ASICs, 2P domain K channels) HCN channels and of voltage-dependent Na+ K+ and Ca2+ channels.

Under pathological conditions (inflammation, surgical injury, dryness of the ocular surface) activity of ocular sensory nerve fibers changes markedly as the result of short-term changes in ion channel expression secondary to local release of inflammatory agents and growth factors, and of long-lasting modifications in gene expression. This leads to the development of spontaneous activity and of abnormal responsiveness to natural stimuli.

Each of the functional types of corneal sensory fibers can be stimulated selectively in humans, using an instrument (the Belmonte esthesiometer) that delivers gas pulses of variable flow at neutral temperature (mechanical stimuli), CO^2 concentrations (acidic stimuli) and cooled or warmed air at subthreshold flow levels (cold and heat stimuli) onto the ocular surface. Stimulation of the different functional populations of nerve fibers of the ocular surface evokes a specific quality of sensation that includes a variable component of unpleasantness. The relationship between activation of the different classes of ocular surface sensory fibers under normal and pathological conditions and the quality of the experienced sensation is now being elucidated.

In addition to their role in the production of conscious innocuous and noxious sensations referred to the eye surface, sensory fibers appear to play a role in the maintenance of the ocular surface homeostasis, including basal and reflex modulation of tearing and trophic maintenance of corneal and conjunctival tissues.

Supported by grants BFU2005-08741 and CONSOLIDER-INGENIO 2010 CSD2007-00023 from the Government of Spain.

Clouding lens, swap or stop?

SÖDERBERG P
Uppsala University, Ophthalmology, Dept Neuroscience

Ophthalmic Research

Road to fulfillment (not perdition): taming immune response to restore vision

DICK A
School of Clinical Sciences (Bristol)

Understanding immune regulation that maintains retinal function whilst interrogating immune responses during retinal inflammation has illuminated avenues to harness for future therapy of many disorders including uveitis and neovascular age-related macular degeneration. The retina is endowed with a network of a continual turnover of myeloid derived cells. The default response is to regulate inflammation, however during inflammation the over burdening infiltration of activated T cells or macrophages generates damage and homeostasis is difficult to refirm. By harnessing approaches of suppressing infiltration via inhibiting trafficking of cells into the tissue, or inhibiting activation of cell infiltrate and then restoring homeostasis via recapitulating natural mechanisms of control will prevent damage, facilitate healing and regeneration and maintain immunoregulation.

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.

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Courses

• 1211

Unilateral optic disc swelling: history and examination

KAWASAKI A
Lausanne

Purpose To review the important aspects of the history and fundus examination that serve as clues toward diagnosis

Methods Didactic lecture

Results In the patient with unilateral disc swelling, it is important to discern if the patient has noted accompanying visual loss and / or pain. If visual dysfunction is noted, is it unilateral or bilateral, acute or subacute? If pain is an accompanying feature, is it localized pain or diffuse headache, is it associated with eye movements or constant?The examination should first affirm that the swollen disc appearance is not due to a congenital anomaly like buried drusen, hamartoma or hypoplasia. In the event of true, acquired optic disc swelling, certain features such as segmental edema, pallid swelling or the presence of retinociliary shunt vessels point strongly to specific diagnoses.

Conclusion History and careful examination are the first steps to diagnosis in the patient with unilateral disc swelling.

Commercial interest

• 1212

Unilateral optic disc swelling : differential diagnosis and evaluation

GOLNIK K
Cincinnati Eye Institute

ABSTRACT NOT PROVIDED

• 1213

Bilateral optic disc swelling: differential diagnosis and approach to investigation

LEE AG (1, 2, 3)
(1) Ophthalmology, Houston
(2) Weill Cornell Medical College, New York
(3) Baylor College of Medicine, Houston

Purpose To define bilateral optic disc swelling and the differential and approach to investigation

Methods Case based learning, evidence based medicine, practice based learning and systems based practice

Results Common things are commonNeuroimaging followed by lumbar puncture is standardMost cases are pseudotumor cerebri

Conclusion A systematic approach to bilateral disc edema will allow the clinician to diagnose and treat bilateral disc edema appropriately

• 1221
In vitro techniques for ocular cell biology and tissue engineering

UUSITALO H (1, 2)
(1) SILK , Department of Ophthalmology, University of Tampere, Tampere
(2) University Hospital, Tays Eye Center, Tampere

Purpose In vitro techniques form the basis for ocular cell and molecular biological approaches in basic and translational research. They are valuable tools with several benefits like their cost efficiency. They are after they have been validated usually relatively easily and quickly performed and in most cases suitable for automated analyses. In many cases their use can replace in vivo studies with experimental animals and thus they are ethically sustainable. By using valid in vitro techniques it is also possible to simplify the research frame from very complex in vitro situation and to set more specified hypothesis. Therefore these alternative in vitro techniques have gained popularity, although they are not able to totally replace in vivo techniques and the use of experimental animals.

Methods There are, however, several drawbacks in the use of in vitro techniques. The results of them should be analyzed critically and the validity of the used in vitro technique should be rechecked on the basis of the new knowledge. It should also be kept in mind that an in vitro technique valid for one specific signalling cascade can be totally unacceptable for an other. Techniques based on immortalized cell lines in most cases are simple and cost effective, however, having several and sometimes serious restrictions, due to their altered cellular behavior. Therefore their use in each specific case should be validated and the results compared with those obtained by using primary cell cultures or cells differentiated from hESC's or iPSC's or in vivo studies.

Results The simplified techniques can very seldom reveal the complex cell signalling cascades the various cell in tissues are interacting with each others.

Conclusion In vitro techniques should therefore be critically evaluated.

• 1222
In vitro methods, biomarkers and proteomics in eye research

BEUERMAN RW (1, 2, 3), WEON SR (1), CHEW J (1), ZHOU L (1, 3), ZHU HY (1), RIAU AK (1)
(1) Singapore Eye Research Institute, Singapore
(2) DUKE-NUS SRP NBD, Singapore
(3) Ophthalmology, NUS, Singapore

Purpose To understand biochemical pathways using cell culture models simulating certain aspects of eye disease combined with several modes of analysis. The use of primary cells and cell lines was explored as well as the use of laser capture micro dissection to reveal the roles of specific cell types of the ocular surface and meibomium glands.

Methods Primary human conjunctiva cells were obtained from eye bank material as well as a conjunctiva cell line, IOBA cells. Additionally, limbal, conjunctival and eyelid tissues were obtained from human and mouse eyes. Full thickness cryostat tissue sections were made for laser microdissection (PALM Combi system) which were collected in 0.5ml tubes with 40ul or either Trizol for RTPCR or lysis buffer for protein extraction.

Results Understanding the role of specific cells and their receptor specificities, the interaction of various epithelial cell layers with the environment in the conjunctiva and limbal regions has been difficult. The use of laser dissection has begun to clarify some of these relationships. In the meibomium gland neural receptors for NYP1, VIP1, SP and all five muscarinic receptors in the various cell types. In conjunctival tissue epithelial microregulators of found site specific distribution which may be related to the stem cell niche. Finally, laser dissection has allowed the properties of human basal layer limbal cells to be differentiated from the more anterior cells.

Conclusion The ocular surface remains a challenge for understanding the interactions of the various epithelial cell types, the response to stress and the unique characteristics of the stem cells.

• 1223
How to study autophagy in RPE cells?

KAARNIRANTA K
Department of Ophthalmology, Kuopio

Protein turnover control is particularly important in post-mitotic cells such as in retinal pigment epithelial (RPE) cells, where accumulation of malfunctioning proteins may be highly detrimental. In eukaryotic cells, proteolysis occurs mainly in proteasomes or in lysosomes. Autophagy is a strictly regulated lysosomal pathway that degrades cytoplasmic material and organelles. In macroautophagy, a portion of the cytoplasm to be degraded is first wrapped inside a specialised autophagosome, which then fuses with lysosomal vesicles and delivers the engulfed cytoplasm for degradation. Recently, it has been shown that autophagy and the release of intracellular proteins via exosomes by the aged RPE may contribute to the formation of drusen. In this course all central molecules and techniques to examine autophagy are discussed.

• 1224
In vitro techniques for assessing differentiation and functionality of human pluripotent stem cell -derived RPE cells

JUUTI-UUSITALO K
Institute of Biomedical Technology, University of Tampere, Tampere

Human embryonic stem cells (hESC) and induced pluripotent stem cells (iPSC) serve an unlimited source of cells capable of differentiating retinal pigment epithelial cells. These cells may be used in in vitro drug testing and in cell transplantation therapies. Small population of pluripotent hESCs and iPSCs spontaneously differentiate to RPE cells. At present most differentiation methods are based on this rather inefficient method. Maturation of RPE cells from pluripotent stem cells occurs via multiple developmental phases. In those phases cells express genes and proteins that are characteristic to neuroectodermal, optic vesicle, optic cup and in the end mature RPE cells. Differentiation and maturation process of RPEs is slow, taking several weeks. However, attempts to improve the yield and the rate of maturation with biological and chemical supplements are ongoing in the laboratories around the world. The differentiation potency and maturation status is dependent on the cell line and the culture environment, furthermore hESC and iPSC derived RPE cells are also capable to trans-differentiatiate. In addition to the basic cell and molecular biological characterizations it is vitally important to assess the differentiation and maturation status of acquired cells with functional tests. In this lecture methods to derive RPE cells from hESC and iPSC as well as functional test to assess functionality of acquired cells will be addressed.

• 1231

Modern pterygium surgery

DUA H
Queens Medical Centre,, Nottingham

ABSTRACT NOT PROVIDED

• 1232

Limbal stem cell transplantation techniques

GICQUEL JJ
Ophthalmology, Poitiers

Limbal epithelial stem cells (LSC) are essential for the regeneration of the corneal epithelium. Limbal stem cell deficiency (LSCD) that can develop in traumatic, immunologic, or genetic diseases affecting the ocular surface is a major cause of corneal transparency loss.Limbal stem cell transplantation (LSCT) aims to restore a corneal epithelial phenotype, essential to maintaining the corneal transparency. The source of donor tissue containing LSC for in vivo expansion, can be the healthy fellow eye (Conjunctivo Limbal Autograft (CLAU)), living-related (LR) Conjunctivo Limbal Allograft or cadaveric (Kerato Limbal Allograft (KLAL)). Sheets of ex vivo expanded bioengineered epithelial cells (from autologous origin (LSC / oral mucosa) or LR (LSC) are an alternative. Before and after transplantation a proper control of the ocular surface inflammation is essential. Systemic and topical immunosuppressive treatment is also needed in all allograft recipients. In order for the surgical restoration of the corneal transparency to be complete, lamellar and penetrating keratoplasty are often required.

• 1233

Penetrating keratoplasty

DIGHIERO P
CHU de Poitiers - BP 577, Service d'Ophtalmologie

ABSTRACT NOT PROVIDED

• 1234

Anterior and posterior lamellar keratoplasty

NUBILE M
University Chieti-Pescara, Ophthalmology, Chieti

ABSTRACT NOT PROVIDED

• 1235

Indications and limitations of amniotic membrane transplantation

DUA H
Queens Medical Centre,, Nottingham

ABSTRACT NOT PROVIDED

• 1241
Pathophysiology of uveitis

DICK A
School of Clinical Sciences, Bristol

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

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

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

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

• 1242
Classification of uveitis

ANDROUDI S
Thessaloniki

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

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

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

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

• 1243
Symptoms and signs of anterior uveitis

NERI P (1), ARAPI I (2)
(1) Ocular Immunology Unit, The Eye Clinic-Polytechnic University of Marche, Ancona
(2) The Eye Clinic-Polytechnic University of Marche, Ancona

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

Methods Review of symptoms and signs of AU.

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

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

• 1244
Symptoms and signs of posterior uveitis

KHAIRALLAH M, KAHLOUN R
Ophthalmology, Fattouma Bourguiba University Hospital, 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 chorioretinal 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 cuffing or sheathingOther 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.

• 1245

Laboratory work-up and specialized investigations

PLEYER U
Charite, Campus Virchow, Augenklinik, Berlin

ABSTRACT NOT PROVIDED

• 1246

Imaging: techniques and indications

HERBORT C
University of Lausanne & Centre for Ophthalmic Specialised Care, Ophthalmology

ABSTRACT NOT PROVIDED

• 1261
Diagnostics of adult ophthalmic tumours: role of clinical history, symptoms and signs

KIVELÄ T
Helsinki

Purpose To summarise signs and symptoms useful in diagnosing adult ophthalmic tumours.

Methods Personal experience of the author and relevant data from literature.

Results According to studies from the United Kingdom, Finland and United States, 28-42% of adult patients with intraocular tumours may experience delays because the lesion is either misdiagnosed (e.g. as macular degeneration, naevus, rhegmatogenous retinal detachment) or missed at the initial visit. Of these patients, 72-87% have symptoms attributable to the tumour such as blurred vision, photopsia, floaters, metamorphopsia, and visual field loss. These symptoms can also be caused by many benign conditions (e.g. vitreous detachment) but should not be interpreted as innocent without adequate fundus examination. Signs specific for iris and ciliary body tumours include a visible mass, sentinel vessels, acquired astigmatism and cataract. Choroidal tumours may induce serous retinal detachments, subretinal and vitreous bleedings and, sometimes, lipid exudation. Finally, orange subretinal pigment suggests the diagnosis of a uveal melanoma whereas uniform drusen point to a long-standing naevus.

Conclusion Signs and symptoms of ophthalmic tumours are mostly nonspecific, calling for an appropriately high level of suspicion and a systematic approach to clinical examination to avoid missed diagnoses. Earlier diagnosis could be achieved especially if dilated fundus examinations were performed without exception and if all suspicious naevi were referred for a second opinion.

• 1262
Diagnostic tools for adult intraocular tumours

ZOGRAFOS L
Jules-Gonin Eye Hospital, Lausanne

Indirect ophthalmoscopy and fundus drawing, fundus photography, standard and 150° ICG, standard and 150° fluorescein angiography, auto fluorescence, OCT, ultrasonography, UBM, MRI and in selected cases intraocular biopsy are the main diagnostic tools used in ocular oncology.The tumors can be documented either by composite standard fundus pictures, or panoramic fundus photographies.Modifications of the pigment epithelium are observed either by standard fluorescein angiography and by standard ICG or by autofluorescence. Hemodynamic modifications of the choroide and the retina are observed with panoramic fluorescein angiography and ICG.Modifications of the retina on the surface of the tumors and modifications of the macula are studied with high resolution OCT.The shape and the height of the tumors are measured with standard 20 or 10 MHz, B mode ultrasonography. The intra tumoral reflectivity and attenuation are studied with A mode ultrasonography. The volume and the shape of tumors located in the anterior segment are observed and studied with non contact 50,35 or 20 MHz high resolution ultrasonography.In selected cases, MRI, cytology and cytogenetics are used in order to define the diagnosis.In small tumors the final diagnosis is often established following a documented tumor growth.

• 1263
Technique and role of biopsies in intraocular tumours

DAMATO BE (1), COUPLAND SE (2)
(1) Ocular Oncology Service, Liverpool
(2) Pathology Department, Liverpool

Purpose This presentation will give an overview of intraocular tumour biopsy with special reference to techniques, results and complications.

Methods The methods include: (a) aspiration biopsy, using a fine needle or vitreous cutter, passed through the sclera or through the retina; (b) incisional biopsy; and (c) excisional biopsy, removing either the tumour or the entire eye. Close liaison with the pathologist is required, especially in the case of vitreous biopsy for suspected retinal lymphoma. Immunohistochemistry has greatly enhanced diagnostic accuracy.

Results Biopsy is usually successful at obtaining sufficient material for diagnosis and prognostication. The chances of failure are greatest with small tumours. Others complications include: vitreous haemorrhage, rhegmatogenous retinal detachment, endophthalmitis and tumour seeding. Prognostication is more accurate if the biopsy results are assessed together with clinical data, also taking age and sex into account.

Conclusion Biopsy is useful for diagnosis and prognostication in selected cases, but requires surgical expertise and a highly-skilled laboratory team.

• 1264
Diagnostic techniques for adnexal tumours

SEREGARD S
St. Erik's Eye Hospital, Stockholm

ABSTRACT NOT PROVIDED

• 1265
Diagnostics of retinoblastoma

DESJARDINS L
Institut Curie, Paris

Purpose Retinoblastoma is the most frequent malignant intra ocular tumors in childhood. The incidence is one out of 15000 to 18000 births. The median age at diagnosis is 24 months for unilateral and 12 months for bilateral.The genetic predisposition is autosomal do

Methods In 1971 Knudson made the hypothesis that 2 genetic alterations in the same retinal cell were necessary. In bilateral disease there is one germline and one somatic mutation and in unilateral non hereditary, 2 somatic mutations. The Rb1gene is located on chromosome 13 q 1-4 . The Rb 1 protein is a pocket protein involved in the cell cycle regulation

Results Most frequent symptoms are leukocoria and strabismusLater symptoms include heterochromia iridis,rubeosis, buphtalmia, pseudo hypopion, uveitis, inflammatory pseudo tumor and exophtalmia. Diagnosis of retinoblastoma is made by fundus examination. Imaging of the orbits and brain should be performed using MRI if possible. Ultrasonography with B and A scan is also useful as well as the use of Retcam .Differential diagnosis is sometimes easy when there is colobomas ,persistance of hyperplastic primary vitreous ,hamartomas or astrocytomas It can be difficult in cases of advanced Coats disease or when there is diffuse infiltrating retinoblastoma.

Conclusion We have made a retrospective study on patients sent for suspicion of retinoblastoma in our institute from January 2003 to December 2005 If we compare this serie to the serie published in the literature we can say that the pourcentage of well diagnosed retinoblastoma is improving. We have found 16% of wrong diagnostics. There was 30% in the serie of Balmer in 1988 and 42% in the serie of Shields in 1991. The most frequent differential diagnosis reported in all series is Coats disease

• 1266
Diagnostics of phakomatosis

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ABSTRACT NOT PROVIDED

• 1311

Anatomy & etiology

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The anatomical position of the upper and lower eyelids is dominated by the balance between forces closing the eyelids (protractive) and forces opening the eyelids (retractive). The protractive forces of the lower eyelid are maintained by the orbicularis oculi muscle (OOM), innervated by the VII nerve, whereas the protractive forces of the upper eyelid are the gravitational traction as well as the action of OOM. In the case of VII nerve malfunction, an imbalance of protractive and retractive forces in favor of the latter. In the upper eyelid, this leads to elevation (retraction) of the eyelid margin with poor depression upon voluntary eyelid closure (lagophthalmos). In the lower eyelid, this results in defective support against gravitational traction, depression and progressive eversion of the lower eyelid margin (paralytic ectropion) as well as deficient tear drainage through the active mechanism of lacrimal pump, which is largely maintained by the action of OOM. The resulting epiphora leads to a persistent vicious circle of ocular irritation and digital rubbing by the patient, creating repeated mechanical stress on the anatomical supporting elements of the lower eyelid, i.e. the medial and lateral canthal tendons, which may become destabilized or completely detached. The combined action of the above mentioned components leads to damage to the ocular surface, such as corneal epithelial defects, which may threaten the integrity of the eye through infection or corneal perforation. The anatomy and pathophysiology of VII nerve malfunction as well as their clinical and imaging assessment are discussed.

• 1312

History of disease, facial nerve grading systems & clinical evaluation

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Obtaining an accurate history of the onset, progress and associated symptoms of newly acquired facial nerve palsy is extremely helpful in determining the potential cause of the palsy. More importantly it serves as a guide for prognosis and timing of any necessary surgical intervention. Acute versus chronic facial nerve palsy, complete versus incomplete facial nerve palsy, recovery and recurrence of the disease will be discussed.The gold standard for grading facial nerve function is the House-Brackmann grading scale. Due to the limitations and subjectivity of this scale, several new scales of various degrees of objectivity and ease of use have been introduced. These include the Nottingham system, the Sunnybrook scale, the Yanagihara and the Sydney system, all with their advantages and disadvantages.Clinical evaluation of a patient with facial nerve palsy include evaluation of upper eyelid retraction, blink reflex, lagophthalmos, brow ptosis, paralytic ectropion, midface ptosis, mouth symmetry, platysma muscle strength, hearing, corneal sensation, Bell's phenomenon, tear function and synkinesis.

• 1313

Management of corneal exposure & lagophthalmos

BOBORIDIS K
Aristotle University of Thessaloniki

ABSTRACT NOT PROVIDED

• 1314

Management of epiphora & facial synkinesis

CHALVATZIS N
Bristol Eye Hospital

ABSTRACT NOT PROVIDED

• 1315

Periocular cosmesis & facial dynamic procedures

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(2) Dept. Plastic Surgery, Athens Airforce Hospital, Athens

Purpose To present Periocular Cosmesis & Facial Dynamic Procedures, that can be performed in severe and refractory facial nerve palsy cases.

Methods Didactic course lecture

Results Facial reanimation using dynamic procedures is a multidisciplinary rehabilitative type of management which may be undertaken in longstanding and severe facial nerve palsy. This management includes facial nerve repair, facial nerve substitution and temporalis muscle transfers.Peri-ocular aesthetic issues need to be addressed in severe and refractory facial nerve palsy cases. Brow lift, midface lift and facial lift can be performed to improve functionality and cosmesis.

Conclusion These procedures can provide a moderate to significant degree of improvement in facial nerve functionality and periocular cosmesis

• 1321

Corneal bacterial infections

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Ophthalmology, 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.

• 1322

Herpes ans Zoster keratitis

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Herpes simplex virus (HSV) and varicella-zoster virus (VZV) are two leading causes of corneal infection with potential severely impaired visual acuity. These two viruses share multiple characteristics, including the ability to become latent in the trigeminal ganglia, before reactivation and migration along the trigeminal fibers innervating the cornea. The clinical settings of keratitis may vary from an epithelial defect (dendritic of geographic) to a more severe disease involving the stroma and/or the endothelium. Classically, HSV keratitis occurs from the second decade of life, and associated skin disease is not frequent and only involves the eyelids. In contrast, VZV keratitis mostly occurs after the sixth decade, as an associated finding of herpes zoster ophthalmicus (HZO). However, several studies recently highlighted that the rate of HSV keratitis increases with age, even in elderly, and some other studies reported VZV keratitis in children, either isolated or associated with HZO. Antiviral drugs currently available are highly efficient to reduce the severity on ongoing HSV- or VZV keratitis, but preventive treatments still have to be optimized. For HSV keratitis, the usual preventive treatment, as defined by the HEDS study, only reduces the rate of relapses in a two-fold manner, and the optimal dosage has not been settled for patient with severe herpetic disease. For VZV, the two vaccines against chickenpox and HZO probably will lead in the future to a reduction of the incidence of keratitis, but they are not widely used, even in most of developed countries.

• 1323

Fungal infections

KESTELYN P
UZ Gent

ABSTRACT NOT PROVIDED

• 1324

Can amniotic membrane help treating severe corneal infections

DIGHIERO P
CHU de Poitiers - BP 577, Service d'Ophtalmologie

ABSTRACT NOT PROVIDED

• 1325

Infectious crystalline keratopathy and its management

DUA H
Queens Medical Centre, Nottingham

ABSTRACT NOT PROVIDED

• 1331
Introduction to KPros

LIU CS
Sussex Eye Hospital, Brighton

ABSTRACT NOT PROVIDED

• 1332
Patient assessment

LAM FC
Sussex Eye Hospital, Brighton

ABSTRACT NOT PROVIDED

• 1333
Psychological assessment

BUSUTTIL A
Sussex Partnership NHS Foundation Trust UK

ABSTRACT NOT PROVIDED

• 1334
Osteo-odonto-keratoprosthesis - surgical technique and complications

LIU CS
Sussex Eye Hospital, Brighton

ABSTRACT NOT PROVIDED

• 1335
Boston Type 1 KPro - patient selection

LAKE D
The Queen Victoria Hospital, East Grinstead

ABSTRACT NOT PROVIDED

• 1336
Boston Type 1 KPro - surgical technique

CORTINA S
University of Illinois at Chicago

ABSTRACT NOT PROVIDED

• 1337
Management of Boston Type 1 KPro complications

ETXEBARRIA J
Spain

ABSTRACT NOT PROVIDED

• 1341
Infectious anterior uveitis

PLEYER U
Charite, Campus Virchow, Augenklinik, Berlin

ABSTRACT NOT PROVIDED

• 1342
Infectious posterior uveitis

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ABSTRACT NOT PROVIDED

• 1343
Pediatric uveitis

BODAGHI B
Ophthalmology, Pitié-Salpêtrière Hospital, Paris

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

• 1344
B27-associated uveitis

WILLERMAIN F
Hospital St. Pierre, Brussels

B27 associated uveitis is a very frequent form of 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 interactive course will be mostly based on clinical cases and focused on the most controversial aspects of the work up, treatment, and complications of B27 associated uveitis.

• 1345

Behçet disease, sarcoidosis, VKH

ABU EL ASRAR A
King Abdulaziz University Hospital, Riyadh

ABSTRACT NOT PROVIDED

• 1346

White dot syndromes: from MEWDS to serpiginous choroiditis

HERBORT C
University of Lausanne & Centre for Ophthalmic Specialised Care

ABSTRACT NOT PROVIDED

• 1347

Complications of uveitis and their management

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(2) The Eye Clinic-Polytechnic University of Marche, Ancona

Purpose To review the uveitis complications and their management.

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

Results Visual recovery in uveitis is hampered all too often by the onset of complications arising from the frequent, recurrent episodes of inflammation. The most frequent complications in uveitis are: cataract, cystoid macular edema (CMO), glaucoma, neovascularization, and vitreous opacities. Moreover, these sequela may progress, despite an apparent good control of the ocular inflammatory disease. An early recognition, as well as an appropriate and timely management are mandatory for a successful outcome. In addition, the treatment alternatives for these entities should be considered, depending on the severity of the condition.

Conclusion Several sequela have been described in uveitis. A prompt recognition may orient correctly the ophthalmologist towards the best treatment option, lowering the risks of severe and irreversible ocular damages.

• 1348

Immunosuppression and biologic agents

DICK A
University of Bristol

Purpose To overview the contemporary therapeutic approaches to treatment of non-infectious non-infective ocular inflammatory disease. Treatment of non-infectious uveitis has over past 15 years expanded from the use of traditional therapies including corticosteroids and immunosuppressants to the deployment of targetting the immune response with biologic therapies with monoclonal antibodies and immunoadhesins. Such use will be exemplified with case reports during the talk.

Methods The talk will overview the evidence of effect of immunosuppressants in the treatment of uveitis, the role of predicting steroid responsiveness, the use of monotherapy with immunosuppression and finally the pathways and evidence of success of biologic therapy.

Results The concommitant use of immunosuppression is an important aspect to the adequate treatment of uveitis. This ensures adequate control of inflammation whilst reducing the need for comcomitant steroids thereapy. Moreover, monotherapy is equally efficacious in the control of some forms of uveitis.Neverthless there are patients who remain refractory to therapy, and in particular treatment of sight threatening Cystoid macular oedema. The use of targetted biologic therapy has gained increasing evidence to now lead to clinical trials in the use of anti-TNF and anti-IL17 agents

Conclusion There is now a recognised algorithm to treat aggressively and early patients with sight threatening disease. The appropriately timed use of immunosuppression and moreover increasingly earlier intervention with biologics has the promise to alter prognosis and outcome of such blinding disorders.

EVER 2011
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Oral presentations

• 2111
Cholesterol from diet to the retina

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Institut Patseur De Lille

Plasma cholesterol is carried in the blood by lipoproteins. Lipoproteins contains lipids (free and esterified cholesterol, triglycerides, and phospholipids, and apolipoproteins). There are in the fasting condition three kinds of lipoproteins : very low-density lipoproteins which are coming from the liver, and contain triglycerides and cholesterol ; low-density lipoproteins which contain mainly cholesterol and apolipoprotein B, and high-density lipoproteins which are involved in the reverse transport of cholesterol. Lipoproteins bring cholesterol to the tissues and cells which use it (gonads and adrenal glands, liver…) and triglycerides which are source of energy for muscle or are stored in adipose tissueThe regulation of the plasma lipids metabolism is complex under genetic factors controlling receptors, apolipoprotein synthesis, and other proteins (for transfert, exchanges…). Dietary factors and metabolic factors such as abdominal adiposity may modulate the lipid metabolism.A lot of abnonnalities may affect the level of LDL or HDL cholesterol due to genetic defects, or nutritional diseases.The interpretation of a dyslipidemia often needs a global approach in order to identify the mechanisms, the consequences (cardiovascular risk) and the best treatment with hypolipidemic drugs and/or dietary changes.

• 2112
Metabolism of cholesterol in health and disease of the retina

BRETILLON L
Eye and Nutrition Research Group, Dijon

Purpose Cholesterol is the main sterol in the vertebrate retina.

Methods Deposits of free cholesterol and cholesteryl esters at the basement of RPE are hallmarks of aging in humans, and AMD, the leading cause of vision loss in the Western world.

Results Cholesterol in the neuroretina originates from in situ synthesis and extra-retinal sources. The relative contribution of cholesterol coming from the circulation and local biosynthesis remains unknown. Tight junctions between retinal pigment epithelial (RPE) cells limit the intercellular movements of molecules to water and small molecules. RPE cells express various lipoprotein and scavenger receptors which can promote the recognition of cholesterol-rich lipoprotein and enhance the entry of cholesterol in the neurosensory retina. Both the neurosensory retina and RPE cells express proteins which participate to cholesterol export in other tissues than the retina, including CYP46A1. CYP46A1 would represent a mechanism of cholesterol removal from neurons, by catalyzing the hydroxylation of cholesterol at position C24. Other mechanisms than CYP46A1 have been described in the retina, including formation of 7-ketocholesterol or 27-hydroxycholesterol.

Conclusion Interestingly a single nucleotide polymorphism in cyp46a1 gene was associated with a significant risk for glaucoma, the second leading cause of blindness worldwide.

• 2113
Cholesterol, drusen and AMD

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Germany

ABSTRACT NOT PROVIDED

• 2114
Cholesterol and neurodegeneration

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Purpose Based on our previous studies (Mauch et al., 2001 Science; Nieweg et al., 2009 J Neurochem), we hypothesized that retinal ganglion cells (RGCs) depend on the endocytotic import of glia-derived cholesterol and that a breakdown of this import causes neurodegeneration (Pfrieger, 2003). The membrane protein Niemann-Pick C1 mediates the exit of externally acquired cholesterol from the endosomal-lysosomal system. Therefore, we studied, whether mice lacking Niemann-Pick typ C protein1 (NPC1) due to a spontaneous mutation, show pathologic changes in RGCs and elsewhere in the retina. These mice are a model for the lysosomal storage disorder Niemann-Pick type C.

Methods We analysed the retinal phenotype of NPC1-deficient mice by electroretinography, scanning laser ophthalmoscopy and histologic analysis.

Results We observed striking signs of degeneration in retinae from two-months-old NPC1-deficient mice. This included impaired visual function, accumulation of lipofuscin in the retinal pigment epithelium (RPE) layer, degeneration of photoreceptor outer segments, disruption of synaptic layers and upregulation of proteins that mediate cellular cholesterol release under the transcriptional control of the liver X receptor (Claudepierre et al., 2010 MCN). Notably, we observed an increase in LC3, an autophagy marker, specifically in the ganglion cell layer and in the RPE.

Conclusion Our results support the idea that cells in the retina depend on the intercellular exchange of cholesterol via lipoprotein-mediated transport. Moreover, our results suggest that disturbance of lipid metabolism in the retina contributes to neurodegeneration.

• 2121

Changes in retinal neuronal connectivity in a mouse model of dominant optic atrophy

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(3) University Hospital of Wales, Cardiff Eye Unit, Cardiff

Purpose The heterozygous mutation, B6;C3-Opa1Q285STOP which models autosomal dominant optic atrophy results in a 50% reduction in Opa1 transcript and protein in the mouse retina and neural tissues and is associated with visual dysfunction mirroring that found in human patients. We have previously reported retinal ganglion cell dendropathy in the absence of cell loss in this model. This study aims to explore the mechanisms that underlie this retinal ganglion cell dendropathy.

Methods Changes in retinal ganglion cell connectivity were explored in Opa1+/- mutant mice (n = 27) and accompanying age and sex matched controls (wt; n = 27) at 3 time points (12, 14 and 15 months of age) by immunohistochemistry, western blot analysis, TUNEL labelling and electron microscopy.

Results We report RGC dysfunction and changes in RGC connectivity in the absence of soma loss or microglial activation. We observed a dramatic decrease in PSD-95 levels across all ages in the Opa1+/- mice suggesting synaptic atrophy coupled with a selective degeneration of glutamatergic but not GABA-ergic synaptic sites. There was an increase in synaptic vesicle distribution assessed by immunohistochemistry, western blot and electron microscopy. γ-synuclein labelling confirmed stable RGC populations without significant evidence of apoptosis on TUNEL staining.

Conclusion In conclusion; we show discrete changes in RGC connectivity localised to sublamina b. These results highlight the importance of normal mitochondrial fusion balance as influenced by the OPA1 protein in maintaining neural cell connectivity. Changes in connectivity precede the onset of clinical visual loss and structural changes in optic nerve in the absence of significant apoptosis or microglial upregulation.

• 2122

Visual impairment in Leber hereditary optic neuropathy carriers of the same family

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Purpose To characterize the visual phenotype of asymptomatic Leber's hereditary optic neuropathy (LHON) associated with mtDNA 11778G>A mutation in carriers from the same family.

Methods Computerized psychophysical assessment methods (CCT - Cambridge Colour Test and CSF - Metropsis Contrast Sensitivity Function Test) were used to evaluate visual function in a population of 17 subjects of two generations of the family mentioned above (mean age ± SD = 27.94±12.97 years; mean visual acuity ± SD = 1.25±0.11) which was compared with an age-matched control group. This evaluation was completed with electrophysiological assessment (Multifocal ERG, Pattern ERG and Pattern VEP). Stratus-OCT3 was used for structural evaluation. Statistical analysis at a significance level of $p<0.05$ was performed using ANOVA, when applicable (otherwise Mann-Whitney was used).

Results CCT showed evidence for damage of all cone populations ($0.0001<p<0.006$), implying concomitant damage of parvo/ koniocellular pathways. No significant damage occurred in the achromatic contrast sensitivity across the spatial frequency channels studied, suggesting a relatively preservation of achromatic pathways.PERG results were normal, while mfERG (testing preganglionic pathways) showed a decrease in central ring amplitudes ($p=0.006$), corroborating central cone damage. Retinal thickness was decreased in the inner rings (R1:$p=0.012$; R2:$p=0.04$), irrespective of changes in macular nerve fiber layer thickness.Cortical responses (VEP) were delayed (60':$p=0.002$ / 15':$p=0.02$) with normal amplitudes.

Conclusion Our results suggest that, besides the classical concept of ganglion cell dysfunction, damage to outer retinal circuits could also contribute to subclinical impairment in LHON carriers.

• 2123

Retinal ganglion cell neurodegeneration in mitochondrial optic neuropathies: a comparative structural study

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Purpose To compare structural measurements of retinal degeneration between the most frequent hereditary diseases of retinal ganglion cells (RGCs), Leber Hereditary Optic Neuropathy (LHON) and Autosomal Dominant Optic Atrophy (ADOA).

Methods Peripapillary retinal nerve fiber layer (RNFL) and retinal thickness (RT) were assessed by Spectralis OCT (Heidelberg Engineering, Germany) in 14 patients (28 eyes; age=37.57+16.43 years) with ADOA and 15 patients (30 eyes; age=29.27+13.27 years) with LHON (unaffected carriers with gene mutation). These data were compared with age-matched control group. Statistical analysis was performed using Mann-Whitney test at a significant level of $p<0.05$.

Results ADOA group showed a significant reduction in RNFL ($p<.0001$ for all quadrants and average) and RT ($p<.0001$ for average, all quadrants and rings; except ring 1, $p=.001$), when compared with control group. LHON group yielded an increase in RNFL for inferior ($p=.0051$) and temporal ($p=.0129$) quadrants and for average ($p=.0014$); but a significant decrease in RT (temporal quadrant $p=.0079$; ring 1 $p=.0016$; ring 2 $p=.0011$; average $p=.0283$), comparing with controls. Comparing with ADOA group, LHON showed a significant increase in RNFL ($p<.0001$ for all quadrants and average) and also for RT ($p<.0001$ for all measures), except for ring 1 (no significant differences was found between study groups).

Conclusion As expected, ADOA group presents a significant loss of peripapillar RGCs and consequently a significant reduction in RT. LHON group shows an increase in RNFL, which is consistent with a documented swelling of the papillomacular bundle. Surprisingly, we found a decrease in RT that suggests retrograde involvment of other retinal cell type.

• 2124 / 259

Pupillometric quantification of residual rod and cone activity in patients with visual loss due to Leber congenital amaurosis

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(4) Ophthalmolgoy and Visual Science, Iowa City

Purpose Leber congenital amaurosis (LCA) is a group of genetically heterogeneous retinal dystrophies in which severe visual impairment occurs at infancy or during early childhood. We describe the threshold response function of rods and cones, as determined from pupil responses to colored light stimulation over a range of intensities, in 4 patients with LCA with different gene mutations who each had very poor visual function and non-recordable ERG.

Methods Four subjects with LCA and 10 control subjects underwent computerized pupillography under conditions of dark adaptation. The pupil response to a 1 second red (640 ± 10nm) and blue (467 ± 17nm) Ganzfeld light from -4.0 to 2.0 log cd/m2 was recorded continuously. Pupil responses to low light intensities were used to define the response curve of rods and the rod threshold for blue and red light. When rod-related pupil responses were absent, those obtained from red light stimulation at brighter intensities could be used to estimate cone activity.

Results A rod-related pupil response curve was still preserved and defined in only one patient (RDH mutation) using blue light and the repsonse threshold was -3.1 log cd/m2 . This was almost 2 log-units greater than the mean value in normal eyes (-4.9 log cd/m2 blue light). Residual cone activity in all 4 LCA patients yielded response thresholds of -2.3, -0.9, -0.8 and -2.1 log cd/m2.

Conclusion Pupillometry can estimate residual function and threshold responses of rods and cones in advanced stages of LCA. As such, pupillometry expands the dynamic range of photoreceptor activity that can be objectively monitored, either to follow natural progression or to assess effects of intervention.

Commercial interest

• 2125

Functional aspects of hyperautofluorescent ring in retinal dystrophies

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Purpose To further investigate functional aspects of hyperautofluorescent ring, seen in retinal dystrophies.

Methods Full ophthalmologic examination was performed, autofluorescence imaging was done by Heidelberg Engineering Spectralis/OCT, microperimetry with MP1 and electrophysiology.

Results Hzperautofluorescent ring exhibited different characteristics in RP-related diseases and very heterogenous characteristics in cone dystrophies, cone/rod dystrophies and macular dystrophies such as Stargardt disease, Best's disease and other dystrophies affecting central retina.

Conclusion Hyperautofluorescent ring is a specific feature that represents boundary between functioning and disfunctional retina and its origin is at present unknown. Different forms of ring are seen in different diseases and its functional correlations are important to understand the underlying mechanisms.

• 2126

Beijing eye public health care project

JONAS JB (1), XU L (2), CUI TT (2), YOU QS (2), WANG YX (2), YANG H (2), LI JJ (2), WEI WB (2), LIANG QF (2), WANG S (2), YANG XH (2), ZHANG L (2)
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Purpose The Beijing Eye Public Health Care Project was designed to screen all elderly subjects (age 55-85 years) of the rural region of Greater Beijing. It was developed as preparatory step for a telemedicine based public health care system in ophthalmology in China.

Methods Project participants were visited, interviewed and examined by 2500 trained barefoot doctors. If visual acuity was <0.3, subjects were referred to primary health care centers where ocular photographs were taken. Using telemedicine, the photographs were transmitted to a reading center and causes for visual impairment were diagnosed.

Results Out of 692,323 eligible inhabitants, 562,788 (81.3%) subjects participated. Visual impairment in at least one eye was detected in 54,155 (9.62%) subjects, and 30,164 (5.36%) subjects had bilateral visual impairment. Ocular fundus photographs were taken for 37,281 subjects. Cause for visual impairment was cataract in 19,163 (3.41%) of all screened subjects, glaucoma in 1,606 (0.29%) subjects, diabetic retinopathy in 905 (0.16%) subjects, other macular diseases in 2,700 (0.48%) subjects, pterygium in 1381 (0.25%) subjects, and corneal leukoma in 283 (0.05%) subjects. For 5,853 (1.04%) subjects, a diagnosis of urgent cataract surgery was made. After cataract surgery, visual acuity was ≥0.3 in 1464 (91.7%) of 1596 postoperatively re-examined subjects.

Conclusion Using a telemedicine approach, the Beijing Eye Public Health Care Project developed, applied and tested an infrastructure for ophthalmic mass screening of more than 500,000 elderly inhabitants with a response rate of >80%. Besides cataract, retinal diseases including diabetic retinopathy and glaucoma were major causes for visual impairment.

• 2131

Inhibition of mitocondrial complex IV in cell death and the influence of light.

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Purpose Characterise the mechanism by which the mitochondrial complex IV poison sodium azide kills RGC-5 cells (cell line with certain ganglion cell properties) in the dark and determine the influence of white and red light.

Methods RGC-5 cell cultures in 96- or 12-well plates were exposed to different concentrations of sodium azide in the dark or under white (400-700nm, 1000 lux) or red (625-635nm, 1000lux) light. Cells were analysed 24-96 hours later for production of reactive oxygen species (ROS), cell viability (MTT procedure) and for apoptosis (staining for phosphatidylserine and DNA breakdown). Also, cultures were subjected to immunocytochemistry for the localisation of certain antigens or their proteins extracted and subjected to electrophoresis and western blotting for various proteins involved in cell death.

Results Sodium azide (5mM)-induced apoptosis of RGC-5 cells is characterised by positive membrane staining for phosphatidylserine, breakdown of DNA, a generation of ROS production, the activation of p38 MAPK and by inhibition with the caspase inhibitor z-VAD-fmk. Sodium azide also caused p38 MAPK to be translocated from the nucleus to the cytoplasm and the stimulation of alpha fordrin and caspase-3 content. White light exacerbated and red light reduced the effects of sodium azide that occurred in the dark.

Conclusion Red light as opposed to white light acting directly on the retina might protect neurones from dying by apoptosis where their mitochondria are affected.

• 2132

Resveratrol, rapamycin and MG-132 as inducers of autophagy in ARPE-19 cells

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Purpose To investigate the effect of the polyphenol resveratrol (3,5,4'-trihydroxy-trans-stilbene), rapamycin (RAP) and proteasome inhibitor MG-132 on cell death and autophagy in human retinal pigment epithelium-derived ARPE-19 cells.

Methods ARPE-19 cells were exposed to different treatment regimens: 10-50microM resveratrol, 50-100 nM RAP, 50 microM chloroquine (CQ) and 50-100 nM MG-132 over 48 hours. The levels of LC3-II, mammalian target of rapamycin (mTOR), Hsp70, p62 were determined by Western blot analysis; autophagic vacuoles (AVs) formation was detected by acridine orange, pDendra2-hLC3 expression and transmission electron microscopy; cell death was quantified using annexin-V-FITC/propidium iodide (PI) labeling on flow cytometry.

Results Exposure to RAP and MG-132 caused a time- and concentration dependent induction of autophagy that could be inhibited by 3-methyladenine (3-MA), while the induction of an active autophagic flux could be verified with CQ treatment, a blocker of the autophagosome-lysosome fusion. Similarly, resveratrol alone could induce autophagy in ARPE-19 cells, serving as a pro-survival signal in ARPE-19 cells. Inhibition with 3-MA increased the death rate of resveratrol treated ARPE-19 cell, further proving the autophagy-related protective role of resveratrol.

Conclusion Resveratrol at lower concentrations, RAP and MG-132 can provide a pro-survival stimulus to ARPE-19 cells by inducing autophagy. This property can possibly be used for prolonging the lifespan of retinal pigment epithelium in diseases such as age-related macular degeneration.

• 2133

Quantification of GFAP and NF-200+ retinal ganglion cells in contralateral mice retina to experimental glaucoma

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Purpose To analyze the effects of laser-induced ocular hypertension (OHT) in the macroglia and retinal ganglion cells (RCGs) of eyes with OHT (OHT-eyes) and contralateral eyes two weeks after lasering

Methods Adult Swiss mice were divided into two groups: naïve (n=6) and lasered (n=6). Retinal whole-mounts were immunostained with antibodies against GFAP and NF-200, the latter used to analyze the presence of degenerated RGCs. The GFAP-labeled retinal area (GFAP-RA) and the number of astrocytes and NF-200+RGCs were quantified

Results In comparison with naïve: i) astrocytes were more robust in contralateral eyes and had less GFAP immunoreaction and secondary processes in OHT-eyes; ii) GFAP-RA was increased in contralateral eyes ($p<0.032$) and decreased in OHT-eyes ($p<0.001$); iii) in both contralateral and OHT-eyes, GFAP was upregulated in Müller cells. No differences in astrocyte number were found among naïve, contralateral, and OHT-eyes. NF-200+RGCs were observed in OHT-eyes (503+/-145 cells) with a trend for the GFAP-RA to decrease and for the NF-200+RGC number to increase from the center to the periphery ($r=-0.448$)

Conclusion Two weeks of laser-induced OHT produced macroglial retinal changes in both contralateral and OHT eyes. The differences in NF-200+RGCs counting among contralateral and OHT-eyes support a possible contribution of retinal macroglia to neuronal homeostasis in contralateral eyes. On the basis of the macroglial changes detected in the present work, the use of the contralateral eye as an internal control in experimental induction of unilateral OHT should be reconsidered

• 2134

MHC-II glial upregulation in contralateral mice retina to experimental glaucoma

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Purpose To analyze the effects of laser-induced ocular hypertension (OHT) in MHC-II expression in the glia of eyes with OHT (OHT-eyes) and contralateral eyes two weeks after lasering.

Methods Adult Swiss mice were divided into two groups: naïve (n=6) and lasered (n=6). Retinal wholemounts were immunostained with antibodies against GFAP, Iba-1 and MHC-II.

Results In the naïve retinas, a weak constitutive MHC-II expression was scarcely found in some Iba-1+ cells and rarely in astrocytes. A small dendritiform subpopulation of Iba-1+ cells, located in the juxtapapillary area and in the marginal region of the retina, had a strong MHC-II immunoreaction. In comparison naïve results, in the contralateral eye, MHC-II was expressed in Müller cells and was upregulated in Iba-1+ cells as well as in the astrocytes. In contralateral macroglia, MHC-II was preferentially expressed by astrocytes. In OHT-eyes, Iba-1+ cells showed MHC-II immunoreactivity similar to contralateral and no MHC-II astrocytes were observed; however, MHC-II expression was upregulated in several groups of Müller cells thoroughout the retina and was preferentially located in the end-foot of the cells.

Conclusion Two weeks of laser induced-OHT produced macro and microglial retinal changes in MHC-II expression in both, contralateral and OHT-eyes. Our results suggest that the gliotic behavior in contralateral untreated eyes could be related to the immune response. On the basis of the glial changes observed, the use of the contralateral eye as a control in experimental unilateral OHT should be reconsidered.

• 2135

A hypothesis about structural changes of the posterior pole based on scleral deformation during ocular movements

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Purpose To propose a theoretical model of the pathogenesis of various macular diseases based on structural deformation of the stratified posterior pole during ocular movements

Methods CT, MRI and OCT scans show evidence of significant deformation of the posterior sclera wall during ocular movements.The posterior pole is seen as a stratified model of multiple layers with different elastic properties.The morphology of lessions of various macular diseases is examined as a consequence of the compression of the stratified posterior pole using basic principles of mechanics.

Results The clinical expression of various macular diseases such as age-related macular degeneration, macular hole, central serous choroidopathy could be explained by a unifying mechanism of structural changes that includes the role of the choroidal bed as a dampening stroma.

Conclusion The structural behavior of the multilayered stratified posterior pole during ocular movements may open a new field of research and treatment of the posterior pole diseases.

• 2136 / 206

AICAR induces autophagy in ARPE-19 cells

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Purpose The pathogenesis of age-related macular degeneration involves impaired protein degradation in retinal pigment epithelial (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 the present study, the effects of AICAR (AICA ribonucleotide, 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside) and MG-132 (proteasome inhibitor) on autophagy regulation in ARPE-19 cells were evaluated.

Methods The AMP activated protein kinase (AMPK), p62 and ubiquitin protein levels were analyzed by western blotting. pDendra2-hLC3 construct was used to detect macroautophagy in confocal microscopy analysis. Transmission electron microscopy was used to detect protein aggregates and autophagosomes. Cellular permeability was measured by analyzing lactate dehydrogenase levels in culture medium.

Results MG-132 (5 microM) triggered the accumulation of perinuclear aggregates that strongly colocalized with p62 and ubiquitin. AICAR (2mM) induced autophagy clearance of p62 and ubiquitin positive protein aggregates without increasing cellular permeability. Cellular energy status regulator AMPK or p-AMPK levels were not significantly changed in response to AICAR treatment.

Conclusion Our findings open new avenues for understanding the mechanisms of proteolytic processes and indicate that AICAR could be useful in the acceleration of protein clearance in RPE cells.

• 2137 / 208

BDNF-deficiency upregulates SIRT2 expression but does not affect cellular metabolism in mouse retina

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Purpose Brain derived neurotrophic factor (BDNF) is essential for cell development, function and survival. Mammalian sirtuins (SIRT) are deacetylase enzymes that are known to play an important role in longevity. In the present study we aimed to compare SIRT1 and SIRT2 expression in retinas of mice that lack brain derived neurotrophic factor (BDNF+/-) and their wild type littermates (WT) at young age in relation to cellular metabolism.

Methods Eyes from 2-months old WT and BDNF+/- mice (The Jackson Laboratory, Bar Harbor, ME, USA) were used. SIRT1 and SIRT2 protein levels in retina were determined by Western blotting. Paraffin-embedded retinal sections were immunostained for SIRT1 and SIRT2 to determine their localisation and abundance in various retinal layers. Metabolic state of mouse retinal cells was assessed by measuring NAD+, NADH and total NAD levels using resazurin-based assay.

Results Western blot analysis of the whole retina showed that SIRT1 expression is similar in WT and BDNF+/- mice. However, there was a significant upregulation of SIRT2 protein level in BDNF+/- mice compared to WT littermates. Assessment of NAD+, NADH and total NAD levels showed similar cellular metabolic state in retinas of WT and BDNF+/- mice.

Conclusion Our results indicate increased tubulin deacetylation in retinas of BDNF+/- mice, which is independent from cellular energy metabolism.

• 2141
T Cells and the eye

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Purpose Experimental Autoimmune uveoretinitis (EAU) is a clinico-pathological model of human non-infectious uveitis. This review is to illuminate the dynamics of T cell infiltration in the eye during the course of EAU, the control of T cell activation and proliferation of T cells at the target site and ultimately control of inflammation.

Methods Using models of EAU we are able to accurately dissect and enumerate T component, cyokine liberation and interrogate interactions of myeloid-T cell compartment within the local environment during autoimmune inflammation.

Results During the course of EAU, the early T cell infiltrate is seen prior to clinical disease. During acute inflammation there is a mixed T cell response, predominantly CD4+ Th1 and Th17 response. In later stages, Treg cells accumulate along with minor populations of CD8+ and NK T cells. Throughout there is close interaction with myeloid-derived cells governing response of T cell activation and proliferation and vice versa mediated in part by TNF and TSP.

Conclusion The cellular interactions within the local microenvironment regulate T cell expression.

• 2142
Macrophages and the eye

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The members of the antigen-presenting cell family are known under many names, such as macrophages, Langerhans cells, dendritic cells and monocytes. They can be found in all ocular tissues, and depending on their activation state and characteristics, these cells can either stimulate or inhibit immune responses. Furthermore, macrophages may play a role in wound healing or angiogesis. These differential roles will be illustrated by showing their function in ocular tumors and in corneal diseases.

• 2143
Conjunctival antigen presenting cells: sentinels for ocular surface inflammation

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Purpose To evaluate the role of conjunctival antigen presenting cells (APC) in experimental dry eye disease (EDE) and in the immune rejection of corneal allografts.

Methods Ocular surface APC were depleted by subconjunctival injection of liposomes containing clodronate. APC depletion was confirmed by immunohistochemistry using anti-CD11c (dendritic cells) and anti-Iba1 (macrophages) antibodies. EDE was induced by exposing mice to desiccating stress (DS) for 5 days and pathogenic CD4+ T cells were to T cell-deficient nude mice. Experiments were also performed in a murine model of keratoplasty.

Results Injection of clodronate liposomes produced 65% and 86% reductions in conjunctival macrophages and DC respectively. Depletion of APC prior to DS inhibited the generation of autoreactive CD4+ T cells and prevented EDE. APC deletion in nude mice prior to their receiving EDE-producing CD4+ T cells significantly mitigated EDE. APC depletion prior to keratoplasty completely prevented corneal allograft rejection. However, depleting APC in nude mice prior to transferring CD4+ T cells did not affect corneal allograft rejection indicating that primed CD4+ T cells do not require secondary activation by APC to mediate graft rejection.

Conclusion Ocular surface APC play an important role in the generation of autoreactive pathogenic CD4+ T cells that mediate EDE and for secondary activation of these cells at sites of ocular surface inflammation. Ocular surface APC are also crucial for the induction of corneal allograft rejection, but secondary activation of previously primed allospecific CD4+ T cells by resident ocular surface APC is not required. Targeting ocular surface APC may be a facile therapeutic modality for managing ocular surface inflammation.

• 2144
PMNs and the eye

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Polymorphonuclear leukocytes (PMNs) are an important modulator of many types of infection. The purpose of this presentation will be to review the characteristics and functional capabilities of these cells and to discuss their role in the pathogenesis of HSV-1 ocular infection.

• 2151

From persistent epithelial defect to corneal ulceration: induction of proteases and epithelial-stromal interactions

MENASHI S
France

ABSTRACT NOT PROVIDED

• 2152

Corneal ulcerations associated with allergy and meibomian gland dysfunctions

DOAN S
Hopital Bichat, Paris

ABSTRACT NOT PROVIDED

• 2153

Infectious corneal ulcers: pathogenesis and management

BOURCIER T
Hôpital Civil, Strasbourg

ABSTRACT NOT PROVIDED

• 2154

Herpes simplex and Herpes zoster associated corneal ulcerations

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Corneal ulcerations are the landmark of viral infections of the ocular surface. The clinical patterns of these ulcerations may vary according to the virus, the type of infection (epithelial or stromal) and the history of the patient. Dendritic ulcers are the most typical findings of Herpes Simplex Virus (HSV) infection, but may also be seen during Varicella-Zoster Virus (VZV) infection. They share common feature such as rapid diffusion of fluorescein beneath the edges of the ulcer. Inversely, this diffusion is usually not seen in pseudo-dentritic ulcers, which may be related to either some other infectious agents, or toxicity of eyedrops, or corneal denervation. Geographic ulceration is usually due to HSV infection mistreated with topical steroids, especially if the size of the defect is rapidly progressing. In contrast, a slowly progressing geographic ulcer, with amorphous margins, rather results from neurotrophic conditions. Finally, deep corneal ulcerations, involving both the epithelium and the stroma should be first treated as HSV or VZV necrotic keratitis, but other agents like bacteria, acanthameba and even fungi may lead to similar findings. Such cases thus need a daily control of the evolution to find optimal treatment.

• 2155

Therapeutic approach in sterile corneal melts

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Purpose The aim of this instruction course is to present the medical and surgical management of chronic corneal melts.

Methods Interactive clinical cases.

Results Modulation of epithelial wound healing using different technics such as epihelial debridement, inlay and overlay amniotic membrane transplatation, lamellar or penetrating keratoplaty are presented.

Conclusion Delayed epithelial wound closure is the main risk factor of sterile corneal melts. Early diagnosis for the medical and surgical management of corneal ulcerations

• 2161
Radiation cataracts: epidemiology and biology

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Purpose The lens is one of the most radiosensitive tissues in the body. Ocular ionizing radiation exposure results in characteristic, dose related, progressive changes leading to cataract formation. While initial, early stages of such opacification may not cause visual disability, the severity of such changes progressively increases with dose until vision is impaired and cataract extraction surgery may be required. The latency of such changes is inversely related to dose.Within the past few months, the ICRP released new guidelines and recommendations concerning ocular ionizing radiation exposure, significantly lowering the presumptive threshold for radiation cataract to 0.5 Gy, regardless of acute, protracted or chronic exposure. Similarly, the occupational lens exposure limit was lowered, from 150 mSv/yr to an average of 20 mSv/yr over 5 years, with no single year exceeding 50 mSv.

Methods Recent human epidemiological studies have helped refine radiation cataract risk in various exposed populations. Nevertheless, considerable uncertainties remain concerning the precise pathobiology and the relationship between cataract development, age at exposure, threshold dose and genetic determinants of radiosensitivity.

Results Recent findings will be reviewed and new data on the genetic and individual basis of radiation cataract risk will be presented.

Conclusion New ICRP recommendations are likely to have significant implications for presumed radiation cataract risk, especially in radiosensitive individuals, as well as the need for occupational eye protection in fields such as interventional medicine. Cellular and molecular pathways leading to radiation cataract have fundamental relevance to that in other tissues and likely involves genomic damage, abberent division and abnormal differentation.

• 2162
Monitoring the eye lens

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Purpose To prevent the induction of cataracts by ionizing radiation (photons or betas), the International Commission on Radiological Protection (ICRP) has lowered the annual dose limit for the eye lens from 150 mSv down to 20 mSv for occupational exposures. Thus, protecting the eye and monitoring the lens dose to prevent exceeding the dose limit is more necessary than formerly assumed.

Methods Different kinds of dosemeters were investigated to give guidelines on monitoring the lens dose when necessary.

Results Hp(0.07) dosemeters are constructed to monitor the local skin dose in 0.07 mm depth as the radiation-sensitive epidermis lies about 0.07 mm below the surface. In pure photon radiation fields, e.g. in interventional radiology, Hp(0.07) dosemeters are appropriate to monitor the lens dose when worn near the eye and if the back of their case consists of thin plastic. In beta radiation fields, e.g. in nuclear medicine, Hp(0.07) dosemeters may overestimate the lens dose by a factor of 100 or more. Thus, they are unsuitable here.Hp(3) dosemeters are constructed to monitor the lens dose as the radiation-sensitive part of the lens lies about 3 mm within the eye. Only very few Hp(3) dosemeters exist, but, by construction, they should monitor the lens dose also in beta fields correctly. However, this has not yet been demonstrated.Hp(10) dosemeters are constructed to monitor the whole body dose as the inner organs are assumed to lie about 10 mm within the trunk. Hp(10) dosemeters usually underestimate the lens dose and are, thus, unsuitable.

Conclusion Protection measures such as lead glass shields or glasses should be used. In case exposures cannot be avoided, appropriate dosemeters must be worn near the eye behind devices used to shield the eyes but not behind a shield worn on the trunk (e.g. a lead apron).

• 2163
Lens opacities among physicians occupationally exposed to ionizing radiation--a pilot study in Finland

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Purpose The aim of this study was to estimate the prevalence of lens opacities among physicians occupationally exposed to radiation - overall and by occupational factors - and to assess the feasibility of a large-scale study for risk assessment.

Methods Based on a nationwide registry of 1312 physicians, mostly radiologists with occupational exposure to ionizing radiation, 120 subjects were invited to participate, of which 59 (49%) consented. The inclusion criteria included (i) age 45-70 years, (ii) cumulative recorded radiation dose >10 mSv, and (iii) duration of work with dose monitoring >15 years. The participants completed a questionnaire regarding occupational history and other risk factors for lens opacities. A full ophthalmological examination was performed. Lenticular changes were graded using the Lens Opacities Classification System, version II (LOCS II), and the Nidek EAS-1000 Scheimpflug slit-imaging videophotography system.

Results Lens opacities were detected in 42% [95% confidence interval (95% CI) 29-55] of the 57 physicians without prior cataract surgery. Nuclear opacities were found in 14% (95% CI 6-26), cortical in 7% (95% CI 2-19), and posterior subcapsular in 5% (95% CI 1-15) of the subjects. The prevalence of lens opacities increased with age, smoking, and cumulative recorded radiation dose. After controlling for age, gender, and smoking, the excess odds ratio for any lens opacity was 0.13 (95% CI -0.02-0.28) per 10 mSv of cumulative radiation dose.

Conclusion Our preliminary results show cortical and posterior subcapsular lens opacities among physicians exposed to occupational radiation, consistent with recent studies on low dose radiation exposure. A full study with an unexposed reference group for risk estimation is warranted.

• 2164
Occupational cataracts and lens opacities in interventional cardiology (O'CLOC Study)

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Purpose Interventional cardiologists - ICs, are exposed to ionizing radiations (X-rays), which may induce early cataracts known as radiation-induced cataracts. To test the existence of an increased risk of cataracts among ICs, the O'CLOC study was performed in France.

Methods This study is a cross-sectional study including an exposed group of ICs and a comparable unexposed group of non medical workers. Individual information on risk factors of cataracts (age, diabetes, myopia, etc. ...) and catheterization laboratory activity for ICs, were collected during a phone interview. Clinical eye examination including papillary dilatation and slit lamp examination was performed. LOCS III classification was used to detect lens opacities (nuclear, cortical or posterior subcapsular)

Results The study included 106 ICs (mean age=51.1±7.3 yrs.) and 99 unexposed people (mean age =49.6±6.7 yrs.). There was no significant difference between both groups in terms of sex ratio, BMI, smoking status, diabetes, myopia, corticosteroids use. Regarding nuclear and cortical lens opacities, no significant difference was observed: 61% for ICs vs. 69% for unexposed group, p=0.23, and 23% for ICs vs. 29% for unexposed group, p=0.29, respectively. In contrast, posterior subcapsular lens opacities were significantly more frequent among ICs (17% vs. 5%, p = 0.006), corresponding to a crude OR=3.89 [1.39–10.93] which remained significant even after adjustment for age, sex, BMI, smoking status, diabetes, myopia and corticosteroids use (OR=3.85 [1.30–11.40], p=0.015).

Conclusion In order to limit the exposure to the eyes and the risk of radiation-induced cataract, we recommend ICs to wear lead glasses and use protective equipment against X-rays.

• 2171

Novel methods to maintain corneal transparency while increasing the strength of LASIK flaps

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Purpose To reduce the incidents of keratectasia after LASIK we have been attempting to increase the strength of the flap using various methods1. We now are aiming to improve this by transplanting stromal fibroblasts, oral fibroblasts (a scarless reparative cell type) or stromal progenitor cells into LASIK corneas.

Methods LASIK flaps were created in ovine corneas and human oral fibroblasts or human stromal progenitor cells were applied on the flap bed. Stromal flaps in bovine corneas were treated with stromal fibroblasts from the same species. LASIK corneas without any treatment acted as controls. All samples were placed in organ culture and allowed to heal for up to 3 weeks. The mechanical strength of the flaps was measured using a vertical extensometer in a "pull to break" test. Transparency was assessed by making spectorphotometric measurements across the visible spectrum. Cell phenotype was examined by anti-alpha smooth muscle actin immunostaining.

Results All approaches improved the strength of LASIK flaps but the bovine stromal fibroblasts compromised the tissue's transparency. Both human cell types maintained corneal transparency but the oral fibroblast approach was the most efficient one in the 3 week culture period, perhaps due to the scarless reparative phenotype of these cells.

Conclusion LASIK flap strength can be increased biologically but the challenge now is to apply these methods in an animal model to assess the long term of the efficacy of increasing flap adhesion strength and maintain corneal transparency and its potential use in medical intervention.1. Mi S, Dooley EP, Albon J, Boulton ME, Meek KM, Kamma-Lorger CS. J Cataract Refract Surg. 2011; 37(1):166-72

• 2172

A new method of the eye refraction correction under non-ablative laser radiation

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Purpose The aim is to present a new approach of cornea reshaping using termomechanical effect of pulse repetitive laser radiation both on sclera and cornea.

Methods Experiments were performed in vitro with eyes of pigs, rabbits, cadavers, and in-vivo with rabbit eyes using an Erbuim glass fiber laser of 1.56 microns in wavelength. Thermomechaniucal properties of sclera and cornea during laser heating were studied with an indenter test and using thermo mechanical analyzer. The alterations in eye refraction was measured with various optical techniques including coherent tomography, confocal microscopy and shlieren visualization. Histological technique was used to study possible alterations in tissues structure.

Results The results have shown different thermomechanical properties of cornea and sclera allowing to change eye refraction under nondestructive laser irradiation. Denaturation thresholds for stromal collagen of the cornea were measured for various laser wavelengths. Optimal laser settings were established allowing obtain vision correction without visible damage and denaturation of the eye tissues. The maximal change of eye refraction obtained was of 6 diopters. The stability of rabbit eye refraction was established during at least 6 months. Hystological analysis did not revile substantial alterations in cornea structure.

Conclusion The advantages of the new approach are provided by the following factors (1) noninvasive and potentially reversible nature of exposure on the cornea and sclera, (2) minimal exposure on the central zone of the cornea, (3) availability of a feed back control system that prevents denaturation and damage of the cornea, (4) possibility of a repeated procedure.

• 2173

I-LASIK retreatment of residual refractive errors after microkeratome and femtosecond assisted LASIK

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Purpose To evaluate the efficacy and safety of femtosecond-assisted sub-bowman keratomileusis (I-LASIK) retreatment for residual refractive errors after either I-LASIK or microkeratome assisted LASIK.

Methods We performed i-lasik retreatment in 14 eyes of 10 patients (mean age 37) for residual myopic and astigmatic refractive errors after previous both i-lasik and lasik procedures. All patients had stable residual refractive errors for at least 2 years. I-lasik was performed in all cases with AMO's IntraLase™ FS and STAR S4 IR™ Excimer Laser System, corneal flap thickness was 100µm and hinge position was 90 degrees with reverse 120° side cut. The optical zone of the ablation was from 6.5 to 7 mm, transition zone from 8 to 9 mm.

Results Controls were made at 1day, 1 and 3 months. Anterior segment OCT and corneal confocal microscopy were performed in every case. No flap decentration was observed in any case, we had 2 cases of epithelial ingrowth, 4 cases of dry eye, no cases of corneal ectasia and no retinal complications. All spherical equivalent results were within 0.50 diopters.

Conclusion In our experience I-lasik procedure demonstrated itself to be safe and effective also in patients with residual refractive errors from previous i-lasik and lasik treatments.

• 2174

Comparative evaluation of photorefractive keratectomy with the use of an excimer laser and a solid state laser system

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Purpose To compare refractive results of photorefractive keratectomy (PRK) with the Solid State laser and Excimer laser.

Methods This retrospective cohort study comprised eighty patients (153 eyes) who received PRK with the excimer laser Allegretto 400 Wave Eye-Q (group 1), and 79 (156 eyes) who received PRK with the solid state laser Pulzar Z1 (group 2). All patients had a complete ophthalmic examination preoperatively to exclude ocular disease. All procedures were performed using an identical technique. Groups were matched in terms of age sex, preoperative refraction and visual acuity (VA).Preoperative and postoperative assessments included uncorrected distance VA, corrected distance VA, manifest and cycloplegic refractions, slitlamp examination and corneal topography.

Results No statistically significant differences were found 1 year postoperatively between the two groups in terms of patient's corrected distance VA (p=0.23), uncorrected distance VA (p=0.20),and remaining refractive error (difference between achieved and attempted correction) (p=0.60).

Conclusion Both systems performed similarly in terms of efficacy and predictability. The use of the Solid State laser for the correction of myopia with photorefractive keratectomy is an effective alternative for the Excimer laser.

• 2175

Evaluation of tear film osmolarity after mechanical LASIK, femtosecond laser-assisted sub-Bowman keratomileusis and LASEK

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Purpose To evaluate the tear osmolarity in patients that underwent LASIK (performed with a microkeratome or a femtosecond laser) or LASEK three months before.

Methods We performed a prospective observational study of consecutive eyes that had LASIK performed with a mechanical microkeratome (MM-LASIK), with a femtosecond laser (FS-LASIK) or that had LASEK. Three months postop, tear osmolarity was measured with the TearLab TM Osmolarity System. This measure was performed only in one eye per patient. A normality value of 308 ± 5 mOsm/L (provided by the manufacturer) was used to clasify the tear osmolarity.

Results 105 eyes of 105 patients were included in the study (35 eyes in each group). No significant differences were found in the mean preoperative refractive defect and patient age between groups. Three months postop, mean osmolarity values were 304.8 ± 20.2 mOsm/L (range, 275 to 371) in the MM-LASIK group; 306.8 ± 17.7 mOsm/L (range, 280 to 342) in the FS-LASIK group and 307.9 ± 17.6 mOsm/L (range, 280 to 374) in the LASEK group. After three months, there was no statistically significant difference in tear osmolarity between the groups.

Conclusion Our results suggest that tear film osmolarity measured with the TearLabTM Osmolarity system tends to achieve normal values three months after MM-LASIK, FS-LASIK and LASEK.

• 2176

Dynamic corneal wavefront aberrations and quality of vision in patients with dry eye disease

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Purpose This clinical, prospective, and comparative study was conducted to evaluate the time-course of corneal optical quality along with patient-centered visual deterioration in dry eye.

Methods Twenty patients diagnosed for dry eye and twenty controls were included. Clinical evaluation of the ocular surface included tear break-up time (BUT) measurement, Schirmer's test, corneal and conjunctival staining scores. Dynamic corneal aberrometry was performed using KR-1W aberrometer (Topcon, Tokyo, Japan). Patient-centered quality of vision was evaluated according to the Ocular Surface Disease Index (OSDI). Corneal aberration (CA) dynamics were compared between both groups then analyzed regardless to other clinical data.

Results Mean slope for aberration time-course was significantly higher in dry eye patients than in controls (P=0.01). Dry eye was associated with an increase in corneal high-order aberrations from 3 to 10 seconds after blinking (P<0.001) mainly due to rapid increase in third- and fourth-order CAs. Correlation matrix revealed significant relation between CA dynamics and BUT (P<0.001), corneal staining (P<0.001), OSDI vision-subscore (P=0.009) and OSDI overall score (P=0.02). BUT and Oxford's score were found to correlate with CA dynamics in multiple regression analysis.

Conclusion Dynamic corneal aberrometry appears as a new objective tool to better understand visual disturbances due to dry eye, and it could constitute a repeatable and reproducible method to follow the disease and improve the therapeutic management.

• 2177 / 405

Long-term results of simultaneous topo-guided photorefractive keratectomy followed by corneal collagen cross-linking for keratoconus

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Purpose To present the long-term results after simultaneous photorefractive keratectomy (PRK) followed by corneal collagen cross linking (CXL) for keratoconus

Methods In this prospective case series, 26 patients (31 eyes) with progressive keratoconus were included. All patients underwent customized topography guided photorefractive keratectomy (PRK) immediately followed by corneal collagen cross linking with the use of riboflavin and ultraviolet-A irradiation. Epithelium was removed by transepithelial phototherapeutic keratectomy (t-PTK) in all cases

Results Mean follow-up was 19.53 +/- 3.97 months (range 12 to 25 months). Mean preoperative spherical equivalent (SE) was –2.3 +/- 2.8 diopters (D) while at the last follow up examination was significantly (p<0.001) reduced to -1.08 +/- 2.41 D. LogMAR uncorrected (UDVA) and corrected distance visual acuity (CDVA) were significantly reduced by 0.46 and 0.084 LogMAR units, (p<0.001) at the last follow up examination. Mean steep and flat keratometry readings were reduced by 2.35 D (p<0.001) and 1.18 D (p=0.013) at the last follow-up examination

Conclusion Simultaneous topo-guided PRK followed by CXL seems to be an effective and safe treatment without any complications in our series of keratoconic patients

• 2211

High-mobility group box-1 and biomarkers of inflammation in the vitreous from patients with proliferative diabetic retinopathy

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Purpose To measure levels of high-mobility group box-1 (HMGB1), and soluble receptor for advanced glycation end products (sRAGE) in the vitreous fluid from patients with proliferative diabetic retinopathy (PDR) and to correlate their levels with clinical disease activity and the levels of the inflammatory biomarkers monocyte chemoattractant protein-1 (MCP-1), soluble intercellular adhesion molecule-1 (sICAM-1), interleukin-1 (IL-1) and granulocyte macrophage colony-stimulating factor (GM-CSF). In addition, we examined the expression of HMGB1 in the retinas of diabetic mice.

Methods Vitreous samples from 29 PDR and 17 nondiabetic patients were studied by enzyme-linked immunosorbent assay. Retinas of mice were examined by immunofluorescence analysis and Western blotting.

Results HMGB1 was detected in all vitreous samples and sRAGE was detected in 5 PDR samples. IL-1 was detected in 3PDR samples and GM-CSF was not detected. Mean HMGB1 levels in PDR with active neovascularization were 2-fold and 3-fold higher than that in inactive PDR and nondiabetic patients, respectively. Mean HMGB1 levels in PDR patients with hemorrhage were significantly higher than those in PDR patients without hemorrhage and nondiabetic patients ($p=0.0111$). There were significant correlations between levels of HMGB1 and levels of MCP-1 ($r=0.333$, $p=0.025$) and sICAM-1 ($r=0.548$, $p<0.001$). HMGB1 expression was also upregulated in the retinas of diabetic mice.

Conclusion Subclinical, chronic inflammation might contribute to the progression of PDR.

• 2212

Alteration of plasmalogens in erythrocytes of patients with diabetic retinopathy

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Purpose Plasmalogens are phospholipids characterized by a vinyl ether bond and the preferential esterification of polyunsaturated fatty acids (PUFA). We have shown that the lack of plasmalogens leads to abnormal retinal vascularisation. Because we hypothesize that plasmalogens are negative regulators of vascular development, we aimed to check their circulating levels in patients having a retinal pathology with vascular proliferation.

Methods Blood samples were collected from 4 control subjects and 42 patients having proliferative or non-proliferative diabetic retinopathy (DR). Patients were classified according to the stage of DR. The plasmalogen content and the fatty acid composition of erythrocyte phospholipids were determined using gas chromatography. Individual species of phospholipids, including plasmalogens, were quantified by liquid chromatography coupled with a triple quadrupole mass spectrometer (HPLC-ESI+MS/MS).

Results Gas chromatographic analyzes did not reveal any change in plasmalogens. The analysis of individual species of phospholipids by HPLC-ESI+MS/MS showed reduced levels of plasmalogens in patients with DR. Five species of plasmalogens having PUFA were at reduced concentrations in erythrocytes of DR patients. In parallel, the amounts of conventional phospholipids having docosahexaenoic acid (DHA) were altered in DR patients when compared to control subjects.

Conclusion Mechanisms responsible for the reduction in blood levels of plasmalogens and DHA in patients with DR are unknown. Since erythrocyte membrane lipid composition is admitted to reflect the lipid composition of nervous tissues, including the retina, one may suggest that DR patients have altered retinal concentrations of plasmalogens and DHA.

• 2213

Health related quality of life in patients with diabetic retinopathy

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Purpose To assess Health-Related Quality of Life (HRQoL) among Greek patients with Diabetic Retinopathy (DR) and Maculopathy(DMac) and to compare the results with data from existing studies.

Methods Patients were recruited from the Diabetic Eye Clinic of the Hellenic Red Cross Hospital while attending their scheduled appointment. The study comprises of 85 patients with DR/DMac. HRQoL was measured using three different types of measurement, the NEI VFQ-25, the SF-12 and the EQ-15D independently of their treatment.

Results The response rate was 86.73%. There were 51 males, the average age was 57.7±16.4 years and the average duration of diabetes was 10.9±6.6 years.Patients with proliferative DR and existing DMac scored lower on all VFQ-25 subscales compared to patients with non-proliferative DR and those without DMac, respectively, especially in the dimensions "General Health"(34.2±24.9 versus 74.3±15.7 and 25.1±18.7 versus 69.8±19.2) and "Role Difficulties"(33.7±28.3 versus 87.7±25.2 and 23.6±23.1 versus 79.9±26.7). In the SF-12 questionnaire the mean value in the Physical Component Scale (CS) was 45.6±11.3 and in the Mental CS was 45.2±16.8 while values in general Greek population are 49.4 and 48.9,respectively. In the EQ-15D the mean value was significantly lower,0.761,while published values in Greek diabetic patients without DR are 0.813.

Conclusion This study confirms that Greek patients with DR and DMac report poorer HRQoL than the general population. Therefore, the prvention and management of DR and DMac is essential to improve quality of life for these patients.

• 2214

Treatment accuracy and patient pain compared in retinal navigated laser (Navilas®) versus conventional laser in diabetic macular edema

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Purpose Treatment accuracy and patient pain were evaluated using a novel navigating laser (NAVILAS) compared to conventional laser treatment in clinically significant macular edema (CSME).

Methods Focal Navilas laser was performed in 42 patients. On color images (CI) and OCT laser spots were analyzed regarding accuracy spot placement compared to planning. Treatment pain was quantified on a visual-analogue-scale (VAS) and compared to a matched control. Up to one year clinical follow-up investigated retreatment and visual acuity compared to a control of 113 patients treated by conventional laser.

Results 79% of laserspots were visible on CI, of which 96% were within 100µm from the planned target. OCT confirmed that laser effects were limited to the outer retina . The number of laser spots per patient was 115+/-97 with Navilas, (43+/-36) with conventional laser. Pain on VAS was mean 1.6 (SD 1.0), 4.4 (SD 1.8) for the control. Kaplan-Meier analysis showed separation of the retreatment curves after 4-5 months with less retreatments for Navilas.

Conclusion Compared to conventional laser, significantly more laserspots were placed with Navilas, patient reported pain was significantly lower. the tendency for lower retreatment rates tend with Navilas may be important when considering possible combination laser and anti-VEGF drug therapy.

Commercial interest

• 2215

Diabetic retinopathy macular edema: treatment by series of 3 ranibizumab injections after 3 years follow-up

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Purpose To evaluate the functional, anatomical, vascular,anti-exudative effects of intravitreal injections (IVT) for Diabetic Retinopathy Macular Edema, by a protocol with 3 Ranibizumab IVT series, and the recurrences frequency at 3 years evolution.

Methods 44 eyes of 26 patients, 16 men, 10 women, with Diabetic Retinopathy Macular Edema. Patients received intravitreous Ranibizumab, 3 times, every 4 weeks in an inductive treatment. The next injections (IVT) depended on the follow-up results and were done by series of 3. First and 2 months' interval follow-up exam included ETDRS visual acuity (VA), complete ophthalmic examination, optical coherence tomography (OCT),fluorescein (FA) angiography. VA and OCT were done before each IVT. We want to evaluate the incidence of this protocol on the exudation and frequency of recurrence of exudation and so on the number of IVT needed.

Results VA improved in 79% cases, stabilized in 10,5%. Diffuse edema was 77% normalised ,total thickness was 55% less in the average follow-up, cysts 100% disappeared in 75% cases, in 40% were diminished in size , volume and number, by OCT. At Angiography, no leakage in 64% cases, cystic macular edema disappeared, microaneurysm's size and number diminished. Most of patients had good functional, anatomical results, with few IVT needed, no scars in the retina. Inductive treatment was sufficient in 6 cases, needed 2 IVT series in 30% eyes, failed in no cases. This protocol was compared ,discussed .

Conclusion The results, with improved visual function, reduction of exudation on OCT, lack of fluorescein leakage, few recurrences, suggest this protocol, with series of 3 Ranibizumab IVT seems effective, more retinal protective. This protocol seems attractive, specif

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The distribution of retinal thickness in healthy eyes and its use in the objective analysis of optical coherence tomography (OCT) scans

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Purpose OCT provides quantitative data but interpretation remains subjective. We have developed a statistical method to detect abnormal retinal thickness in OCT scans.

Methods High resolution macula topography maps, which were identified as normal by a retinal specialist, were exported from a spectral domain OCT/SLO machine. A Matlab® algorithm was written to perform image registration to a model macula. A reference map was constructed for each eye consisting of mean thickness and standard deviation at each point. Kurtosis and skewness were calculated. To analyse pathological scans areas > 2 SD from the mean were deemed abnormal.

Results 151 left eye scans and 112 right eye scans were analysed. The mean foveal thickness was 190.7 microns (SD 1.8) for the left and 189.2 microns (SD 1.6) for the right. Skewness and kurtosis were assessed over the macula. The mean skewness was 0.34 (-0.39 to 0.39) for the left and -0.0154 (-0.45 to +0.45) for the right. The mean kurtosis was 0.95 (SE 0.39, range -0.8 to 0.8) for the left and -0.0324 (SE 0.45, range -0.90 to 0.90) for the right.20 abnormal scans from patients with diabetes were aligned with the reference maps. The mean percentage area of abnormality >2 SD was 28%, 2-3 SD was 8%, 3-5 SD was 7%, 5-10 SD was 8% and >10 SD 5%. There was a linear correlation of area >2 SD with areas 3-5 SD (R2 = 0.65) and 5-10 SD (R2 = 0.73) indicating that larger lesion area is associated with greater oedema.

Conclusion The data show a normal distribution of retinal thickness in healthy eyes. A quantified image of statistical abnormality in a diseased eye can be generated which is helpful for standardising interpretation.

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Cytokine concentration in aqueous humor of eyes with diabetic macular edema

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Purpose To measure cytokine concentrations in aqueous humor of eyes with diffuse diabetic macular edema.

Methods The study included a study group of 23 patients with diffuse diabetic macular edema and a control group of 22 patients undergoing cataract surgery were compared. Cytokine concentrations were measured in aqueous humor samples using a Luminex xMAP suspension array technology.

Results In the study group as compared to the control group, significantly higher concentrations were measured for epidermal growth factor (EGF)(P<0.001), human growth factor (HGF)(P<0.001), intercellular adhesion molecule-1 (ICAM1) (P<0.001), interleukin 1a2 (IL1a2)(P=0.04), interleukin 6 (IL6)(P=0.001), interleukin 8 (IL 8)(P<0.001), interferon-gamma induced protein (IP10)(P=0.004), monocyte chemoattractant protein-1 (MCP-1)(P<0.001), monokine induced by interferon gamma (MIG)(P<0.001), matrix metalloproteinase 1 (MMP1)(P=0.02), matrix metalloproteinase 9 (MMP9)(P<0.001), plasminogen activator inhibitor 1 (PAI1) (P<0.001), placenta growth factor (PlGF) (P<0.001), tissue growth factor beta (TGF-ß) (P=0.003), vascular cell adhesion molecule (VCAM)(P<0.001), and vascular endothelial growth factor (VEGF)(P<0.001). Retinal macula thickness was significantly associated with the concentrations of the EGF, ICAM1, IL3, IL6, IL8, MCP-1, MIG, MMP9, TGF-ß, PlGF, VCAM, and VEGF. In multivariate analysis, macular thickness remained to be significantly associated with the concentration of ICAM1 (P=0.006;r=0.40).

Conclusion Numerous cytokines are associated with the presence and the amount of diabetic macular edema. Among these cytokines, ICAM1 was the most significantly associated with the disease parameters.

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Experimental study of distinguishing small retinal haemorrhages from dust artefacts using HLS colour space

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Purpose Many ophthalmologists consider it difficult to distinguish small retinal heamorrhages of early diabetic retinopathy from dust artefacts on fundus cameras.

Methods Photographs of the fundi of five patients with diabetic retinopathy were taken. Paint Shop Pro v. 8.0 was used to measure HLS colour spaces of both hemorrhagic area and the area around the heamorrhage at two locations of each photograph. We constructed the experimental device, which has an illumination optical system and a photographic optical system separated by a mirror having a hole with 4 mm diameter. The device consists of a canon EOS 50D camera, an EF 50mm f/1.8-2 camera lens, a Speedlite 270EX flash, an object lens, four double-convex lenses, two aperture stops and four artificial eyes. The eye ground is a half sphere made of polythene terephthalate painted by four mat colour sprays: red, white brown, ochre and yellow. Five fragments of house dust on the object lens were photographed under each artificial eye. Paint Shop Pro 8.0 was used to measure the HLS colour spaces of dust artefacts and the area around the artefacts.

Results The evaluation space of house dust was calculated using the HLS data obtained from the experimental device. Hue was red, −7.1±16.9; white brown, −5.7±7.4; yellow, 3.4±1.6 and ochre 0.3±2.3. Lightness was red, 10.7±3.4; yellow, 9.9±3.0; ochre, 9.5±1.8 and white brown, 8.2±2.1. Saturation was red, 25.5±23.5; white brown, 22.6±12.2; yellow, 15.1±12.3 and ochre, 5.0±2.8.

Conclusion The lightness of the HLS colour space helped in distinguishing dust from heamorrhage in all colour spectra. However, hue and saturation could distinguish dust from heamorrhage only under certain conditions.

• 2221

Mutation in Pxdn encoding peroxidasin causes small lenses and kinky tails in the mouse

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Purpose The mouse mutant KTA48 was identified within the recessive Munich ENU Project among offspring of treated C3HeB/FeJ mice. It is characterized by a kinky tail, white belly spot and small dull eyes.

Methods Linkage analysis was performed using SNP-based technology and microsatellite markers. Sequence analysis, histology and in-situ hybridization were performed according to standard techniques.

Results The genome-wide linkage analysis mapped the KTA48 mutation on chromosome 12; positional candidate gene analysis detected a mutation in the Pxdn gene (encoding peroxidasin) co-segregating with the mutation. The Pxdn-mRNA of the KTA48 mutants contains a T->A mutation at pos. 3816 (T3816A) creating a new Alw26I restriction site; the mutation converts the Cys at codon 1272 into a stop codon (Cys1272X). The mutation co-segregates with the phenotype in the breeding colony; it is not present in several wild-type strains.The lens phenotype is slightly variable. During an early stage of eye development (E12.5), Pxdn is expressed in the posterior part of the lens and in the central part of the retina without obvious changes. At the end of embryonic development (E17.5), we observed small lenses outside the optical axis and rupture of the lens capsule. Later, microphagia is accompanied by deformed cornea and multilayered retina. At P21, the small lens is attached to the cornea, and in some cases, the eye is completely disorganized..

Conclusion The recessive mouse mutation KTA48 is caused by a premature stop codon of the Pxdn gene. The function of Peroxidasin is still unknown; there is no mutation known neither in humans nor in mice.

• 2222

CTNND2 is a genetic variant for high myopia

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Purpose To determine novel genetic variants for high myopia in Singaporean Chinese.

Methods A meta-analysis of 2 genome-wide association (GWA) datasets in Chinese and a follow-up replication cohort in Japanese.Two independent datasets of Singaporean Chinese individuals aged 10 to 12 years (Singapore Cohort Study of the Risk factors for Myopia [SCORM]: cases = 65, controls = 238) and more than 21 years (Singapore Prospective Study Program [SP2]: cases = 222, controls = 435) for GWA studies, and a Japanese dataset aged more than 20 years (cases = 959, controls = 2128) for replication. Genomic DNA samples from SCORM and SP2 were genotyped using various Illumina Beadarray platforms (>HumanHap 500). High myopia, was defined by spherical equivalent (SE) ≤ -6.00 diopters (D) and controls defined by SE between -0.50 and +1.00 D.Single-locus association tests were conducted for each dataset with meta-analysis using pooled z-scores. The top-ranked genetic markers were examined for replication in the Japanese dataset. Fisher P was calculated for the combined analysis of all 3 cohorts.

Results Two SNPs (rs12716080 and rs6885224) in the gene CTNND2 on chromosome 5p15 ranked top in the meta-analysis of our Chinese datasets (meta P = $1.14 \times 10(-5)$ and meta P = $1.51 \times 10(-5)$, respectively) with strong supporting evidence in each individual dataset analysis (max P = $1.85 \times 10(-4)$ in SCORM: max P = $8.8 \times 10(-3)$ in SP2). Evidence of replication was observed in the Japanese dataset for rs6885224 (P = 0.035, meta P of 3 datasets: $7.84 \times 10(-6)$).

Conclusion This study identified a strong association of CTNND2 for high myopia in Asian datasets. The CTNND2 gene maps to a known high myopia linkage region on chromosome 5p15.

• 2223

A meta-analysis of studies on the hetitability of myopia

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Purpose Recently there has been considerable interest in the issue of mssing heritability - the quite common problem of difficulty in matching the high heritability for some complex diseases with associated genomic variation. The aim of this analysis was to determine whether the heritability values for myopia and ocular biometry dervied from twin studies, broader family studies and population-based studies were similar or different.

Methods Relevant studies were collected by using as search words "myopia","refractive error", "axial length","corneal curvature", "corneal power" and "heritability" in the PubMed database. Reference lists of the papers identified were also searched to identify additional references. Studies on populations enriched in myopia or refractive error due to the selection criteria for inclusion were excluded from the analysis,

Results The heritabilites determined for myopia from twin studies were significantly higher than those from family studies and population-based studies. Fewer studies were availalbe on the heritability of axial length, but there appeared to be a similar trend in the data. Studies on the heritability of corneal power were even fewer in number, and the results were inconsistent.

Conclusion The decline in the heritability of myopia with broader population base to the study suggests that the high heritability determined in twin studies is not generalisable, and may be associated with the low level of environmental variation within twin pairs. The heritability of axial length also depends on study design, although not as markedly as for myopia. Despite the high heritability determined in twin studies, evidence for major environmental effects is obtained with a broader population base.

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Analysis of locus 2q13 in Ecuadorian family with keratoconus

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Purpose Keratoconus (KTCN) is described as a non-inflammatory thinning and anterior protrusion of the central cornea which results in altered refractive powers, and loss of visual acuity. The etiology of KTCN remains unknown. Both genetic and environmental factors are associated with the disorder. The purpose of this study was to identify novel genetic factors involved in familial form of KTCN by extensive analysis of multigenerational Ecuadorian family.

Methods A total of 22 individuals from KTCN-019 family were included into this study. Genomic DNA samples of all members of KTCN-019 family were genotyped with highly polymorphic microsatellite markers. After linkage was established, two positional and functional candidate genes, IL1A and IL1B, were examined with polymerase chain reaction amplification, and direct sequencing of all exons, and intron-exon boundaries was performed.

Results The disease susceptibility locus was mapped on 2q13 chromosome in KTCN-019 family. Sequencing analysis of the candidate genes, IL1A and IL1B have revealed numerous alterations in coding and non-coding sequences of both genes including several novel single nucleotide polymorphisms. No mutations segregated with KTCN phenotype have been identified.

Conclusion Analysis of IL1A and IL1B genes revealed no mutations segregating with affected phenotype in large Ecuadorian family, indicating that other genes are involved in KTCN causation in this family.

• 2225 / 261

Identification of novel germline mutations in the VHL gene in Hungarian von Hippel-Lindau patients

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Purpose Von Hippel-Lindau disease is an autosomal dominantly inherited highly penetrant tumor syndrome predisposing to retinal and central nervous system hemangioblastomas, renal cell carcinoma and pheochromocytoma among other less frequent complications. Our goal was to establish genotype-phenotype correlation in Hungarian von Hippel-Lindau patients.

Methods Fourteen members (9 patients and 5 healthy family members) of 6 unrelated families with type 1 VHL disease underwent clinical and molecular genetic examination. The effect of a novel missense mutation was predicted using molecular modeling.

Results Retinal angioma was detected in seven patients; six patients had central nervous system hemangioblastoma and three patients developed RCC. Molecular genetic investigations detected four novel (c.232A>T, c.340+1G>A, c.163G>T, c.555C>A) and two previously described (c.583C>T and c.472C>G) germline mutations in the VHL gene, including four mutations leading to protein truncation and two missense mutations.

Conclusion RCC only associated to MLTP among our patients, in accordance with previous findings. The novel c.163G>T mutation associated to bilateral RCC and retinal angioma in a 15-years-old male patient, which is the earliest occurrence of RCC in VHL disease reported so far. Molecular modeling of the VHL-Elongin C complex predicted that the c.232A>T mutation responsible for the p.Asn78Tyr amino acid exchange remarkably changes the 77-83 loop structure of the VHL protein destabilizing the VHL protein and the VHL- Elongin C complex. Therefore it is predicted to cause type I phenotype, as seen in our patient indeed. Our results can be useful for genetic counseling and follow-up of VHL patients.

• 2231
iPS cells - an alternative source of RPE?

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Purpose We have previously shown that human embryonic stem cells spontaneously differentiate into RPE, and, after transplantation into the dystrophic RCS rat, maintain visual acuity. Recent advances in the generation of stem cells from somatic cells have led us to investigate the use of induced pluripotent stem cells (iPS) as a potential source of therapeutic RPE.

Methods iPS cells spontaneously differentiate after removal of bFGF from the culture medium. Isolated pigmented colonies were dissociated for expansion. The enriched population was then characterised morphologically and at the gene and protein expression level. Functionality of iPS-derived RPE cells was assessed by RPE phagocytosis of retinal debris in vitro and in vivo. The therapeutic effect of iPS-derived RPE was examined by injection of cells into the subretinal space of the dystrophic RCS rat.

Results In culture iPS-RPE were morphologically similar to, and expressed many markers of developing and mature RPE. These cells also phagocytose photoreceptor material, in vitro and in vivo following transplantation into the RCS dystrophic rat. Preservation of the neural retina layers and maintenance of visual acuity was observed 13 weeks following transplantation, however at this stage very few human cells remained and a number of large pigmented macrophages were observed in the subretinal space.

Conclusion iPS cells can readily differentiate into functional RPE which facilitate the short-term maintenance of photoreceptors. However, long-term maintenance of the dystrophic RCS rat neural retina is likely to be due to a protective host response initiated against the xenografted cells. The use of iPS-RPE as a cell therapy requires further investigation, however these cells provide a new model system in which to study RPE specific diseases in vitro.

• 2232
Towards xeno-free differentiation of rpe cells

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Purpose Stem cell therapy is a potential approach for the replacement of degenerated retinal pigment epithelial (RPE) cells essential for vision. For therapeutical use, the differentiation of RPE cells from human pluripotent stem cells (hPSC) should be performed in a culture environment fulfilling clinical quality requirements. For example the use of xeno-products should be avoided as this bears the danger of interspecies transfer of viruses and incorporation of immunogenic molecules.

Results Animal-derived substances, such as fetal bovine serum, mouse fibroblasts, and Matrigel are widely used in the differentiation and culture of hPSC-RPE cells. Recently, some protocols utilizing human feeders in the culture of pluripotent cells and small molecules in the differentiation process have been published. In our studies, we have also successfully differentiated pigmented cells from hPSC lines without the use of animal cells or serum. These cells show characteristics of RPE cells such as morphology, polarity, expression of genes and proteins typical for RPE cells, and phagocytosis of photoreceptor outer segments.

Conclusion Tissue engineering holds a great promise for treating retinal degenerative diseases. To date, RPE-like cells have been successfully produced from hPSCs and lately the protocols have been developed further towards xeno-free and defined culture systems enabling clinical grade cell production.

• 2233
The role of RPE in the regulation of VEGF

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Vascular endothelial growth factor (VEGF) has emerged as a major player in retinal diseases and is strongly involved in choroidal neovascularisation in exudative age-related macular degeneration (AMD) or in the development of macular edema in diabetic retinopathy. An important source of VEGF in the retina is the Retinal Pigment Epithelium (RPE). The RPE is a highly polarized cell layer situated between the choroid and the photoreceptors and among its many functions is the secretion of cytokines. RPE-derived VEGF is important for the development of the vasculature of the retina in the premature eye. In the adult eye, the RPE constitutively secrets low amounts of VEGF, mainly on the basolateral side, in order to maintain the choroid and protect endothelial cells. Also, neuroprotective properties of (apical) VEGF have been described. Main isoforms of RPE-secreted VEGF are VEGF165 and, to a lesser extent, VEGF121. Also, minor amounts of VEGF189 are can be found. VEGF165b, an anti-angiogenic isoform, might also be secreted by the RPE. Under different noxious stimulations, RPE cells increase their VEGF secretion, via several, stimulus specific, pathways. Among these stimuli, hypoxia, oxidative stress, hyperglycemia, several cytokines and endoplasmic reticulum stress might be closely connected to the pathogenesis of exudative AMD and other neovascular alterations of the retina. Loss of polarity might also contribute to inappropriate VEGF secretion and subsequent neovascular changes. The dichotomy of protective physiological and vision-threatening pathological VEGF secretion renders the differences of physiological and pathological VEGF expression regulation a highly interesting target for the development of long-term VEGF inhibiting drugs.

• 2241

Behçet's uveitis: why biologicals are predestined to become the first line treatments

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ABSTRACT NOT PROVIDED

• 2242

Laser flare photometry: why is it going to be the gold standard for the assessment of intraocular inflammation

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Purpose Laser flare photometry is a noninvasive, objective and quantitative method to measure intraocular inflammation.

Methods The reproducibility and accuracy of flare measurements was proven by laboratory tests and by clinical studies showing low inter- and intra-observer variability. Laser flare photometry values correlate with clinical grades of flare based on slit lamp examination. However, this technique provides a wide range of values for each clinical grade and there are overlapping ranges between grades. Besides,it allows the detection of subclinical blood aqueous barrier disruption.

Results Laser flare photometry has many clinical applications : 1-Uveitis Laser flare photometry shows better sensitivity than the slit lamp grading of cells and flare in monitoring anterior chamber inflammation, in both acute and chronic inflammation. It helps to define the inflammatory profiles of various types of anterior and posterior uveitis.It allows the assessement of the response to treatment and the prediction of the disease relapse.Relationships of laser flare photometry with complications permit to determine the prognosis of uveitis.2-Post-surgical inflammationAn objective evaluation of the blood aqueous barrier disruption after different surgical procedures is provided. The effects of different molecules on the post-surgical inflammation can be evaluated and compared.3-Several other conditions associated with some degree of blood-aqueous barrier disruption such as diabetic retinopathy

Conclusion Laser flare photometry is an objective and precise technique. It should be the gold standard for the assessment of intraocular inflammation.

• 2243

How OCT changed the appraisal of macular inflammatory disease

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ABSTRACT NOT PROVIDED

• 2244

Birdshot chorioretinopathy: why is sustained immunosuppression going to be the standard of therapy in most cases

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ABSTRACT NOT PROVIDED

• 2245

Vogt-Koyanagi-Harada disease: why indocyanine green angiography-assisted therapy is going to become the standard of care

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Purpose To assess the potential of ICGA in the monitoring of treatment of acute Vogt-Koyanagi-Harada (VKH) disease by detecting early recurrences.

Methods Retrospective/prospective study including patients in the initial acute phase of VH disease treated early with high dose inflammation suppressive therapy who were followed by indocyanine green angiography. (ICGA) at regular intervals.

Results The angiographic characteristics of ICGA in VKH in acute phase include hypofluorescent dark dots, fuzzy leaking choroidal vessels in the early and intermediate angiographic phase followed by diffuse choroidal hypperfluorescence in the late phase, and in very severe inflammation disc hyperfluorescence and pinpoints with subretinal fluid can be seen. All those signs disappear with early and intensive anti-inflammatory therapy. ICGA was effective in objectively detecting recurrence in apparently controlled disease by showing re-appearence of choroidal lesions (mainly dark dots) before biomicroscopy or fluorescein angiography manifestations, allowing early and fine adjustement of treatment during tapering period.

Conclusion By detecting subclinical choroidal inflammatory lesions ICGA allows detection of subtle recurrent lesion and refine therapeutic adjustement in order to avoid evolution toward chronic form and prevent sunset glow fundus.

• 2246

Choriocapillaritis : why is ICGA due to become the standard to monitor evolution and response to therapy

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ABSTRACT NOT PROVIDED

• 2247

Inflammatory choroidal neovascularization: how combined anti-VEGF and inflammation suppressive therapy is going to become the treatment of choice

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Purpose To describe the treatment strategy in the management of inflammatory choroidal neovascularization (CNV).

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

Results CNV can be one of the most severe sequela in patients with uveitis. The outcome of subfoveal inflammatory CNV is poor if untreated: several procedures have been considered, even though there is lack of guidelines.On the other hand, the better knowledge of CNV pathophysiology may suggest a suitable treatment strategy.The combination of steroids and immunosuppression represents an important aspect of inflammatory CNV treatment. This ensures suitable control of inflammation as well as the reduction concomitant steroids dose. Neverthless there are cases which do not show a fully satisfactory response. Recently, the role of intravitreal anti-Vascular Endothelial Growth Factor (VEGF) has become primary in the treatment of neovascularizations. At this time, the combination of anti-VEGF drugs and immunesuppressives has become the recommended strategy for the management of inflammatory CNV.

Conclusion CNV secondary to uveitis is a severe sequela, which can lead to significant visual impairment. Although no guideline is provided, the current medical literature can give the basis for a successful treatment strategy, suggesting that combination of immunesuppresives and anti-VEGF is recommended.

• 2251

Agreement between structural and functional classifications in glaucoma diagnosis

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Purpose To evaluate the agreement between the Moorfields regression analysis classification (MRA) of the Heidelberg retina Tomograph 3 (HRT3; Heidelberg Engineering, Heidelberg, Germany) and the functional classification of white-on-white Heidelberg Edge Perimetry (HEP, Heidelberg Engineering).

Methods Fifty-seven normal subjects and 89 age-matched glaucoma subjects were selected.Only one eye per subject was randomly included in the statistical analysis. All glaucoma patients had an intraocular pressure higher than 21 mmHg and abnormal Humphrey visual fields. The glaucoma group was divided into three subsets, according to the subject's level of visual field loss (Hodapp-Parrish-Anderson score). All participants underwent a comprehensive ophthalmic examination, at least a reliable Humphrey perimetry, at least a reliable HEP and imaging with the HRT3. The agreement between color-coded classifications of both, MRA and HEP, was calculated for each sector of the optic nerve head: nasal-superior

Results Mean age was 52.9 ± 9.5 years in the control group and 55.5 ± 9.7 years in the glaucoma group (p=0.104). In the control group, the best agreement was found for NI sector (100%), while the worst agreement was observed for TI sector (93%). Patients with mild glaucoma (n=59) had the best agreement at NS sector (79.7%) while patients with moderate glaucoma (n=18) had the best agreement at NS, TS and TI sectors (88.9%), and patients with severe glaucoma (n=12) had the best agreement at NS, TS, TI and T sectors (83.3%).

Conclusion In general, MRA and functional classification of HEP showed moderate to good agreement. The best agreement between both classifications was observed in healthy and patients with mild glaucoma.

• 2252

Rates of visual field progression before and after trabeculectomy

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Purpose To compare the rates of change in the visual field (VF) in patients with glaucoma before and after trabeculectomy.

Methods 52 eyes of 52 patients over 35 years of age with different types of chronic glaucoma who underwent primary trabeculectomy were evaluated retrospectively. Pre- and postoperative automated visual fields measured by the same technique were compared to detect differences in rates of progression.Rates of VF loss before and after trabeculectomy were calculated using global indices, mean defect (MD) and pattern standard deviation (PSD) and linear regression analysis per cluster. Linear mixed models were used to compare the evolution of the VF before and after trabeculectomy.

Results The mean follow-up period pre-trabeculectomy was 3.88 years (min 0.92, max 10.72) and post-trabeculectomy 3.82 years (min 2.03, max 8.02). The intraocular pressure (IOP) decreased significantly from 18.12 ± 4.71 mmHg before trabeculectomy to 11 ± 2.87 mmHg at the last follow-up after trabeculectomy ($P < 0.0001$). The rate of progression of MD decreased with 55%, from −0.36 dB/year before surgery to −0.16 dB/year after surgery ($P = 0.15$). The rates of progression of PSD decreased from −1.69 dB/year before to −0.018 dB/year after surgery ($P = 0.03$). Of the 10 predefined clusters, only in cluster 10, situated infero-temporally, the difference between the slopes was statistically significant (0.64 dB/year, $P = 0.0021$).

Conclusion Trabeculectomy significantly decreased the rates of glaucomatous VF progression.

• 2253

Location of visual field defect and optic disc assessment by confocal scanning laser ophthalmoscope in early normal tension glaucoma

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Purpose To compare topographic optic disc measurements in patients with central 10-degree and outer arcuate visual field (VF) defects in early normal tension glaucoma (NTG)

Methods Early NTG patients with a mean deviation of -10 dB or better in 24-2 Humphrey VF analyzer, and glaucomatous optic disc were included in this retrospective study. Patients were divided into central VF defect group (CFD) with VF defect in 10-degree radius in total deviation plot and peripheral VF defect group (PFD) with outer arcuate VF defect. Global and sectoral optic disc stereometric parameters were obtained with the Heidelberg Retina Tomograph (HRT) III and compared between CFD and PFD group. Mean deviation (MD) of central and nasal peripheral 12 points in mean deviation plot compared between superior and inferior hemifields in both groups.

Results Mean deviation and pattern standard deviation values showed no significant difference between 27 patients in the CFD group and 29 patients in the PFD group. The cup area, cup disc area ratio was significantly decreased in CFD group compared to PFD group only in inferotemporal sector, not in other sectoral parameters and global parameters of HRT. The MD of VF in the CFD group was significantly decreased in superior central 6 points (-9.23±8.12 dB) compared to inferior central 6 points (-3.36±4.18 dB). The MD of VF in the PFD group showed no significant difference between superior (-5.24±6.06 dB) and inferior (-8.10±6.42 dB) nasal peripheral 6 points.

Conclusion The change of optic disc in early NTG was more localized in the CFD group than the PFD group and central VF defect was more prominent in the superior hemifield.

• 2254

Correlation of the rate of progression of visual field loss between guided progression analysis (GPA II) and PeriData® program in glaucoma patients: pilot study

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Purpose To assess the correlation of progression rate measured by GPAII using visual field index (VFI%) and PeriDataTM employing functional equivalent score (FES) in glaucoma patients.

Methods Retrospective, observational study including 54 eyes of 37 medically treated glaucoma patients with at least 5 reliable visual field examinations in minimum 2 years. Only patients with a negative rate of progression with VFI were taken into account to calculate their rate of progression and loss of FES. Patients who underwent filtering surgery or laser trabeculoplasty during the follow-up period were excluded.

Results Mean age was 75.7 ±13.4 yrs. the patients performed their visual field with Humphrey standard automated perimeter (Sita Standard 24-2). The mean follow-up was 7.5 ± 2.5 yrs.The mean of progression by GPA (%/year) and PeriData FES index (%/year) were: -2.0 ± 2.2 (range= -10.6 to -0.2 per year) and -3.18 ± 2.5 (range: -9.3 to 2.8 per year) respectively. There was an excellent correlation between GPAII index VFI% loss per year and PeriData FES loss per year (<0.001) for the total group. In contrary when the group was limited to low- moderate progressors (VFI% loss per year ≥ -2), there was no correlation between the two different indexes.

Conclusion In this study we couldn't find any correlation between VFI% and FES% in the clinically low to moderate visual field progression.

• 2255

Increased hydrostatic pressure does not cause loss of retinal ganglion cell viability in human organotypic retinal cultures

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Purpose Raised intraocular pressure is the major risk factor for glaucoma. It is therefore vitally important to understand how increased pressure impacts on retinal ganglion cells (RGC) viability. These experiments investigate the effect of "pure" hydrostatic pressure on RGC survival in human organotypic retinal cultures (HORCs).

Methods In order to achieve this, we have designed and built a highly sophisticated controlled environment pressure chamber to expose cells to increased hydrostatic pressure while maintaining constancy of other parameters.

Results Exposure of HORCs to constant (60mmHg) or fluctuating (0-100 mmHg; 1 cycle/min) pressure for 24 or 48h resulted in no loss of structural integrity compared to controls (n=4). No significant changes in levels of RGC markers (THY-1 mRNA or NeuN) or LDH release were observed (n=4; $p>0.05$). RGC-5 cells, used for comparison, showed no change in cell viability (MTS; n=4), LDH release (n=3) or apoptosis (TUNEL; n=3) with pressure at 24 or 72h ($p>0.05$). Oxygen/glucose deprivation in HORCs reduced RGC number (~40%) at 24h (n=9; $p<0.05$) and increased LDH release (~80%; n=10; $p<0.05$). p38 and JNK activation remained unchanged in HORCs exposed to pressure (n=3; $p>0.05$) whereas OGD increased activation of both (n=3; $p<0.05$).

Conclusion These data clearly show that increased hydrostatic pressure on its own is insufficient to cause loss of cell viability, suggesting that direct hydrostatic pressure is not responsible for degeneration of RGCs occurring in glaucoma.

• 2256

Mitigation of the IOP elevation associated with non-supine sleep positions

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Purpose When a person sleeps in a non-supine position, the load path through which the weight of the head is transferred to a supporting surface (a pillow, the mattress, an arm, etc.) generally includes one eye. This research quantifies the forces that act on the eye and the potential for extended periods of intraocular pressure (IOP) elevation when the eye is a load bearing element in the "head-to-bed" load path.

Methods An engineering model of the load path is used to quantify nominal loads on the eye when in side- and face-down sleep positions. The eye is modeled as a fluid filled, thin walled pressure vessel and is included as a load-bearing structural element in the head-to-bed load path. The model is used to simulate a device that provides as alternative load path to mitigate sleep position related elevation of IOP.

Results Predictions from a lumped parameter model indicate that individuals who sleep in non-supine positions will experience elevation of IOP of 3-5 mmHg. A more sophisticated eye model is used to incorporate deformation of the eye and to show the lumped parameter model estimates of IOP elevation are conservative. This result is supported by a recently published experimental study of measured IOP elevation in dogs during eye manipulation [Keing et al., 2011] which suggests that relatively modest deformations of the eye can nearly double measured IOP levels. A non-invasive method for alleviation of the external forces that act on the eye during non-supine sleep is described as a means for altering this load path.

Conclusion These results suggest that patients with normal IOP levels during the day may experience significant elevation of IOP levels due to sleeping in non-supine positions. An approach to mitigate this mechanism of IOP elevation is presented.

• 2257

Posture-induced IOP changes in treated and untreated primary open angle glaucoma patients

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Purpose To compare posture-induced intraocular pressure (IOP) changes in controls, medically treated, and untreated primary open angle glaucoma (POAG) patients.

Methods One eye from each of 20 age-matched controls, 21 treated and 14 untreated POAG patients was included. IOP was measured with a Perkins tonometer and arterial pressure (AP) with a sphygmomanometer consecutively in the sitting, supine and 20 degrees Trendelenburg positions, allowing for a period of 5 minutes between positions. Differences in IOP and mean AP between the sitting, supine and Trendelenburg positions were calculated.

Results Mean±SD sitting IOP was 13.5±1.9 mmHg in the control group, 22.0±4.4 mmHg in the untreated POAG group and 13.5±2.5 mmHg in the treated POAG group (one-way ANOVA, $p<.001$). The IOP change from the sitting to supine position was 0.9±1.3 mmHg in the control group, 2.3±1.7 mmHg in the treated POAG group and 3.1±1.9 mmHg in the untreated POAG group (one way ANOVA $p<.001$). The IOP change from the sitting to the Trendelenburg position was 1.7±1.6 mmHg in the control, 4.2±2.2 mmHg in the treated POAG and 4.3±3.1 mmHg in the untreated POAG groups, respectively ($p<.001$). Post hoc pairwise comparisons revealed significant differences between each POAG group and controls ($p<.01$). No difference was observed in IOP changes between treated and untreated POAG patients for the sitting-to-supine ($p=.14$) and the sitting-to-Trendelenburg transitions ($p=.90$). No significant posture-induced AP change was observed in any group (repeated measures ANOVA $p>.1$).

Conclusion Irrespective of treatment, POAG patients exhibit a bigger posture-related IOP change compared to controls. This change is bigger when assuming the Trendelenburg position.

• 2261

Emil von Behring, the first Nobel prize laureate in medicine or physiology, and his ophthalmic interests

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Purpose Emil von Behring (1854-1917) received the Nobel Prize in 1901 for his work on serum therapy, especially its application against diphtheria. There are many publications about the life and work. It is thus surprising, that his interests and relationship to ophthalmology were only rarely mentioned, usually presented incorrectly and never analyzed thoroughly. The aim of this work is to fill this gap.

Methods The study was based on the detailed analysis of materials from National Archives in Berlin and in Poznan, cities where Behring lived and and Behring's works, including his doctoral dissertation.

Results Behring was trained and worked as anophthalmologist. He also wrote his doctoral dissertation on "Neurotomia opticociliaris" (optociliary neurotomy) whilst in Berlin under Carl Schweigger (1830-1905). He later worked as an assistant and co-worker with the prominent Polish ophthalmologist Boleslaw Wicherkiewicz (1874-1915), in Poznan where he described an interesting ophthalmic case in a scientific journal.

Conclusion Behrings' biography and achievements in serotherapy are well-known, however his interest in ophthalmology was not previously analyzed in detail. Both his doctoral dissertation and later his work as an assistant to Wicherkiewicz' ophthalmic hospitals in Poznan reveal his deep concern in ophthalmology in the early period of his medical career.

• 2262

Detection of retinal nerve fibre layer defects in Alzheimer's dementia using SD-OCT

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Purpose To examine the clinical value of spectral-domain optical coherence tomography (Spectralis OCT) to detect retinal nerve fiber layer defects in patients with clinically defined Alzheimer´s dementia (AD).

Methods Design: Cross-sectional studyA heterogenous cohort of AD patients (n = 25; 50 eyes) underwent a series of high-resolution OCT examinations of the peripapillary retinal nerve fiber layer (RNFL) thickness using the Spectralis 3.5-mm circle scan protocol with ART-Modus and eye tracking. The obtained results were compared to age- and sex-matched healthy control subjects (n = 25, 50 eyes) and RNFL thickness correlated with vision testing scores (ETDRS chart), Humphrey visual field testing, visual evoked potential testing (VEP).

Results In the AD group, independently of disease duration, no significant difference in RNFL thickness compared to controls (mm vs mm) as well as normal VEP values were observed. In contrast, determination of RNFL thickness in eyes of severe AD patients showed minimally reduced RNFLT values (without statistical significance). The detected RNFL thinning in patients of severe AD correlated moderately with visual acuity and VEP.

Conclusion As examined by spectral domain OCT, patients with AD did not show marked changes in the retinal nerve fiber layer.

• 2263

Dyschromatopsy and visual allesthesia in a glioblastoma multiforme patient

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Purpose To report a case of glioblastoma multiforme with dyschromatopsy and visual allesthesia.

Methods A 46 – year old male presented in emergency ophthalmologic department with recent color perception disturbance complaints noticed during his occupation (PC technician). The patient underwent a thorough ophthalmological examination and then he was referred to the neurological department for further management.

Results Patient presented an atypical pattern of color perception disturbance revealed by color blindness Ishihara test and Fransworth-Munsell D-15 test. Patient's best corrected visual acuity decreased progressively during his hospitalization and he also experienced paroxysmally illusory left homonymous transpositions of subjects viewed in the right homonymous visual field. The transposition occurred from normal to the defective visual field. This condition is called visual allesthesia. The visual field evaluation revealed homonymous left hemianopsia and magnetic resonance imaging revealed glioblastoma multiforme localized in the right occipital lobe with compressive effects on the occipital horn of the right lateral ventricle. The diagnosis was confirmed by biopsy.

Conclusion A thorough ophthalmologic and neuro-imaging control in patients with sudden color perception disturbance is suggested. Visual allesthesia is a rare condition experienced by patients with temporal or occipital cortex damage. Glioblastoma multiforme localized in the right occipital lobe was the underlined causative lesion.

• 2264

The pupil in pupillometry - to dilate or not to dilate

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Purpose To evaluate the influence of the size of the light exposed pupil in one eye on the consensual reflex in the other.

Methods Using a prototype chromatic pupillometer, the left eye in each of 10 healthy subjects was exposed to 20 s of monochromatic light of luminance 300cd/m2, first red (660nm)and in a following session, blue (470 nm) light. The consensual contraction of the right pupil was measured simulataneusly before, during and after light exposure. Tropicamid or pilocarpine was subsequently instilled into the left eye and the entire sequence repeated after allowing the left pupil to dilate or contract.

Results The AUC (Area Under the Curve, i.e. the "integral" of contraction amplitude versus time) of the right pupil was determined for each individual sequence. Prior dilatation of the left pupil augmented the post light AUC to blue ($p<0.0001$), but not to red light. The contraction during light exposure did not change. Prior contraction of the left pupil decreased the late (10-30s) post-stimulus AUC to blue light ($p<0.02$), but not any other AUC.

Conclusion The size of the light exposed pupil influences the magnitude of the response to blue, but not not to red light of the contralateral pupil. Thus prior dilatation may prove useful, when the response to blue light (as a marker of melanopsin containing retinal ganglion cell function) is of interest, especially when this response is weak. Prior dilatation may also be useful in exchanging long duration of stimulus with short duration, thus making the examination faster, less prone to artefacts and not least, less tiresom to the patient.

• 2265
Toxic optic neuropathy secondary to disulfiram: a case series

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Purpose To describe the presentation, ophthalmic features and electrophysiological findings in 4 patients with disulfiram (Antabuse) related optic neuropathy.

Methods Observational case series involving 4 patients. All patients underwent an extensive ophthalmological work-up, including psychophysical and electrophysiological testing.

Results All patients took disulfiram (Antabuse) tablets in varying doses and length of time before developing profound, bilateral visual loss. Three patients were smokers and one patient suffered from schizophrenia. Ophthalmic examination in combination with automated and manual perimetry showed reduction of visual acuity, disturbed colour vision and visual field defects consistent with bilateral optic neuropathy. Electrophysiological testing revealed delayed and reduced amplitudes on pattern VEP. After cessation of disulfiram, visual acuity, perimetry and electrophysiological testing gradually returned to normal or near-normal levels.

Conclusion Disulfiram is a rare cause of reversible toxic optic neuropathy. Patients who take disulfiram are more likely to abuse tobacco and possibly other drugs, or have psychiatric or psychological comorbidity. These patients may also be labelled as cases of malingering. Careful history and examination should alert the clinician to the possibility of disulfiram optic neuropathy.

• 2266 / 301
Endothelin-1 (ET-1) plasma levels in multiple sclerosis (MS) patients

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Purpose The aim of this study was to estimate endothelin- 1 (ET-1) plasma level in multiple sclerosis patients.

Methods Material was 49 patients (13 males, 36 females, mean age: 40 year, range: 22-62 years) suffering from multiple sclerosis according to McDonalds rule. The healthy controls consisted of 3 males and 28 females (mean age: 38 year, range: 19- 61 years). The protocol was approved by the Ethical Committee of the Postgraduate Medical Education Centre in Warsaw, Poland. Endothelin- 1 (ET-1) plasma levels were determined by ELISA Test (Immuno- Biological Laboratories. Co, Japan with tenderness : 8 fmol/ml). Statistical analysis were performed using the U- Mann- Withney test.

Results Endothelin- 1 (ET-1) plasma levels were significantly decreased in MS patients when compared to age matched controls (P= 0.0075).

Conclusion Statistically significant ET-1 plasma levels difference between examined patients and controls indicates, that vascular dysregulation may exists in MS patients. The outcomes will be discussed.

• 2267 / 302
Anisometropia and amblyopia in children

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Purpose To asses the quality of life for children with anisometropic amblyopia.

Methods A retrospective study for 53 children (33 girls and 20 boys) performed in ambulatory clinic in 2010. The average age at first diagnosis is 7.1415 ± 2.9317 years old (limits between 2 and 16 years). During the study the average age of children is 9.4943 ± 3.8422 years (limits between 3 and 20 years). Tracking interval is 1 year in 33.95%, between 2 and 5 years in 60.37% and over 5 years in 5.64%. Clinical parameters observed are: sex, age, visual acuity, optical correction, the type of correction (glasses, contact lenses), strabismic deviation and genetic factor.

Results Uncorrected visual acuity average at the right eye is 0.4353 ± 0.3640 and for the left eye is 0.3934 ± 0.3158. Corrected visual acuity average at the right eye is 0.6626 ± 0.3552 and for the left eye is 0.6468 ± 0.3519. Mean objective refraction (in spherical equivalent) at the right eye is -5.8214 ± 4.4651 and -5.52 ± 5.89 for the left eye. The average cylinder value is -0,7783 ± 1,1671 (with a range between maximum = -4.75 and minimum = -1). For 60.37% of patients, cylinder value is less than 0,75. There is a genetic transmission in 23.21% of cases, predominantly in mother (9.43%) and sister (9.43%). In 39.62% of cases there was esotropia. For 11.32% of cases, optical correction was made with contact lenses.

Conclusion 1. As early the diagnosis of anisometropia is made, visual acuity is more easily recovered.2. The average age of diagnosis in the our cases is 7.1415 ± 2.9317, noting that in Romania children are late diagnosed. 3. It is required a collaboration between the pediatrician, an ophthalmologist and the family for an early diagnosis of refraction errors.4. Anisometropic amblyopia can be corrected using contact lenses.

• 2268 / 303
Retinal nerve fiber layer thickness measured by optical coherence tomography correlates with Expanded Disability Status Scale (EDSS) in multiple sclerosis (MS)

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Purpose To determinate if retinal nerve fiber layer (RNFL) thickness was correlated with Expanded Disability Status Scale (EDSS) score in patients with definite multiple sclerosis (MS)

Methods 74 consecutive patients (extracted from the prospective Lorraine Multiple Sclerosis Registry) were included. A neurological examination with determination of the EDSS score and an ophthalmological examination with visual acuity, visual field testing, and RNFL measurements with optical coherence tomography (OCT3-Carl Zeiss Meditec, Dublin California USA) were performed.

Results Mean age was 44,5 years and 66% were women. EDSS average score was 3. Prior optic neuritis was present in 83% OD and 41% OS. EDSS score was negatively correlated with RNFL thickness (-0,28 p=0.04 OD and -0.2 p<0,1 OS). There were no correlation between RNFL thickness and MS subtype or any of other ophthalmological tests. At the opposite, RNLF thickness was significantly lower among eyes with prior optic neuritis (74 vs 90 OD and 76.8 vs 90.3 micrometers, p<0.01). In addition we did not find any correlation between EDSS and other ophthalmological tests.

Conclusion Our study demonstrates that RNFL thickness is statistically correlated with EDSS score. RNFL thickness measured by OCT appears to be an interesting structural biomarker to detect global axonal loss in MS patients. Larger studies are warranted to confirm if RNFL thickness could serve as a surrogate of EDSS score.

• 2271

Spectacle independence and subjective satisfaction of multifocal intraocular lens after cataract or presbyopia surgery

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Purpose Multifocal implantation represents nowadays in the world the first surgical option for presbyopic correction because of their ability to truly provide spectacle independence in more than 80% of cases, despite their goal is to only compensate the loss of accommodation and not to restore it.

Methods Actually the success of these lenses and the achieved visual performances have increased with last design refinements that have been brought on diffractive (aspheric, toric, trifocal) or refractive (bifocal aspheric, toric) multifocal IOLs in addition to the adjustment of calculation nomograms, for: better predictability of refractive correction, improved quality of vision with less pupil dependency and custom choice of the IOL model according to each patient needs. Moreover, the use of photoablation or LRI as an enhancement procedure in case of residual refractive error represent a nice option that has allowed to obtain glasses removal in more that 95% of operated patients.

Results However selection of patient appears to be the key factor and should be carefully considered in order to guarantee the good surgical outcome: beside anatomical contraindication such macular, retinal problem, severe amblyopia ..., preoperative refraction, patient expectations and needs are very important to evaluate. No doubt at that time that hyperopia and age of more than 55 years determine the best candidate. However, indications can be widely enlarged, when informations about limits especially in qualitative vision, postoperative evolutive profile are well explained and accepted before the surgery.

Conclusion We will describe the interest of last generations of multifocal IOLs, and report some comparative results between the different concepts.

• 2272

Wavefront guided or topo-link? Which one and when?

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Based on the refractive outcomes and postoperative wavefront aberrations measurements, in large series of patients who underwent photorefractive keratectomy with topography-guided, or wavefront-guided ablation, we will help you decide when to use each of these "premium" refractive surgery techniques.

• 2273

Would you recommend PresbyLASIK to your best friend?

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ABSTRACT NOT PROVIDED

• 2274

Spherical aberration: friend or foe?

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Purpose To determine the level of residual spherical aberration that gives the best objective and subjective quality of image after cataract surgery with intraocular lens (IOL) implantation.

Methods Six months after microincision (1.8 mm) cataract surgery with aspheric IOL implantation, total aberrations were computed using a Wavescan aberrometer. The modulation transfer function (MTF), Strehl ratio, and objective index of scattering were measured using the Objective Quality Analysis System. Objective depth of focus was computed as the focus range at which the Strehl ratio did not fall below 50% of maximum. Subjective depth of focus was calculated as the difference between the vergence of the punctum remotum and that of the punctum proximum.

Results Thirty patients (54 eyes) were evaluated. The MTF cutoff values were higher with decreasing total ocular spherical aberration ($r = 0.56$; $P<.05$). Objective and subjective depth of focus were positively correlated with total spherical aberration ($r = 0.26$ and $r = 0.46$, respectively; $P<.05$).

Conclusion A final spherical aberration of zero obtained by compensation of IOL asphericity gave the greatest improvement in objective quality of vision and better MTF contrast. However, a final target ocular spherical aberration between 0.07 µm and 0.10 µm should be considered to be the best compromise between subjective depth of focus and objective contrast sensitivity.

Azithromycin: clinical efficacy and safety in infants

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Purpose Purulent bacterial conjunctivitis affects all ages with high frequency in newborns and children. Our aim was to analyze in children especially in infants, the efficacy and safety of azithromycin 1.5% eye-drops in the treatment of this disease.

Methods Two multicenter, randomized, investigator-masked, parallel-group study, included infants, children and adolescents presenting a purulent conjunctivitis comparing azithromycin 1.5% eye-drops twice daily for 3 days and tobramycin 0.3% 1 drop every two hours for 2 days then four times daily for 5 days. Cultures, signs and symptoms were studied and safety and efficacy were evaluated at baseline, Days 3 and 9.

Results Results in term of positive cultures, signs and symptoms are exposed. Bacterial strains were identified precisely. Both treatments were effective. No adverse effects were noted on the ocular surface.

Conclusion The distribution of positive culture in bacterial conjunctivitis in infants and children is of interest for a better understanding of bacterial conjunctivitis. A short-treatment course can be easily used in children, thus improving the quality of life of them and their parents.

Commercial interest

Antibiotic prophylaxis in cataract surgery: what about the guidelines?

ROBERT PY
Limoges

ABSTRACT NOT PROVIDED

Management of the infectious risks in Cataract surgery in Sweden

BEHNDIG A
Umeå

ABSTRACT NOT PROVIDED

• 2311

Characterization of neuroepithelial progenitor cells in patients with proliferative vitreoretinopathy

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Purpose Proliferative vitreoretinopathy (PVR) is an important cause of retinal diseases such as retinal detachment (RD). In lower vertebrates, retinal damage is known to activate neuroepithelial stem cells (NSCs) in the ciliary margin in an attempt to regenerate the neuroretina. Cells expressing some markers of NSCs are also present in the retina and the ciliary body epithelium (CB) of the adult human eye. We hypothesized that if NSCs exist in the adult human eye, they should be activated by PVR formation.

Methods Cells isolated from vitreous samples (n=25) obtained during vitrectomies for RD were directly fixed or cultured in a stem cell-promoting medium, and compared to cells isolated from post mortem CB and peripheral retina (PR) using sphere-forming assay, immunohistochemistry, molecular biology and electron microscopy. Markers of NSCs were also studied in whole retinal control/PVR sections obtained from enucleations.

Results Spheres formed in 7/10 vitreous samples from patients with PVR compared to 2/15 samples from patients with no known PVR. These spheres stained for markers of NSCs both in vivo and after repetitive passages. Their mRNA and immunohistochemical profile resembled sphere-forming cells from the PR with only a few characteristics of CB cells. In situ characterization of the CB revealed that although there were higher numbers of dividing cells in PVR eyes than in controls, we did not detect markers of NSCs. Interestingly, markers of NSCs were evident around PR cysts with some evidence of activation following PVR formation.

Conclusion A population of NSC-like cells are found in the vitreous of patients with PVR. These cells seem to be originated from the retina itself and not the CB.

• 2312

Compared effectiveness of brilliant blue G for internal limiting membrane peeling in idiopathic epiretinal membrane in novice and experimented surgeons

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Purpose To evaluate the reliability of expected peeled surface after internal limiting membrane (ILM) removal by junior and senior surgeons with or without Brilliant Blue G (BBG) dye.

Methods We conducted a prospective study based on videorecordings of epiretinal membrane surgeries. Surgeries were performed by a senior vitreoretinal surgeon (SS) and two junior surgeons (JS). Patients were included into two groups: SS(group 1) and JS(group 2). In each surgery, after the ILM peeling, the surgeon described the expected peeled area (A1). Then, the instillation of brilliant blue G stained the actual peeled area (A2). The third area (A3) corresponded to the additional surface peeled with the help of BBG. Areas were measured in square millimeters using the software ImageJ 1.43 µ.

Results 15 patients were included in each group. In the group 1, A1 was 15.1+/-5.1 mm2, A2 was 13.0+/-8.0 mm2 and A3 was 16.3+/-5.0 mm2. In the group 2, A1 was 6.5+/-4.4 mm2, A2 was 5.9+/-5.3 mm2 and A3 was 11.2+/-5.1 mm2. In both groups, there was no stastical difference between A1 and A2 (P = 0.1875 and P = 0.5186 respectivally in group 1 and 2). A2 in the group 1 was significantly larger than A2 in the group 2 (P = 0.0195)as well as A3 (P = 0.0166).

Conclusion In our study, both senior and junior surgeons were able to determine the surface of ILM peeled without BBG. However, the surface of ILM peeled with the dye was larger with BBG with both junior and senior surgeons.

• 2313

Customized intraocular telescope implanted in high myopic patients with advanced maculopathy

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Purpose To evaluate the results of intraocular personalized telescope implantation toimprove distance best corrected visual acuity (BCVA) in high myopic patients having cataract surgery.

Methods This prospective non randomized observational study included 16 eyes of 9 consecutive patients with advanced maculopathy associate to high myopia having cataract surgery. Bilateral implantation of the intraocular telescope was performed after phacoemulsification in patients having the requisites. The telescope consists of two lenses a positive high power lens is implanted in the anterior chamber and a negative one is implanted in the posterior chamber. The lenses power, magnification and residual refraction were calculated for each eye using our own software. A complete ophthalmologic exploration and measurements of eye characteristics (keratometry, axial length…) refraction and VA were performed to the eye both before and after surgery.

Results The mean preoperative BCVA was 2/43. The mean postoperative BCVA was of 2/5 or better in 35% of eyes and 2/12.5 or better in 60%. The mean VA was 2/20 and only one eye had VA less than 2/40 (also before surgery). The prediction for the mean residual refraction (spherical equivalent, SE) was of -1.5 diopters (0.8 standard deviation, SD) and the achieved mean refraction was of -0.58 diopters SE (1.8 SD).

Conclusion Intraocular personalized telescope is an effective option for these low vision patients; which improves magnification and distance VA without significant adverse effects in one year follow up.

• 2314

Reasons for reduced vision after anatomically successful retinal detachment surgery

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Purpose To identify the cause of reduced visual acuity in patients with successful anatomical result after retinal detachment surgery.

Methods We retrospectively reviewed files of patients that underwent retinal detachment surgery in our clinic. Patients with anatomically successful operation and a postoperative visual acuity ≥ 0.18 logMAR were identified. Patients were called and they underwent thorough re-examination including BCVA after refraction, slit lamp examination, fundus biomicroscopy, OCT and fluorescein angiography if considered necessary.

Results We reviewed the files of 78 patients with anatomically successful operation. 26 patients (33%) had a visual acuity better than 0.18 LogMAR. The remaining 52 (67%) patients had a visual acuity ranging from 1.1 LogMAR to 0.18 LogMAR. The reduced visual acuity was attributed to anterior segment problems in 8 patients (15.4%) (in 7 patients to cataract and 1 to bullous keratopathy), to cystoid macular edema in 18 patients (34.6%), to residual subretinal fluid in 5 patients (9.6%), to macular atrophic changes in 5 patients (9.6%), to epiretinal membrane in 11 patients (21.2%), to macular hole in 3 patients (5.8%), to optic nerve atrophy in 1 patient (1.9%) , while in 1 patient (1.9%) no apparent reason for reduced vision was found.

Conclusion Macular changes represent the most frequent reason for reduced visual acuity after anatomically successful retinal detachment surgery. Strategies to prevent or improve these alterations might improve the functional result of retinal detachment surgery.

• 2315
Transferrin and prealbumin: indicators of PVR and risk of recurrence in retinal detachment

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Purpose Proliferative vitreoretinopathy (PVR) is the leading cause of failure in retinal detachment surgery. Increased levels of transferrine have been found in proliferative vitreoretinopathy. A relationship between the level of prealbumin and the functional outcome has been previously reported. The purpose of this prospective study was to look for a link between the vitreous levels and preoperative PVR or post-operative outcome.

Methods The vitreous samples of patients with epiretinal membrane and rhegmatogenous retinal detachment (RD) were obtained at the initial phase of surgery without previous intraocular infusion. The levels of transferrine (TF) and prealbumin (PA) were determined in all cases. The functional (visual acuity) and anatomical outcome (OCT mean foveal thickness, RD recurrence) was assessed.

Results The vitreous levels of TF (193 mg/l vs. 44mg/l; p=0.038) and PA(115 mg/l vs. 15mg/l; p=0.0002) were significantly higher in the RD group(n=23) than in the macular surgery group(n=35). In eyes with RD, the intravitreal levels of TF in eyes with PVR A and B were higher than in eyes with PVR C (121 mg/l vs.356 mg/l; p=0,0233). In eyes with PA > 200 mg/l, 2 cases of RD recurrence were observed, when PA < 200 mg, no recurrence was observed (p=0.0296).

Conclusion Increased prealbumin levels in the vitreous appear to correlate with an increased recurrence rate of retinal detachment. The predictive value of prealbumin for the occurrence of postoperative proliferative vitreoretinopathy in patients undergoing retinal detachment surgery remains to be demonstrated and requires a prospective multicenter study.

• 2316
Measurement of scleral rigidity in patients with age-related macular degeneration

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Purpose It has been hypothesized that altered mechanical properties of the sclera may contribute to the pathogenesis of age-related macular degeneration. Unfortunately, the determination of structural stiffness of the sclera in vivo is difficult. In this study, we present a new technique to estimate sclera stiffness in vivo. In addition, we aim to test the hypothesis that sclera stiffness is altered in patients with AMD.

Methods 44 patients with AMD and 22 healthy subjects, matched for age, sex and intraocular pressure were included in the study. Ocular pulse amplitude(PA) and pulsatile ocular blood flow were assessed using pneumotonometry. Ocular fundus pulsation amplitude(FPA) was measured by the means of laser interferometry. A coefficient for ocular rigidity(E1), based on the Friedenwald equation was calculated relating PA/FPA,as a measure for structural stiffness.

Results FPA was decresased in patients with AMD when compared to the healthy group ($p = 0.025$). However, no difference was observed PA between patients with AMD and healthy subjects ($p = 0.34$). E1 was significantly higher in the patients with AMD (0.91 ± 0.11AU) than in the control subjects (0.70 ± 0.07AU; $p < 0.001$).

Conclusion Our data indicate that the mechanical properties of the sclera are different in patients with AMD compared to healthy subjects. In particular, our data indicate an increased sclera stiffness in the AMD group. Whether this causatively involved in the pathogenesis of AMD or a consequence of the disease, has yet to be shown.

• 2317 / 335
New cyanine dye for ILM staining

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Purpose To investigate the biocompatibility and staining properties of a new cyanine dye (DSS: 3,3´-Di-(4-sulfobutyl)-1,1,1´,1´-tetramethyl-di-1H-benz[e] indocarbocyanine).

Methods Dye concentrations of 0.5%, 0.25% and 0.1% were evaluated (osmolarity between 290 and 295 mOsm). Toxicity was assessed using a colorimetric test measuring the inhibition of ARPE 19 cell, human primary RPE cell and human Müller cell proliferation. Exposure time was 30, 60, 120 and 300 seconds. Indocyanine green (ICG) (0.5%, 0.25% and 0.1%) served as a control. Besides staining of porcine and human lens capsule, internal limiting membrane (ILM)-staining was assessed by applying 0.25% and 0.5% DSS over the macula in two human post-mortem eyes.

Results The dye DSS did not reveal any toxicity on ARPE-19, primary human RPE cell and human Müller cells proliferation in all concentrations and exposure times investigated. The absorption maximum is found at 591 nm, the even more bathochromic fluorescence proceeds with a common Stokes' shift where maxima at 620 and 660 nm with a quantum yield of 32% were found. The fluorescence is sufficiently hypsochromic and the fluorescence quantum yield high enough for an easy visual detection. The contrast and staining properties at the ILM was excellent because of matched optical properties and allowed for a controlled removal of the ILM during surgery. No penetration into deeper retinal layers was noted.

Conclusion Our results indicate that this new cyanine dye DSS may represent an alternative for ILM staining due to its matched absorption concerning visibility and fluorescence qualities as well as its good biocompatibility. The dye is superior compared with ICG where there is no matching of the UV/Vis spectra.

• 2318 / 336
Acute intraocular pressure after intravitreal injections, what is the mechanism?

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Purpose To evaluate the mechanism of acute intraocular hypertension after intravitreal injections (IVI) of anti-VEGF therapies.

Methods A prospective study was performed to evaluate the IOP increase immediately after IVI of 0,05ml ranibizumab in 50 patients. We have also studied the correlation between IOP immediately after IVI and axial length, then with lens status. Moreover we have analysed the anterior chamber anatomic changes (anterior chamber volume and irido corneal angle), measures were taken before and 5mn after IVI by scheimpflug camera from Oculyzer® (Alcon).

Results The IOP peak immediately after IVI was higher than 45 mmHg in 67,3% of patients. It was transient, decreasing after 15mn and returning to baseline in all patient after 45 mn. We found no statistically significant difference between pseudophakic eyes (n=30) and phakic eyes (n=20, p=0.80). No correlation was found between the axial length and the IOP spike (r=0.042, p=0,85). The mean change for the anterior chamber volume (ACV) is mild (0,33 mm3).The ACV increased in pseudophakic eyes (+15,64 mm3, +7,7%), but decreased in the phakic eyes (-7,24 mm3, -4,4%). The mean change for irido corneal angle (ICA) is not significant (-1,61°), it decreases in phakic eyes (-2,97°, -7,2%) versus a quite neutral effect in pseudophakic eyes (+0,78°, + 1,5%).

Conclusion The IOP spike is not correlated either with axial lengh or with lens status. ACV and ICA variations are different according to the lens status but remains mild. These results enhance the importance of the scleral biomechanical properties, and highlight an unpredictable peak. This could be an argument to propose a systematic prophylactic hypotensive treatment before IVI.

• 2321
Principles of genetic counseling

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Purpose To present the genetic counselling needs of families with inherited eye disease and examine the ethical and emotional issues around genetic testing

Methods The presentation will focus on the psychosocial impact of inherited eye disease and the dilemmas in counselling and testing using case discussions and data from qualitative studies.

Results Genetic counselling is a process of communication to provide information about a genetic condition, inheritance and support decision making and adjustment in families. Genetic testing for inherited eye diseases is rapidly advancing with massive improvements in high throughput molecular testing. While this can allow accurate diagnosis and information, the issues of genetic heterogeneity, variable penetrance and overlapping phenotypes mean that the provision of accurate information particularly challenging for genetic eye disease. These scientific advances have also led to increased patient demand and expectations. Complex cases presenting to the multi-disciplinary genetic eye clinic in Manchester will be presented to highlight the needs of families requesting genetic counselling including approaches to complex situations such as pre-symptomatic testing, childhood testing and pre-natal diagnosis.Qualitative data involving in-depth interviews with families with inherited retinal dystrophy describes the burden of living with the risk of blindness and decision making around genetic tests. Research evidence also demonstrates that families feel their needs are not met by current services, suggesting a need for improvements in evidenced-based practice.

Conclusion Families with inherited eye disease have complex genetic counselling needs requiring multidisciplinary services to provide accurate diagnosis, information, genetic testing, decision-making, support and follow-up.

• 2322
Molecular ophthalmic genetics tools

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Purpose To provide an overview of recent developments in molecular genetic tools applied in ocular genetics.

Methods Genomewide strategies for copy number screening (arrayCGH), identity-by-descent (IBD) mapping and massive parallel sequencing (MPS) or next-generation sequencing (NGS) technologies (targeted resequencing, whole exome and genome sequencing) will be discussed.

Results Genetic variation, comprising both copy number variation (CNV) and sequence variation, has a great impact on ocular genetic disease. Recent advances in genomewide technologies such as arrayCGH, SNP chip based IBD mapping and NGS have revolutionarized the concept of gene identification and diagnostics of ocular genetic disorders. Examples will be given of applications of arrayCGH in gene identification and molecular diagnostics of developmental ocular disease and the power of IBD mapping and NGS in gene identification and routine diagnostics of retinal dystrophies.

Conclusion The throughput and quality of these genomewide technologies now bring DNA-based personalized diagnostics within immediate reach for research, routine diagnostics and treatment strategies of ocular genetic disease.

• 2323
Inherited ocular developmental disease

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Purpose High throughput technologies offer considerable opportunities to understand the genetic basis of developmental ocular disorders, both common and rare. This presentation will provide an overview of recent progress illustrated with specific examples including early-onset corneal, cataract and retinal disorders.

Methods A review, including case presentations, to illustrate insights into genes underlying developmental ocular disorders including the understanding of novel pathways underlying common and rare developmental disorders and the utility in clinical practice of high throughput technologies including next generation sequencing.

Results Although individually rare, the group of developmental ocular disorders are an important contributor to childhood visual disability. Many of the issues regarding diagnosis and counselling apply to the entire group allowing the development of a unified care pathway. An important challenge is to improve diagnosis. Currently diagnostic genetic testing still focuses on single genes; this will be illustrated for ocular conditions such as brittle cornea syndrome (ZNF469, PRDM5) and Lenz microphthalmia syndromes (BOCR). Future prospects will employ high throughput technologies (e.g. next generation sequencing, microarray analysis). Examples will include inherited congenital cataract phenoptyes.

Conclusion The recent identification of genes underlying disorders of the anophthalmia/microphthalmia spectrum, of corneal development and of congenital cataract sheds light on the pathways and processes underlying a range of the biological processes underlying ocular development. Their identification has a direct bearing on clinical management, allowing the development of individualised care pathways.

• 2324
Electrodiagnosis in inherited retinal disease

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The presentation will use a case based approach to describe the value of electrophysiological assessment in the diagnosis and management of patients with inherited retinal disease.

• 2331

Morphology and function of the inner lid margin – history and recent findings

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Purpose The eyelid margin is a region that often receives little interest but, in contrast, is of utmost importance for ocular surface health and disease. The posterior lid border is a pre-requisite for perfect distribution of a thin pre-ocular tear film that is reformed with every blink.

Methods Own findings on the zonal differentiation of the normal lid margin and observations in pathology are presented in the context of the literature on this region.

Results The lid margin is not a homogenous entity but composed of different sub-zones which comprise at least the anterior and posterior lid borders as opposed to the free lid margin. The posterior lid border is again subdivided into three zones that are all characterized by a specific epithelial structure. The termination of the cornified epidermis posterior to the orifices of the Meibomian glands (MG) explains hyperkeratinization as the main pathology of the MG. The mucocutaneous junction (MCJ) has a parakeratinized surface that represents the natural stainable line of Marx. The inner aspect of the posterior lid border is covered by the epithelial lip of the lid wiper with conjunctival structure and goblet cells. The line of Marx, proposed as the bottom of the tear meniscus, has occasionally been suggested as the area wiping over the globe but several lines of evidence point to the lid wiper as the contact interface between lid and globe.

Conclusion Better knowledge of the structure and function of the eyelid margin will provide better tools for the understanding of its function, clinical diagnosis and therapy of frequent diseases at the ocular surface, namely dry eye disease. Support DFG KN 317-11

• 2332

Goblet cells in the conjunctival lid wiper elevation provide a built-in lubrication system

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Purpose The lid wiper is an epithelial elevation at the posterior lid border apposed to the globe that distributes the thin pre-ocular tear film during the blink. To minimize the high risk of friction it can be assumed that it is provided with an advanced lubrication system.

Methods The structure of the lid wiper epithelium is explained together with an overview of historical reports. Theoretical models of lubrication at the lid-bulbus interface are discussed.

Results A thickened epithelium was described early but the immediate functional implications for the distribution of the preocular tear film over the bulbar surface were noticed only much later. More recently "Lid wiper epitheliopathy" (LWE), a respective vital stainable epithelial alteration, was reported as first sign of tear film deficiency and increased friction in dry eye patients. The structure of the lid wiper was generally assumed to consist of a squamous non-cornified epithelium, however in recent investigations we could show that it has in fact a conjunctival structure with goblet cells and goblet cell crypts that secrete mucins of different types.

Conclusion The conjunctival structure of the lid wiper for distribution of the thin pre-ocular tear film with goblet cells and goblet cell crypts implies the presence of a thick mucin-water gel at the surface. This provides the structural pre-requisite for the assumption of a hydrodynamic type of lubrication and can explain how the lid margin continuously travels over the bulbar ocular surface without wounding it.Support: DFG KN 317-11

• 2333

A grading system for alterations of the lid wiper zone in ocular surface disease

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Purpose The lid wiper is a part of the lid margin, with many important functions for the ocular surface. Until now changes of the lid wiper where said to be symptoms of dry eyes. This study should observe the changes according pathogenesis and etiology of ocular surface diseases.

Methods Worse eye of 61 outdoor department patients were observed. We evaluated the etiology according the triple classification and the pathogenesis auf lipids, mucins and water layer as well as the corneal epithel. The wiper was observed by clinical changes of vessels and staining with lissamin green. We observed the relation of these changes with the etiology and pathogenetic cause.

Results There was a correlation of Lid-Wiper changes with inflammation and immune diseases, as well with hormonal disorders. There was a low correlation with psychologic problems and with patient's age.

Conclusion By these observations the grading system could be modified by including vessel changes and locations of lissamin green staining for definition of the ocular surface dysfunction.

• 2334

Prevalence of MGD in a clinical dry eye population

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Purpose The meibomian glands inside the tarsal plates of the eyelids contribute to the superficial lipid layer of the tear film. These lipids reduce evaporation of tears, enhance tear film stability, protect the ocular surface and provide a clear optical image. Meibomian gland dysfunction (MGD) is a common condition and can lead to evaporative dry eye.The purpose of this study was to characterize patients in an Austrian dry eye unit with MGD.

Methods Between 2004 and 2010, 1372 consecutive patients with ocular discomfort from the dry eye unit of the Ophthalmological Department, Medical University Graz, were analysed retrospectively. Subjective symptoms were evaluated with a visual analogue scale. Fluorescein-break up time, Schirmer test without local anaesthesia, fluorescein and lissamine green staining of the ocular surface and evaluation of the lid margins were performed. MGD patients were defined as follows: presence of teleangiectasia, irregularity of the lid margins, altered expressibility of meibomian glands and poor quality of expressed meibomian gland secretions.

Results Overall 70.2% of all patients suffered from MGD. The mean age of these patients was 55.3 ± 16.6 years and 70.9% were women. 52.1% of the MGD patients had Schirmer test values equal or below 10mm/5min and 30.1% of the MGD patients had Schirmer test values equal or below 5mm/5min. Sjögren's syndrome according to the American-European Consensus Group was found in 4% of the MGD patients. The intensity of subjective symptoms did not differ among these patients.

Conclusion MGD is a major cause of ocular discomfort as evaluated in a large clinic-based population of Austria. Tear deficiency is often accompanied with this disorder.

• 2335

The relation of lipid layer structure to meibum - results from a new high resolution microscope

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Purpose Evaporative dry eye is a common disorder, in which the lipid layer of the tear film is a poor barrier to evaporation. We therefore developed a high resolution microscope as an aid in understanding the properties of the lipid layer.

Methods The microscope has a resolution of about 1 um, and uses a stroboscopic light source to prevent blurring from eye movements. Over 10,000 images of a least "fair" quality have been obtained from 375 subjects, including dry eyes and normals.

Results Two characteristics of the images are described here. 1. In some dry eye patients, irregular "islands" and circular "lenses" of lipid are seen within an apparently bare surrounding area. 2. In most images, "droplets" of lipid are observed which may be circular or irregular, and are surrounded by lipid of irregular thickness. Droplets do not appear to change in the inter-blink interval.

Conclusion 1. Rapid evaporation is to be expected through the bare surface between islands and lenses. This pattern may be due to insufficient surfactant (e.g., polar lipid) to help spread lipid over the aqueous layer. 2. "Droplets" do not seem to be generated in the inter-blink interval and it is not obvious how they could be generated by blinks, so their origin may be the "fat droplets" which are observed histologically in meibomian glands (Sirigu et al., 1992, IOVS 33, 2284). It is suggested that meibum is an emulsion of these droplets.

• 2336

Correlation of non-contact meibography to dry eye symptoms and signs in Sjögren`s syndrome and graft-versus-host disease

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Purpose Severe dry eye is often observed in patients suffering from Sjögren's syndrome (SS) or chronic graft-versus-host-disease (cGVHD). Although the underlying pathomechanisms differ, deficient tear production, as well as meibomian gland dysfunction (MGD) are present in both. 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 the correlation of non-contact Meibography to dry eye symptoms in patients suffering from SS or cGVHD.

Methods We examined 37 patients suffering from SS and 11 patients with cGVHD of our dry eye unit. Subjective dry eye symptoms were evaluated with a visual analogue scale and the Ocular Surface Disease Index© (OSDI). Clinical signs of MGD were graded from 0 to 3 according to the Report of the TFOS Workshop on MGD. 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 the meiboscore of Arita and colleagues.

Results The mean age of the study population was 55.3 ± 13.4 years and 91.7% were women. The Meiboscore correlated significantly with the subjective symptoms assessed by visual analogue scale. The grading of the lid margins correlated significantly with the Meiboscore.

Conclusion Non-contact Meibography is a valuable tool in the diagnosis of MGD. Standard ophthalmic angiography cameras equipped with infrared diodes can easily perform it. The meiboscore correlates with the intensity of subjective symptoms and lid margin changes in patients suffering from SS or cGVHD.

• 2341
PCR, principles, advantages and pitfalls: focus in some viral infections of the anterior segment of the eye

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Gene amplification using polymerase chain reaction (PCR) has become the gold standard for microbiological diagnosis in eye diseases, particularly in those related to viruses. Even if the specificity and the sensibility indexes are much higher than conventional methods, gene amplification may present some limits. For example, uveitis with low grade viral replication may induce false-negative PCR results while assessment of the immune charge in aqueous may be positive in such cases. For infections of the ocular surface, PCR is usually much more effective than isolation of the virus in cell culture, but the high sensibility may inversely induce false-positive results. For example, continuous shedding of herpes simplex in tears is known to occur regularly even in asymptomatic patients, which could mask the real diagnosis of any other cause of ocular redness. Even latest technologies, such as real time quantitative PCR, are not completely satisfying since a misuse of this very sensitive technique may also lead to false positive results if effective controls are not systematically used for each assay, due to the self-fluorescence of the PCR mix when the number of thermal cycles increases. Inversely, vital dies, anesthetics eye drops or non-optimal tissues purification may lead to false negative results due to the inhibition of the polymerase reaction.

• 2342
PCR in posterior segment viral diseases

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Since its introduction in the early eighties, PCR has dramatically changed our approach to the diagnosis and understanding of intraocular viral diseases. Even though serology remains the effective diagnostic tool for diseases such as West-Nile virus or dengue-virus retinitis, PCR is the gold-standard for herpetic retinopathies. Two major subtypes have been described including necrotizing and nonnecrotizing herpetic retinopathies. In Europe, diagnosis is performed based on the analysis of the aqueous humor, whereas vitrectomy is more frequently performed in the USA. Less than 100 microlitters of liquid is sufficient for the procedure. Real-time PCR is now available for most of the herpesviruses allowing a quantitative determination of the viral load. The identification of the viral agent is paramount in the management of the disease by adapting the antiviral strategy. VZV, HSV-1, HSV-2 and CMV are the main causes of viral retinitis. Acute retinal necrosis syndrome is mainly observed in immunocompetent patients whereas, progressive outer retinal necrosis syndrome and CMV retinitis occur classically in immunocompromised patients. Intravitreal injection of corticosteroids must be considered as a risk factor. The decrease of the viral load is a major prognostic factor and must be taken into consideration for an optimal management.

• 2343
New test for rapid Acanthamoeba diagnosis

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Purpose Acanthamoeba keratitis (AK) is a sight-threatening infection. Classic PCR enhanced sensitivity but required post-amplification procedures, increasing contamination risks. The reported real-time PCRs are unable to detect all the genotypes associated with pathology. We present a new strategy validated American Type Cell Collection strains and corneal scrapings.

Methods A were detected by a fast PCR (f-d-real-t PCR) and negativity confirmed by SYBR Green. Sequences selected in the mitochondrion were: forward primer: 5'GCAGTCGCGGTAATACGA; reverse: 5'ACCACCTACGCACCCTTTACA and probe: 6-FAM-AGTGTTATTCGCATTGACTGGGTGTAA-TAMRA.

Results The new test detects all A with different lab equipment (1 cyst or less/specimen). A.astronyxis signals are inferior to others; however, primers diluted in SYBR Green mix (without probe) detect 0.1 cyst/µl or less of this strain. For clinical samples microscopic examination and cultures detected 6 out 10 but f-d-real-t PCR 100% with results confirmed by SYBR Green. Other PCRs bracketing different regions (ribosome) detected 80 % and produced false positives for samples containing Salmonella lexinton, C. sporulans, S. marcescens and Propionibacteria.

Conclusion Highly sensitive diagnosis is necessary to administrate efficient treatments at the onset of AK. The strains from the ATCC with higher sensitivity and specificity than techniques previously reported. New approaches based on High Resolution Melting r-t PCR are in development in the CHNO to detect and molecularly characterize in one run different strains of protozoa and Fungi infecting the eye.

• 2344
PCR in acute bacterial endophthalmitis

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Purpose This review aims to summarize studies which assessed the use of PCR in post operative endophthalmitis. Endophthalmitis is a rare but devastating complication of ocular surgeries. There is a need for more rapid and more sensitive microbiological techniques since clinicians should rapidly identify bacterial pathogens.

Methods Different microbiological techniques will be presented, eubacterial PCR, real time PCR

Results Column-based nucleic acid purification allows removal of DNA-polymerase inhibitors. Real time PCR is more sensitive than culture, allows the detection and identification of specific micro-organisms, DNA quantification, and has a faster turn around time (no post-PCR step). The PCR amplification of 16S rDNA uses consensus primers (panbacterial PCR) and is followed by identification from analysis of 16S rDNA sequence (BIBI). 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. A summary of the main published clinicomicrobiological studies will be presented.

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 could help clinicians to identify patients needing a more aggressive treatment and to develop new drugs.

• 2351
CSF pressure and glaucoma: pro

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Purpose The Optic nerve in its orbital is surrounded by cerebrospinal fluid pressure (CSF) with the CSF-pressure. It may therefore make sense to consider the trans-lamina cribrosa pressure difference of intraocular pressure minus orbital CSF-pressure to be important for the physiology of the optic nerve head, in normal eyes and eyes with glaucoma

Methods The talk will present anatomical findings of the optic disc and results of previoous experimental and clinical studies which may support the hypothesis that the CSF-pressure may play some role in the pathogenesis of glaucomatous optic neuropathy.

• 2352
CSF pressure and glaucoma: contra

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Purpose The concept that the low cerebrospinal fluid (CSF) pressure might influence optic nerve neuropathy in glaucoma was recently reappraised. This is to discuss the possible relevance of this concept.

Methods Analysis of the previous clinical and experimental studies, including their results and limitations.

Results The pathogenesis of optic nerve neuropathy in glaucoma is multifactorial and not well understood, thus different new concepts appear to explain the heterogeneity and complexity of the disease. The concept arguing that CSF pressure directly influences the intraocular pressure and is linked to the glaucoma pathogenesis has its proponents and opponents. Evidence based discussion is limited, however, by the fact that the only prospective clinical study raised some ethical concerns and have not been verified yet by any other research center. Moreover, the same ethical concerns might restrain the similar studies in future, what make the scientific discussion of the subject difficult.

• 2353
Deep sclerectomy: pro

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Purpose From the weight of the litterature, deep sclerectomy (DS) certainly is safer than trabeculectomy and as safe as modern trabeculectomy and thus might represent an alternative therapy earlier in the glaucoma process.

Methods The controversy between the IOP-lowering effect of trabeculectomy versus of DS will remain as long as variable definitions of success, different follow-up times, and variable study designs render comparisons between studies very difficult.

Results Although the DS is not the first choice therapy in the angle closure glaucoma, it has a significant advantage (1) in young patients where lower cataract formation occurs following DS, (2) in monocular patients, (3) in patients with high myopia, and (4) in patients with tubular visual fields. The facts that the anterior chamber is not perforating in the original DS and that postoperative intraocular inflammation is minimal make it a good alternative therapeutic choice for (5) uveitic glaucoma cases or (6) glaucoma secondary to iris melanoma. Considering goniopuncture as a failure criterion or as a two-stage penetrating surgery as needed in at least 50% of the cases, could be weighted to considering suture lysis and capsulotomy as failure criteria of glaucoma and cataract surgeries. Performing goniopuncture with caution might avoid the most adverse events like iris incarceration

Conclusion Deep sclerectomy or non penetrating glaucoma surgery continue to evolve in developing new ideas like canaloplasty that would offer better safety and efficacy than the gold standard, namely, trabeculectomy.

• 2354
Deep scelerectomy: contra

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Deep sclerectomy claims to be safer than trabeculectomy. This might have been true in the past but, with modern techniques, "safe trabeculectomy" can be performed with few complications.Deep sclerectomy claims to be a "non-perforating" procedure. It is probably more correct to name it a two-stage perforating procedure since post-operative Yag-laser goniopuncture is necessary in > 50% of the cases. Since an iridectomy is not performed during deep sclerectomy, iris incarceration can occur after goniopuncture and can be easily missed. Furthermore, it is puzzling that new modifications of deep sclerectomy include using an Express implant, converting it right away to a perforating procedure.Finally, a trabeculectomy usually provides lower post-operative IOPs than a deep sclerectomy. Since one of the reasons to operate is to obtain a low target IOP, it is advisable to perform a trabeculectomy.

• 2355

Trend versus event analysis in glaucoma progression

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Analysis of visual field series in order to detect and measure progression may be performed either by event analysis or trend analysis. Event analysis constructs a baseline and compares subsequent tests to the baseline. Trend analysis models the behaviour of the whole series, for example by linear regression.This talk will give examples of how each technique has been used in clinical research and will also present evidence from studies comparing the two.

• 2361

Kinetics of TP53, CASP3 and GADD45 genes expression in the rat lens after in vivo exposure to subthreshold dose of UV-B radiation

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Purpose Subthreshold dose exposures of UVR-B over long time accumulate in the lens to cause cataract. The purpose of this study was to investigate kinetics of p53, caspase 3 and gadd45 genes in the rat lens after in vivo exposure to subthreshold UVR-B around 300 nm.

Methods Forty 6-week-old female albino Sprague-Dawley rats were exposed to subthreshold dose (1 kJ/m2) UVR at 300 nm unilaterally for 15 minutes. The animals were sacrificed at 1, 5, 24 and 120 h following the exposure to UVR-B. p53, caspase 3 and gadd45 mRNA expression of the lenses was analysed by quantitative RT-PCR.

Results p53 is upregulated in 24 h and 120 h groups. Caspase 3 is upregulated in 120 h group. Gadd45 is upregulated in 1 h group.

Conclusion p53 mRNA increased expression precedes caspase 3 mRNA increased expression in the rat lens after in vivo UVR-B exposure. There was initial repair at 1 h showed by increased mRNA expression of DNA repair gene GADD45.

• 2362

Ocular temperature rise and light scattering development in the lens correlating with exposure time after in vivo exposure to 1090 nm infrared radiation

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Purpose To investigate the relationship between light scattering development in the lens and ocular temperature rise after in vivo exposure to high intensity 1090 nm radiation with exposure time up to 60 minutes.

Methods 80 six-weeks-old albino SD rats were anesthetized and the pupils were bilaterally dilated prior to exposure. The animals were randomly divided into four groups of 20 each. All animals were unilaterally exposed to 3.0 W coherent infrared radiation at 1090 nm with a spot size of 2 mm within the pupil for 10, 18, 33, 60 minutes respectively. During exposure, temperature was recorded at the limbus of exposed eye.7 days after the exposure and both lenses were extracted for light scattering measurements and macroscopic photographing.

Results The maximum temperature increase for exposure time of 10, 18, 33, 60 minutes was 7.0, 6.8, 7.6, 7.4 °C at the limbus of exposed eye. 7 days after the exposure, in all the groups there was no statistical difference of light scattering in the lenses between exposed and non-exposed contralateral eyes and no significant lens opacities from the exposed eyes were observed.

Conclusion An irradiance of 96 W/cm2 of 1090 nm projected on the cornea in vivo induces a constant temperature increase of about 7 °Cin the anterior segment of the eye. At a temperature increase of 7°C in the anterior segment, no light scattering development and opacity formation in the lens occurs one week after exposure, indicating that there is no direct either photochemical or thermal effect in the lens under the conditions of the irradiance less than 96 W/cm2 on the cornea and temperature rise below 7°C in the anterior segment for at least 1 hour.

• 2363

Comparison between 2 recent optical biometry devices

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Purpose To compare the refractive precision and the ease of use of 2 recent optical biometry devices.

Methods Fifty patients (50 eyes with grade II and over cataracts according to the Oxford classification) underwent optical biometry measurements with 2 optical biometers, the IOLMaster 500 (partial coherence interferometry [PCI] device) and the Lenstar LS 900 (optical low-coherence reflectometry [OLCR] device. Keratometry was also measured in each patient with the NIDEK ARK 900 keratometer. IOL power calculation was performed using the SRK-T formula. The duration of the actual measurement process was also recorded.

Results IOL power calculation could not be achieved in 2 patients with the PCI biometer (1 post traumatic cataract, 1 dense subcapsular cataract) versus 5 patients with the OLCR device (1 post traumatic cataract, 1 dense subcapsular cataract and 3 loss of fixation).There was an excellent correlation between the keratometric measurements obtained with both biometers and the ones obtained with the NIDEK ARK 900 keratometer.Measurements with the new OLCR device took significantly longer than with the PCI biometer.

Conclusion The accuracy of the IOL Master 500 and Lenstar 900 make them the 2 new gold standards of optical biometry. Both of them are easy to use and due to their non contact technology they prevent the potential transmission of non conventional infectious agents (theoretically possible with contact biometers).

• 2364

Characteristics of the anterior eye segment in patients affected by ehlers-danlos-syndrome

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Purpose Ehlers-Danlos Syndrome (EDS) characterizes an inherited connective tissue disorder caused by a molecular defect in the synthesis of collagen. The refractive, biometrical and densitometrical characteristics of the anterior eye segment in patients affected by various forms of EDS were analysed.

Methods 46 EDS patients in an age-range of 6 to 62 years (mean age 33 years) affected by various types of EDS, as diagnosed by genetic screening or skin biopsies, were recruited on a voluntary basis for this study. They were subjected to a complete orthoptical and clinical examination including documentation of the anterior eye segment with the EAS 1000 (Eye Analysis System, Nidek, Gamagory, Japan). Apart from clinical parameters like visual acuity, ocular motility and intraocular pressure, biometric measurements have been performed for corneal thickness and curvature, anterior chamber geometry, lens biometry and densitometric analysis of corneal and lens light scattering.

Results The EDS patient population comprised 37% classical type, 28% hypermobile type and 13 % vascular type. Among the clinical parameters, prevalence of myopia combined with astigmatism was 33% that of hyperopia combined with astigmatism 28%. Strabismus was found in 11% and about 59% of the EDS patients complained about dry eyes problems. Densitometric aanalyses of the lens revealed a normal age-related scattering profile in all patients. Similarly the biometric data for lens thickness and anterior chamber depth were within the normal range. Patients with the classical type EDS showed thinner corneas compared to the vascular or hypermobility type of EDS.

Conclusion Most of the clinical features described in association with EDS like thin and translucent sclera, keratoconus, lens luxation, retinal detachment or angoid streaks have not been observed in this study. Thinner cornea and perhaps more frequent anterior vitreal detachment were the only consistent pathological findings associated with the classical type of EDS which could be demonstrated in this study.

• 2365
Semi-automatic 3D reconstruction of the anterior segment from high frequency ultrasound scans

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Purpose We propose a new method to perform the semi-automatic 3D segmentation and reconstruction of the anterior segment (AS) using high frequency ultrasound (HFUS) scans. The main application aimed at by this development is the phakic IOL sizing based on the 3D morphological quantification of the AS:ATA, STS

Methods High frequency ultrasound (HFUS) data were acquired by a linear 50 MHz probe (Aviso from QUANTEL MEDICAL), using freehand scanning. An active localization system was used to spatially register each scan in a common 3D coordinates system. The steps of the AS segmentation were defined as follows: 1-3D reference models were previously created using manual US image datasets segmentation. 2-The 3D models were globally registered to the acquired data using the iterative closest point transform. 3-A final manual control / correction ensures the accuracy of the overall procedure. Tests were performed on 12 volumes (containing from 30 to 45 slices) acquired in the same conditions, during the preoperative check up.

Results Our method is much less time consuming than manual segmentation: it took 21 ± 7 min only. The morphological values of the ATA and STS 3D reconstruction were extracted for all the meridians. The ATA had an average minimum and maximum radius of 5.22 ± 0.35 and 6.85 ± 0.5 mm respectively, and an average area of 105.77 ± 6 mm2. For the STS, an average minimum and maximum radius of 4.98 ± 0.32 and 6.81 ± 0.42 mm was determined, and its average area was 103.43 ± 5 mm2.

Conclusion The proposed method offered an accurate and fast 3D segmentation of the ocular anterior segment organs. Future work will aim at reducing the required time and human intervention for each patient datasets processing for better automation.

Commercial interest

• 2366
Age-specific changes of the crystalline lens physical characteristics

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Purpose To study changes of a crystalline lens's physical properties with the years

Methods Patients at the age from 57 to 90. 73 crystalline lens's nuclei with a cataract of the various maturities, received by a method of the extracapsular extraction were investigated. Before operation we determined relative acoustic density of a crystalline lens by an original technique, also we estimated color of a crystalline lens and weight of a lens' nucleus.

Results We revealed that brown color of a crystalline lens's nucleus a little intensify with the years - the correlation factor is equal 0.4 ($p < 0.05$). Average value of relative acoustic density was 0.59 ± 0.01. Average weight of a lens' nuclei was 98.3 ± 1.0 mg. The average density of a lens' nuclei was 1312 ± 12 mg m2. It's revealed that the mature cataract isn't always rigid: the correlation factor is equal -0.4 ($p < 0.05$). If density of a crystalline lens increases, a mechanical hardness increases too– the correlation factor is equal 0.4 ($p < 0.05$). At the same time, a mechanical hardness of a crystalline lens's nucleus reinforces with the years, factor of correlation is 0.74 ($p < 0.05$). It's revealed that the age isn't a determining factor in appearance and cataract progressing.

Conclusion Mechanical properties of a crystalline lens depend on change of its chemical compound, at ageing there is a increasing of brown coloring of a crystalline lens and mechanical hardness of a crystalline lens's nucleus, visual acuity thus can change slightly. Processes of maturing of a cataract and increase in hardness of a crystalline lens are chemically different and go not in parallel each other.

• 2367 / 252
On the impact of multifocal IOL decentration and tilt on retinal image quality

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Purpose The design of advanced (such as multifocal) intraocular lenses (IOLs) is based on the exact alignment of the optical element with the center of the pupil and its optical axis with the line of sight of the eye. It is the purpose of this study to evaluate the impact of multifocal IOL decentration and tilt on retinal image quality.

Methods A series of patients implanted with multifocal IOLs were evaluated with a Scheimpflug imaging device (GALILEI Dual Scheimpflug Analyzer, Ziemer Switzerland), that was utilised to evaluate centration and tilt of the IOLs. Wavefront aberration was recorded using a retinal ray tracing device (iTrace, Tracey Technologies Houston, USA). Induced high order aberrations were correlated to the orientation of tilt and the location of the IOL.

Results In multifocal IOLs, decentration in recpect to the pupil center is more detrimental to retinal image quality than tilt. Moreover, multifocal IOLs are more sensitive to tilt and decentration than monofocal IOLs in respect to the induced aberrations.

Conclusion Modern imaging technologies in combination with wavefront abberation measurements may elucidate the impact of IOL location in the eye in retinal image quality. In certain cases, such as in diffractive lenses, where wavefront sensing has inherent limitations, retinal image quality may be evaluated by appropriate computer modeling.

• 2371

Creating endothelial lenticules with femtosecond laser: the double layer technique

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Purpose Femtosecond laser(FS) enhances reproducibility and accuracy in corneal surgery. However, visual outcomes of Femtosecond Lamellar Endothelial Keratoplasty (FLEK) are still impaired by lenticule irregularities. We aimed to enhance the smoothness of interface of FLEK lenticules.

Methods We proceeded for corneal cuts on experimental human corneas with the 60 and 150 kHz Intralase FS (AMO, USA). Laser settings were optimized to obtain the best interface quality while delivering minimal energy to the corneal stroma. We did each procedure in triplicate with the appropiate settings to test reproducibility. We created posterior lenticules for FLEK with the following FS various cut profiles: a single path profile (SP) performing a 500µm deep full lamellar cut, a double path profile (DP) with an identical lamellar cut performed twice, a double layer profile (DL) performing two successive lamellar cuts at 350µm and then at 150 µm depth. We created 100 µm LASIK free flaps as a control. The stromal interface quality of the so-obtained interfaces was analyzed by scanning electron microscope (SEM).

Results Stromal adherences persisted after both the SP and the DP procedure, creating central irregularities on the endothelial lenticule. The DL profile created the smoothest interfaces with the best reproducibility when FS parameters for lamellar cut were set for diameter (mm), depth (µm), energy (µJ), and spot size/step (µm) respectively on 9.0mm, 350µm, 2.1µJ, 4:4µm and 8.3mm, 150µm, 0.9µJ, 4:4µm. Observed with SEM, EK lenticules created with the DL profile and LASIK flap had similarly smooth interfaces.

Conclusion Femtosecond lasers can creat EK lenticules with a quality of stromal interface comparable to refractive surgery.

• 2372

Riboflavin's time dependent degradation rate induced by ultra violet – an irradiation at 370 nm wavelength

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Purpose To evaluate the time dependent degradation rate of riboflavin standard solution used for corneal cross linking (CXL) treatment, after ultra violet – A irradiation at 370 nm wavelength

Methods Riboflavin solution (> 0.1%) was diluted in nanopurewater to a final concentration of 10 ppm. Two solutions were used, one served as control, while the second was irradiated using an optical system with a light source consisting of an array of UV diodes (370 nm). Four samples of riboflavin solution were retrieved prior to irradiance (time point: 0), at 1, 5, 15, 30 and 60 minutes after irradiation (Group A); while, at the same time points samples of riboflavin were retrieved from the control solution in order to assess environmental time - induced degradation of riboflavin (Group B). All samples were immediately analyzed using liquid chromatograph mass spectrometry to detect riboflavin and its two sub products (lumiflavin and lumichrome)

Results The mean percentage of riboflavin degradation was 2.38, 11.08, 15.30, 20.75 and 34.78 at 1, 5, 15, 30 and 60 minutes after UV-A irradiation for Group A ($p<0.05$), while for group B (no UV-A exposure) there was no change in riboflavin concentration

Conclusion The time dependent degradation of standard riboflavin solution is significant, reaching after 30 minutes of UV-A exposure 20%. It seems that only a small fraction of the overall riboflavin molecules break down since, more than 65% remain intact even after one hour of UV-A irradiation

• 2373

Corneal biomechanical characterization from in vitro eye inflation, optical coherence tomography and finite element modeling

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Purpose Absolute changes in corneal surface area, volume, apex displacement and limbus deformation during in-vitro inflation were used to determine biomechanical properties of the corneal tissue

Methods Whole-globe and corneal button inflation experiments were performed on porcine eyes placed in a temperature and humidity controlled chamber. IOP was increased and decreased (15-55-15 mmHg) at 5mmHg steps, each time acquiring a3-D imaging with a customized spectral anterior segment OCT imaging system. Raw images were corrected from optical and fan distortion. Limbus and apex were detected and the corneal volume and surface area were calculated. The experimental data served as input to optimize a 2D-axis-symmetric, viscoelastic finite-element-model (with cornea-limbus-sclera geometry) written in ANSYS to retrieve elastic (Young's modulus) and viscoelastic (Prony and retardation timeconstants) corneal biomechanical properties.

Results The experimental corneal response upon inflation was well predicted by the FEM simulations. The central cornea deformed more (the apex raised by 60.8 µm at maximum IOP) than the limbal region (factor 3/4 in radial expansion). The limbus expansion caused a flattening of the angle between cornea and sclera. Mean corneal surface was 226 mm2 and changed less than1% Poisson's ratio was found to be 0.49 and Young's modulus 1.24 MPa

Conclusion Measuring and understanding corneal biomechanical parameters is important to predict the outcome of different surgical treatments and could be useful to early detection of several corneal pathologies. Quantitative high resolution OCT imaging in combination with FEM simulation allows to accuratelydetermine meaningful mechanical parameters.

• 2374

Proteases and proteolysis in the tears of people with keratoconus

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Purpose Keratoconus is a degenerating disease of the eye which causes an irregularly shaped cornea leading to impairment of vision.The role of proteases in keratoconus has been a topic of substantial discussion and speculation over many years.This study was designed to examine the levels and activity of proteases in the tear film of people with keratoconus.

Methods A case-controlled study was performed studying the tear proteome of keratoconus patients(K) and controls(N).Basal tears were collected using a capillary tube.Total protein(TP)in tears was estimated using BCA assay;the levels of lactoferrin(Lf),secretory immunoglobin A(sIgA) and serum albumin were measured using specific ELISAs.Levels and activity of tear proteases were studied using Raybiotech® Antibody Array and EnzChek® Assay Kits respectively.

Results There was a two-fold (p=0.0001) decrease in TP levels between K(3.86+1.62 mg/ml) and N(7.00+1.58 mg/ml). Levels of Lf(0.67+0.28 vs. 1.13+0.29 mg/ml) and sIgA(0.78+0.36 vs. 1.70+0.66 mg/ml) were also significantly(p=0.0001) reduced in K.The expression levels of matrix metalloproteinases(MMP)-1,-2,-3,-7,-13,interleukins(IL)-1α,-3,-4,-5,-6,-8,-10 and tumour necrosis factor(TNF)-α,-β were significantly(p=0.01) altered between K and N.Tear proteolysis(gelatinase/collagenase)was expressed as Fluorescence Intensity(FI).The activity of gelatinases(87.54+33.57 vs. 45.79+24.60 FI,p=0.0002)and collagenases(6.11+3.18 vs. 3.56+2.03 FI,p=0.03)were significantly increased in K.

Conclusion The tears of people with keratoconus expressed high levels of proteases, increased proteolysis and a profoundly altered protein profile, which might change with the severity of the disease.These findings may lead the way to understanding or monitoring disease progression.

• 2375
Theoretical basis for estimating the elastic characteristics of individual living human eyes

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Purpose To develop a method for estimating the effective elastic parameters of an individual eye from the data obtainable in various clinical tests with a static load applied.

Methods Our mathematical model that represents the fibrous coat as a system consisting of a soft elastic shell (cornea) and an elastic element characterized by a single elastic constant (sclera and tissues surrounding it) is used for calculating the mechanical behavior of the eyeball during different loading procedures. The calculations were performed for two types of external mechanical loading corresponding to applanation and impression tonometry, as well as for inflating the eye by liquid. The presence in the model of only two important mechanical constants makes it possible to identify them by comparing the data of different tests and then to find the effective elastic characteristics important in diagnostics.

Results A technique of determining the elastic constants of the model from the standard diagnostic tests is developed. This technique is applied to estimating the average elastic characteristics of the human eyeball in vivo basing on the data available from the literature.

Conclusion Our results form a basis for obtaining in standard clinical tests representative individual mechanical characteristics of the living eye. This makes it possible to calculate effective (integral) elastic parameters needed in processing a specific test from the data obtained from other tests, for example, to estimate the volume rigidity from elastometry data. We can now correctly interpret the term "rigidity": in different tests it is commonly used for characteristics that may differ substantially.

• 2376
A biocornea of fish scales – first results of a research model

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Purpose To develop an animal model suitable to evaluate the biocompatibility of a fish-scale derived biocornea. This biocornea has been developed as an alternative for the use of human tissue to replace damaged corneas. Prior to its use in humans, it is essential to determine the behavior and biocompatibility of the biocornea with the natural cornea.

Methods A ±250 µm thick, decellularized and decalcified fish scale-derived collagen matrix was implanted into the corneas of three groups of Fischer 344 male albino rats of 14 weeks old. Rats were anesthetized with isufluorane, oxybuprocaine and marcaine and received corticosteroids postoperatively. The first group (n=6) received an Anterior Lamellar Keratoplasty (ALK). The second group (n=6) had the matrix implanted into an intralamellar corneal pocket and the third group (n=6) subconjunctivally. Discomfort, attachment of the implant, transparency of cornea and implant, epithelial damage and inflammation parameters were observed during 21 days.

Results In rats receiving an intralamellar pocket implantation different degrees of opacity were observed. The anterior lamel started to disappear after day 7. Implants in the ALK group remained transparent despite neovascularization in all cases, but no reepithelialization was observed. Rats with a subconjunctival implant showed local swelling, redness and induration which decreased in time.

Conclusion The artificial cornea is accepted quite well early on, but may lead to corneal melting. The curvature of the implant need be adjusted to better mimic the rats' curvature. Future research is warranted to optimize the Biocornea.

Commercial interest

• 2377 / 404
Mechanical reinforcement of the cornea with an intrastromal in-situ photo-polymerised implant

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Purpose A photo-polymerisable hydrophilic material (PEG/Irg) has been previously evaluated in terms of biocompatibility and toxicity in a series of laboratory animals. It was the purpose of this study to evaluate the bio-mechanical effect of lamellar implants created from PEG/Irg in porcine cadaver eyes.

Methods Twenty porcine corneas where removed along with a 3 mm corneoscleral rim, de-epithelialised and mounted on an artificial anterior chamber. The pressure was maintained at 22 mmHg hydrostatically. In each cornea, a circular lamellar pocket (7mm diameter) was created manually. Thirty microliters of PEG/Irg in liquid form were injected in each pocket. A rigid contact lens was pressed on top of the cornea and the excessive quantity of PEG/Irg was leaked out of the pocket. The cornea was then irradiated with UV light (390nm, 4mW/cm2) and the PEG/Irg underwent a polymerization and the associated phase transition to form a rigid film. Mechanical measurements were performed by means of a purposely-developed device featuring a stepping motor and a load cell. By keeping the pressure constant the role of corneal stiffness is isolated. The force as a function of indentation was recorded for each specimen before and after the in-situ creation of the PEG/Irg film.

Results The mean slope of force versus indentation for the reinforced group was 166.72 (±74.14) and the mean slope for the non-reinforced group was 116.94 (±21.16). The two-tailed P value equals 0.0033, equally meaning that the difference between those two groups was statistically different.

Conclusion According to the results, there was a significant biomechanical reinforcement of the cornea following the in-situ creation of the polymer film.

• 2411

Oxygen and VEGF in venous occlusion

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ABSTRACT NOT PROVIDED

• 2412

Mechanisms involved in vein occlusion related macular edema

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Purpose To describe the pathophysiological processes involved in vein occlusion related macular edema.

Methods Review of the experimental and clinical published data explaining the pathophysiological mechanisms involved in vein occlusion related macular edema.

Results Venous stasis lead to internal blood-retinal barrier breakdown, extravasation of blood vessel content and finally to macular edema. Tissular hypoxia of the internal retinal layers develops secondary to arterial blood flow decrease, followed by Na+/K+ ATPase pump dysfunction, intracellular edema, and neuronal cell death by necrosis and apoptosis. Many vasopermeability factors will be subsequently released, as inflammatory mediators and VEGF. The rationale for clinical treatment of macular edema is based on the understanding and the inhibition of these pathophysiological mechanisms. On the medical side, nonsteroidal anti-inflammatory drugs inhibit the production of prostaglandins and leukotrienes, and modulate fluid movement coupled to chloride movement. Corticosteroids block cyclooxygenase and interleukin, downregulate VEGF and decrease the phosphorylation of occludin, thereby increasing the tightness of the blood-retinal barrier. Anti-VEGF agents restore occludin proteins in the blood-retinal barrier and reduce protein kinase C activation.

Conclusion New advances in understanding the mechanisms involved vein occlusion related macular edema lead to development of new therapeutical strategies which have to be confirmed by clinical randomized trials.

• 2413

Clinical presentations in venous occlusion

JONAS JB
University of Mannheim

Clinical findings in eyes with retinal veouns occlusions, including those observations obtained by ophthalmodynamometry, will be presented and discussed.

Commercial interest

• 2414

Treatment of macular edema in vein occlusion

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Purpose Recent multicenter trials provided us with interesting results of macular edema linked to vein occlusion. Until now, the standard of care treatment of macular edema due to branch vein occlusion remained grid laser in contrast with central vein occlusion where the absence of treatment was still recommended. ,

Methods SCORE, GENEVA, BRAVO and CRUISE studies recently provided us with the following results: SCORE study found triamcinolone to be interesting to treat macular edema due to central vein occlusion but not from branch occlusion. GENEVA study assessed the effect of a delivery system of dexamethasone to treat macular edema due to venous occlusion whatever the clinical form with an improvement of visual acuity. CRUISE and BRAVO studies assessed the effect of ranubizumab which was found to improve the visual acuity of macular edema due to either central or branch vein occlusions. GALLILEO and COPERNICUS reported recent results with another antiangiogenic agents with interesting results but still unpublished.

Results At this stage, to treat macula edema in vein occlusion, we have to consider the characteristics of the patients to decide which treatment should be used: lens status, increased ocular pressure, delay before treatment of the disease, clinical form of vein occlusion as well as the predictable acceptance of repeated injections by the patients.

Conclusion There is an urgent need for comparative studies but these studies should consider separately branch and central vein occlusions.

Commercial interest

• 2421
Genetics and diagnostics of retinitis pigmentosa

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Purpose To utilize next generation sequencing (NGS) and identity-by-descent mapping to identify mutations in known and new genes in patients with autosomal recessive (ar) or isolated (i) retinitis pigmentosa (RP).

Methods We employed Roche 454-NGS to screen the exons of 111 inherited retinal disease (IRD) genes in 12 IRD patients with known compound heterozygous variants and 100 unsolved ar/i RP patients. We used identity-by-descent mapping and SOLiD-NGS to identify novel genes for arRP. We carried out segration analysis in the relevant families using Sanger sequencing.

Results The NGS approach enabled us to robustly identify 21/24 known IRD-associated variants. Taking into consideration that a proportion of the RP patients was previously screened for mutations in selected genes, we could solve 55 ar/i RP cases. Mutations were identified in arRP genes (n=45), X-linked RP genes (n=4), and autosomal dominant RP genes (n=6). In at least 4 families de novo mutations were found.Targeted NGS of exons in selected chromosomal regions based on homozygosity mapping enabled us to identify at least one novel arRP gene. The interpretation of sequence variants derived from whole genome exon (exome) sequencing heavily depends on positional information (linkage analysis, homozygosity mapping).

Conclusion NGS can be used for comprehensive mutation scanning of known IRD genes and for the identification of novel IRD genes. The known RP genes contain 55% of the causative mutations. In a significant proportion of isolated patients, we identified X-linked and de novo autosomal dominant mutations, which has important repercussions for genetic counselling.

• 2422
The bestrophinopathies

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Purpose To describe the phenotypes of conditions due to mutations in BEST1, the gene encoding bestrophin-1.

Methods A case presentation format will be used to illustrate the phenotypes and genotypes of the different bestrophinopathies, with special attention to both the clinical and electrophysiological features that distinguish one phenotype from the other, and those they have in common. In addition, the different BEST1 genotypes will be discussed.

Results The phenotypes of Best vitelliform macular dystrophy (BVMD), autosomal dominant vitreoretinochoroidopathy (ADVIRC), and autosomal recessive bestrophinopathy (ARB) are very different as far as their clinical phenotypes are concerned. Nevertheless at the electrophysiological level, they share an abnormal electro-oculography (EOG) as a common feature. Electroretinography is normal in BVMD, whereas a rod-cone dystrophy is evident in the later stages of disease of ADVIRC and ARB. The BEST1 genotypes differ in that BVMD is due to a heterozygous missense mutation in BEST1, ADVIRC is due to interaction of several bestrophin protein isoforms, and ARB is probably the null phenotype.

Conclusion The phenotypes of the bestrophinopathies are diverse, although they share an abnormal EOG as the common feature. The specific genotypes are also different, leading to different molecular pathogenetic mechanisms.

• 2423
Genetics of Leber's congenital amaurosis

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Purpose To give an overview of our current knowledge of the genetic causes of Leber congenital amaurosis (LCA).

Methods Current literature on the genetic causes of LCA and the function of the defective gene products will be reviewed. In addition therapeutic options for the various genetic subtypes will be discussed.

Results Linkage analysis, homozygosity mapping and candidate gene analysis facilitated the identification of 15 genes mutated in patients with LCA, which together explain approximately 70% of the cases. Several of these genes have also been implicated in other non-syndromic or syndromic retinal diseases, such as retinitis pigmentosa and Joubert syndrome, respectively. CEP290, GUCY2D and CRB1 are the most frequently mutated LCA genes; one intronic CEP290 mutation (p.Cys998X) is found in 20% of LCA patients from north-western Europe, although this frequency is lower in other populations. The LCA genes encode proteins with a wide variety of retinal functions, such as photoreceptor morphogenesis, phototransduction, vitamin A cycling and intra-photoreceptor ciliary transport processes. Rodent, avian and canine models for LCA have been successfully corrected employing adeno-associated virus or lentivirus-based gene therapy. Moreover, phase 1 clinical trials have been carried out in humans with RPE65 deficiencies. In addition, a phase 1 clinical trial with a retinoid compound has been initiated in LCA patients with RPE65 and LRAT mutations.

Conclusion Future LCA 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 for different genetic subtypes of LCA.

• 2424
Gene therapy & pharmacotherapy for inherited retinal disease: current status

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(2) Genetics and therapy of retinal and optic nerve blindness, INSERM U1051, Institute for Neurosciences of Montpellier, Montpellier

Purpose To describe the rationale for gene therapy and pharmacological treatments in retinal dystrophies, and to show a few examples of the undergoing trials.

Methods Gene therapy can be applied to complement (in loss-of-function mutation) or to suppress (in gain-of-function mutation) a mutated gene, in order to correct the specific defect linked to this gene. Gene therapy can also be used to in situ produce a protein whose properties will modify the course of the disease. In a similar way, pharmacological drugs can supplement the metabolic defect linked to a specific gene, or can facilitate photoreceptor survival and/or function whatever the genetic defect.

Results Conditions (photoreceptor dysfunction and degeneration, rate of degeneration, stage at disease diagnosis) to which gene therapy can be applied will be reviewed. Retinal dystrophies linked to RPE65 mutations provide good examples of both gene therapy by complementation and pharmacological therapy by supplementation. Gene repair is a promising approach to reverse mutations into the correct sequence. Rapid descriptions of ongoing trials for congenital achromatopsia, Stargardt disease and retinitis pigmentosa will be showed.

Conclusion Future developments of therapeutic interventions will depend on accurate molecular diagnosis, knowledge of pathophysiological mechanisms and improvement in drug ocular delivery.

• 2431

The eye-associated lymphoid tissue (EALT) - a basis of the anatomy and immunology at the ocular surface

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Purpose Immune protection at the ocular surface is, similar to other mucosal surfaces, governed by mechanisms of the common mucosal immune system. At the ocular surface a local branch of the mucosal immune system, the Eye-Associated Lymphoid Tissue (EALT), maintains the equilibrium between tolerance and immunity and prevents inflammatory diseases.

Methods Own results on the mucosal immune system of the human ocular surface are discussed together with results from the literature.

Results The Eye-associated lymphoid tissue (EALT) is continuous from the ocular surface proper (cornea and conjunctiva) into the mucosal adnexa of the eye (lacrimal gland and lacrimal drainage system). In addition to innate immune factors, this system also contains lymphoid cells and accessory cells that have the task to favour immune tolerance and the secretion of anti-inflammatory IgA antibodies. In inflammatory diseases, however, (as e.g. the dry eye syndrome, ocular allergy or autoimmune disease etc.) and also in certain types of infectious diseases, the mucosal tolerance is overridden and then own tissue constituents or non-pathological antigens become antigenic. In such cases of deregulation, the mucosal immune system may become a promoter of an immune modulated, frequently T-cell mediated, inflammatory disease process.

Conclusion The Eye-Associated Lymphoid Tissue (EALT) formed by physiologic protective lymphocyte populations, accessory cells and protector mechanisms regulates the immunological homeostasis at the ocular surface but may become a player in inflammatory disease when the system is deregulated. Support DFG KN 317-11

• 2432

Overview of the spectrum and therapy of inflammatory ocular surface disease

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ABSTRACT NOT PROVIDED

• 2433

The immunology of allergic ocular surface disease

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Purpose The conjunctiva is normally exposed to picogram quantities of environmental allergens such as pollens, dust mite fecal particles, animal dander and other proteins. When deposited on the mucosa, these antigens are processed by Langerhans cells or other antigen-presenting cells (APC) in the mucosal epithelium, bind to the antigen recognition site of major histocompatibility complex (MHC) class II molecules, and present to naive CD4+ lymphocytes at some unknown location that could be the local draining lymph nodes.

Methods The concentration and distribution of inflammatory mediators or inhibitors in the tear fluid have been extensively used in ocular allergy to find either a 'disease marker', to better understand the immune mechanisms involved in the ocular surface inflammation, or to identify potential targets for therapeutic interventions.

Results Multiple mediators, cytokines, chemokines, receptors, proteases, growth factors, intracellular signals, regulatory and inhibitory pathways, and other unknown factors and pathways are differently expressed, ultimately resulting in the many clinical manifestations of ocular allergic disease.

Conclusion A better understanding of the mechanisms involved in ocular surface immunity is necessary for identifying new classification criteria and new therapeutic strategies.

• 2434

Inflammatory events in trachoma

HUGUET P
Clinical, Clermont Ferrand

Purpose "Trachoma is not a disease of poverty, it is an immune disease – it is like chronic poison ivy" said H Taylor in 2005.Studies done on this topic suggest that inflammation rather than infection is responsible for blindness.This presentation will highlight the ocular surface inflammation induced by Chlamydia in infection and the effectiveness of azithromycin in reducing this inflammation.

Methods Review of the literature on the topic.Medline research with ocular AND inflammation AND azithromycin key words.

Results Trachoma infection usually evolves in two major phases: active or inflammatory trachoma and cicatricial or late trachoma. Active trachoma is characterized by an inflammatory response associated with the variable presence of demonstrable infection (PCR test).Trachoma is considered as a chronic, delayed-type hypersensitivity reaction with subsequent fibrosis.Topical or systemic administration of azithromycin reduces the effects of acute inflammation such as mucus secretion and macrophage infiltration. Azithromycin inhibits inflammatory cytokines gene and protein expressions such as IL-6, MMP-2 activity and NF B.In chronic or cicatricial trachoma a new concept is emmerging: a neglected ocular surface disease.

Conclusion The role of induced chronic inflammation in trachoma is more and more important to be taken in count.These results suggest that azithromycin is not only effective on Chlamydia trachomatis infection but also appears as a promising agent for preventing and treating ocular trachoma surface inflammation in this immuno-inflammatory disease.

Commercial interest

• 2435

Differential control and selective downregulation of cytokines but not chemokines in the normal and pathological tear fluid

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Purpose Overnight eye closure results in a near cessation in tear turnover and the induction of a sub-clinical inflammation as evidenced by PMN cell recruitment and degranulation and the accumulation of pro-inflammatory cytokines and chemokines. What prevents cytokine induced damage to the cornea was investigated.

Methods Open (O) and Closed (C) tears from Ns were subjected to multiple micro well array assays to obtain quantitative data on the distribution of >80 low abundance proteins. Samples were also separated by molecular sieve HPLC and the eluent profiled for the presences of chemokines, cytokines and interactive proteins. Cytokine-protein complexes were identified using a laboratory-developed multiplex assays.

Results Micro-well array assay reveal a marked increase in the concentrations of a wide range of inflammatory and immune modulating cytokines as well as chemokines in the closed eye tears. This was accompanied by increased levels of s-receptors at concentrations greatly exceeding that of the targeted proteins along with the accumulation of α2-M. Protein-protein binding studies and analysis of the HPLC eluent reveals that most inflammatory, angiogenic and immune cytokines eluent in the form of macromolecular complexes bound to s-receptor and α2-M. This serves to inactivate these entities and tags them for up take by macrophages and other cells that express the α2-M receptor. In contrast chemokines which lack s-receptors remain free and bioactive.

Conclusion s-receptors and α2-M co-operatively function in the down–regulation of cytokine and growth factor induced inflammation. Data will also be presented showing its functional role in the control of inflammation elsewhere.

• 2441

Why electrophysiology in children?

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(2) Institute of Ophthalmology, University College London, London

After a description of the appropriate techniques, the presentation will use a case based approach to describe the value of electrophysiological assessment in the diagnosis and management of paediatric patients.

• 2442

Pros of treatment of NA-ION

LEE A
Ophthalmology, Houston

Purpose To define the indications for steroids in NAION

Methods Case based learning, evidence based practice

Results Steroids have been shown to be possibly beneficial in NAION in a patient choice methodology studySteroids have an unproven but biologically plausible mechanism of action in NAION

Conclusion Until a randomized, prospective clinical trial is performed, steroids may be considered as a potential treatment option for NAION in selected cases

• 2443

Cons of treatment of NA-ION

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(2) Medical Faculty, University of Warmia and Mazury in Olsztyn, Olsztyn

Purpose To discuss benefits and risks of steroids use in NAION.

Methods Analysis of evidence based studies.

Results There are no first class evidence based studies confirming that the use of steroids in NAION is of benefit. There are few case series and case reports suggesting the benefit of oral or intravitreal steroids use. These studies, however, have several limitations. Moreover, steroids have many adverse effects, what is especially important in elderly patients with co-existing diseases, the typical profile of NAION patients.

Conclusion There is no effective therapy for NAION supported by first class evidence based study.The use of steroids should be critically analyzed in the context of their possible adverse effects.

• 2444

Pros of steroids use in optic neuritis

LEE A
Ophthalmology, Houston

Purpose To define indications for steroids in optic neuritis

Methods Case based learningEvidence based practice

Results Steroids have a biologically plausible mechanism for improving the speed of visual recovery and for the treatment of possible multiple sclerosis in patients with optic neuritis

Conclusion Intravenous steroids should be considered in the treatment of suspected demyelinating optic neuritis

• 2445

Cons of steroids use in optic neuritis

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(2) Medical Faculty, University of Warmia and Mazury in Olsztyn, Olsztyn

Purpose To discuss benefits and risks of steroids use in optic neuritis.

Methods Analysis of evidence based studies

Results Steroids do not influence the final visual acuity in patients with optic neuritis. Their possible adverse effects will be discussed in detail.

Conclusion Intravenous steroids might be considered in the treatment of optic neuritis after detailed examination of patient's general health status and when possible benefits overcome the risks of adverse effects.

• 2446

Why pulley surgery in strabismus?

BREMOND-GIGNAC D
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Methods The recent innovations in the comprehension of orbital anatomy and extraocular muscles allow a better reflection about practical strabismus surgery. Trochlea anatomy for superior oblique muscle is well defined but Miller in 1987 in monkeys and Demer in 1994 first described functional pulleys for rectus extraocular muscles. These pulleys are based on connective tissue sleeves of collagen, elastin and smooth muscle that surround and stabilize the posterior extraocular muscles paths within the bony orbit. Imaging of the orbit is required to the understanding of variable effect on binocular alignment in strabismus. Different data can be obtained from the MRI as lateral rectus path lengths from orbital apex to first globe conta

• 2451
Your first best glaucoma friend, the slit-lamp

BRON AM
Dijon

New technologies have provided the ophthalmologists with fascinating techniques to evaluating structure and function in glaucoma. Within a couple of minutes we can now obtain very sophisticated mappings, curves, indices, relations etc.The yield of these techniques in the screening, the diagnosis and the follow-up of ocular hypertensive and glaucoma patients is invaluable. However as doctors we 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. This course is designed for young ophthalmologists and we will give a check list to help them in the slit-lamp examination from the lids to the optic nerve head. This rapid and systematic approach will help them to improve their daily clinical practice in glaucoma.

• 2452
Your second best glaucoma friend, function testing

VISWANATHAN A
Institute of Ophthalmology, Epidemiology, London

Accurate and reliable assessment of the results of automated perimetry are of primary importance in the management of glaucoma, both for diagnosis and for the measurement of progression. This aspect of the Course, designed for young ophthalmologists, will give specific, practical guidance on how to derive the maximum amount of useful information from a single visual field test result or from a longitudinal series of results. A simple mnemonic will be described to ensure that no important elements of the analysis are missed.

• 2453
Your third best glaucoma friend, structure evaluation

SUNARIC MEGEVAND G
Switzerland

Glaucoma is characterized by structural changes of the optic nerve and the retinal nerve fibre layer (RNFL) and corresponding functional alterations. Although the glaucoma specialist still depends upon direct fundus examination to assess structural damage, the last ten years has seen the emergence of a variety of new technologies for objective and non-invasive measurement of structural changes. During the course will be discussed the most important parameters for direct fundoscopic analysis of the optic nerve head and RNFL as well as the principals of the 3 most used imaging devices HRT, GDX, OCT.

• 2461

Tips and tricks in grossing and processing ophthalmic specimens

COUPLAND SE
University of Liverpool, Dept. of Pathology, Liverpool

Purpose Ophthalmic specimens range in size and degree of complexity. The diagnostic work-up of ocular ophthalmic biopsies and larger specimens demands close collaboration between the clinician, the pathologist and other specialties, including the plastic surgeon, head-and-neck surgeon as well as the microbiologist.

Methods Documentation of all relevant clinical information in the pathology request form as well as timely discussions between the various specialists (for example, telephone communications just before a biopsy is performed) are essential components of the diagnostic pathway, prior to specimen arrival in the diagnostic laboratory.

Results The laboratory itself should be equipped with experienced technical staff familiar with the specimen protocols, a pathologist with expertise in ocular pathology/fluid samples, and also be supported with a wide range of investigations, including molecular diagnostic techniques.

Conclusion In this way, the yield from these samples can be optimized to reach an unequivocal diagnosis, rapid communication to the clinician, and timely instigation of therapy. Guidelines for these steps are provided.

• 2462

Overview of eyelid and conjunctival tumours

LOEFFLER K
University Klinikum, Bonn

ABSTRACT NOT PROVIDED

• 2463

Anterior-to-posterior "tour" of ocular disease processes

LOEFFLER K
University Klinikum, Bonn

ABSTRACT NOT PROVIDED

• 2464

Overview of orbital tumours

HEEGAARD S
Ojenpatologisk Institut, Copenhagen

ABSTRACT NOT PROVIDED

• 2465

Incorporation of cytogenetic and molecular techniques in ocular pathology

COUPLAND SE
University of Liverpool, Dept. of Pathology, Liverpool

Purpose The roles of molecular techniques in ocular pathology are four-fold: a) Understanding disease pathogenesis; b) diagnosis; c) prognosis; and d) predicting therapy response.

Methods Examples of recent developments in molecular pathology in understanding the pathogenesis of tumours include the sonic hedgehog pathway in BCC; polyomavirus MCPyV in Merkel cell carcinoma; microsatellite instability in sebaceous carcinoma; fusion oncogenes in adenoid cystic carcinoma and mucoepidermoid carcinoma; and A20 gene deletions in conjunctival MALT lymphoma. Molecular techniques, such as IgH-PCR and TCR-PCR, are required regularly for the confirmation of the diagnosis of ocular B- and T-cell lymphomas, respectively. In particular, IgH-PCR is required to provide supportive evidence for the diagnosis of vitreoretinal lymphoma, when evaluating a diagnostic vitrectomy or a subretinal aspirate/chorioretinal biopsy.

Results The main example in ocular oncology where molecular techniques are used for prognostication is uveal melanoma. The presence of monosomy 3 and polysomy 8 was initially detected using FISH. Techniques, which provide more detailed information, such as MLPA, aCGH, and GEP, have been introduced in various ocular oncology centres, with the molecular genetic data being incorporated with clinical and histomorphological features to provide individualized prognostic curves.

Conclusion Advances have been made in some other malignancies in predicting tumour response to therapy. For many ocular malignancies, such a "magic bullet" has not yet been found; however, the principles of predicting "responders" and "non-responders" and the potential targets will be discussed.

• 2466

Comparative ocular pathology

HEEGAARD S
Ojenpatologisk Institut, Copenhagen

ABSTRACT NOT PROVIDED

• 2471

The modern management of ocular surface burns

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Ocular surface burns can be due to the exposition to chemical agents, extreme temperatures or ultraviolet, infrared or ionising radiations. Alkali burns differ from acid burns by the fact that they deeply penetrate in the anterior segment and so are particularly severe.Initial clinical examination (with the help of classifications) tells us how to adapt the treatment and gives us the prognosis. The 4 Grades Ropper-Hall's classification has been replaced by the more precise 6 Grades Dua's one. Surgical treatment aiming to restoring a proper corneal epithelium has improved the prognosis of severe cases. It can address the acute (Amniotic Membrane Transplantation, Sequential Sectorial Epitheliectomies) or the late stage of the disease (Limbal Stem Cell (LSC) Transplantation / in or ex vivo expansion). In all cases, an optimal control of the ocular surface inflammation is essential to the LSC survival.

• 2472

How anterior segment imaging helps in the management of ocular surface cicatrizing diseases

NUBILE M
University Chieti-Pescara

ABSTRACT NOT PROVIDED

• 2473

The amniotic membrane in conjunctival cicatrizing diseases

DUA H
Queens Medical Centre, Nottingham

ABSTRACT NOT PROVIDED

• 2474

An update on muccous membranes management

CLAERHOUT I
UZ Gent

ABSTRACT NOT PROVIDED

• 3111

Anti-VEGF for the treatment of retinal angiomatous proliferation

DATSERIS I
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ABSTRACT NOT PROVIDED

• 3112

Anti-VEGF for the treatment of serous and vascularized RPE detachment and exudative AMD

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Choroidal neovascularization (CNV) associated with retinal pigment epithelial detachment (PED) in AMD is a subtype of AMD with a bad prognosis and a high risk of retinal pigment epithelium (RPE) tear. The efficacy of current treatment options is limited, and the anatomical and functional results are not favourable after both laser photocoagulation and photodynamic therapy (PDT). We will discuss the effect and outcome of anti-VEGF intravitreal injection in treating CNV associated with PED in AMD.

• 3113

Anti-VEGF for the treatment of diabetic macular edema

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Purpose To assess efficacy and safety of intraocular injections of anti-VEGF in patients with diabetic macular edema

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 oedema formation. Trials for different anti-VEGF compounds are nearing completion or are completed. Data regarding dose, injection scheme and practicable application form are reviewed. Combination of laser therapy and anti-VEGF will be reported.

Results For diabetic macular edema, trials of intravitreal pegaptanib and intravitreal ranibizumab have shown short-term benefit in visual acuity. Intravitreal bevacizumab also has been shown to have beneficial short-term effects on both visual acuity and retinal thickness. Furthermore, combined therapies shows promising results. Despite promising early reports on the safety of these medications, the results of large, controlled trials are still expected in order to substantiate the safety and efficacy of anti-VEGF drugs for diabetic retinopathy.

Conclusion New therapeutic approaches based on intravitreal injections of anti-VEGF molecules offer new hope for the management of diabetic macular edema. However, randomized studies are needed in order to attest longterm safety and efficacy profiles.

• 3114

Anti-VEGF for treatment of macular edema secondary to retinal vein occlusions

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Purpose To assess efficacy and safety of intraocular injections of 0.3 mg or 0.5 mg ranibizumab in patients with macular edema following branch and central retinal vein occlusion.

Methods Prospective, randomized, sham injection-controlled, double-masked, multicenter clinical trials. Six-month (monthly injections) and one year (PRN) results of the BRAVO and CRUISE studies will be presented.

Results In the BRAVO study, mean change from baseline BCVA letter score at month 6 was 16.6 and 18.3 in the 0.3 mg and 0.5 mg ranibizumab groups and 7.3 in the sham group (P<0.0001). At 12 months, the corresponding change was 16.4, 18.3 and 12.1 letters respectively.The percentage of patients who gained > or =15 letters in BCVA at month 12 was 56% (0.3 mg) and 60.3% (0.5 mg) in the ranibizumab groups and 43.9% in the sham group; and CFT had decreased by a mean of 314 microm (0.3 mg) and 347 microm (0.5 mg) in the ranibizumab groups and 274 microm in the sham group). In the CRUISE study, mean change from baseline BCVA letter score at month 6 was 12.7 and 14.9 in the 0.3 mg and 0.5 mg ranibizumab groups, respectively, and 0.8 in the sham group (P<0.0001).At 12 months, the corresponding change was 13.9, 13.9 and 7.3 letters respectively.The percentage of patients who gained > or =15 letters in BCVA at month 12 was 47% (0.3 mg) and 50.8% (0.5 mg) in the ranibizumab groups and 33.1% in the sham group;CFT had decreased by a mean of 453 microm (0.3 mg) and 462 microm (0.5 mg) in the ranibizumab groups and 427 microm in the sham group).

Conclusion Intraocular injections of 0.3 mg or 0.5 mg ranibizumab provid rapid, effective treatment for macular edema following BRVO and CRVO with low rates of ocular and nonocular safety events

• 3115
Anti-VEGF for the treatment of CNV secondary to angoid streaks

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Purpose The purpose of this report is to evaluate the safety and efficacy of intravitreal antivascular endothelial growth factors (anti-VEGF) in eyes with macular choroidal neovascularization (CNV) secondary to angioid streaks.

Methods From the present evidence in the literature it may be concluded that anti-VEGF therapy with ranibizumab or bevacizumab, based on the strategy to 'according to need' , is beneficial for the treatment of CNV secondary to angioid streaks.

Results Visual acuity can be maintained or even improved over a prolonged period of time, even with a low number of injections, at high rates ranging from 85.7 to 100% , especially in the early stages of the disease. Later when more widespread atrophic changes of pigment epithelium have occurred ,especially if they related the foveola, the visual prognosis was not favorable. Although at present there are not definite proofs with safety problems of anti-VEGF agents in the treatment of CNV secondary to angioid streaks, patients need to be aware of the off-label nature of the treatment with anti-VEGF..

Conclusion Overall, based on the evidence available, intravitreal treatment with anti-VEGF seems to be the best choice at present to treat patients with CNV secondary to angioid streaks .

• 3116
Anti-VEGF treatment in ocular oncology

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Purpose To present the indications of Anti-VEGF treatment in ocular oncology.

Methods Intraocular anti-VEGF injections were used for:
• The prevention or the treatment of neovascular glaucoma following irradiation treatment of intraocular tumors (uveal melanomas, choroïdal hemangiomas, choroïdal metastasis)

• The control of cystoids macula edema related to the conservative management of intraocular tumors.

• The treatment of secondary retinal detachment related to vascular tumors and pseudo tumors and mainly the Coat's disease.

Results A dramatic decrease of the risk of neovascular glaucoma was obtained with intravitreal anti-vasoproliferative treatment following irradiation treatment of intraocular tumors. The presence of retinal ischemia associated to the secondary exudative retinal detachment is observed with panoramic (150°) fluorescein angiography.The anti-vasoproliferative treatment is delivered during the period preceding the reatachment of the retina which allows a photocoagulation treatment. Anti-vasoproliferative treatment in case of established iris neovascularisation allows a functional success (IOP less than 20mm Hg) in 84% of the cases and anatomical success (reduction of the iris neovascularisation and of diffusion of the dye in fluorescein angiography) in 75% of the cases.Impressive reduction of the secondary retinal detachment is obtained following anti-vasoproliferatives treatment in cases of Coat's disease allowing the photoablation of the reattached retina.

Conclusion Anti-vasoproliferative treatment in ocular oncology is a major contribution for the reduction of side effects induced by irradiation treatment and to maintain useful function in treated eyes.

• 3121

Hyposmotic stress triggers ATP release from porcine lens via connexin and pannexin hemichannels

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Purpose Purinergic receptors in the lens suggest function can be altered by agonists present in aqueous humor. Some agonists may originate from the lens itself. Here, we examine the ability of osmotic shock to trigger ATP release from the intact lens.

Methods Porcine lenses were exposed to hyposmotic (200 mOsm) or hyperosmotic (500mOsm) solution and ATP in the bathing medium was measured by luciferase assay. Because hemichannels are permeable to large solutes, the ability of propidium iodide (PI) (MW 668) to enter the epithelium was examined.

Results ATP release into the bathing medium was stimulated when lenses were exposed to hyposmotic solution. Hyperosmotic solution did not detectably increase ATP release. Hyposmotic solution-induced release of ATP was partially suppressed by the connexin hemichannel inhibitor, 18α glycyrrhetinic acid (AGA) or by probenecid, a pannexin hemichannel blocker, and was abolished by AGA and probenecid added together. Consistent with opening of connexin and/or pannexin hemichannels, lenses exposed to hyposmotic solution displayed a ~4 fold increase in the ability of PI to enter the epithelium. In parallel studies, hyposmotic solution was shown to activate a Src family tyrosine kinase (SFK) and cause an SFK-dependent increase of Na,K-ATPase activity in the epithelium.

Conclusion Hemichannels contribute to ATP release when the intact lens is subjected to hyposmotic shock. The amount of ATP release appeared sufficient to activate purinergic receptors that cause tyrosine kinase-dependent stimulation of active Na-K transport. The responses could perhaps signify an autoregulatory loop initiated by mechanical stress or osmotic swelling.

• 3122

Stimulation of adrenergic β-receptors enhances mydriasis in a porcine eye model

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Purpose In order to achieve an improved mydriasis in human eyes during cataract surgery, the effect of intracameral phenylephrine was compared to the combination of isoprenaline plus phenylephrine, to epinephrine alone and to a negative control, in a porcine eye model.

Methods A total of eighty-nine eyes from newly slaughtered pigs were acquired and randomly split into four groups. In order to gain miosis all eyes received 2.0 mg of acetylcholine intracamerally, and after 60 seconds the eyes were injected with 0.15 ml 0.3% isoprenaline and 0.15 ml 3.0% phenylephrine sequentially with a 90-second interval (n=21), the same substances in the reverse order (n=22), 0.15 ml of 0.025% epinephrine (n=20), or 0.15 ml of saline solution (n=26). The diameter of the pupils were measured every 15 seconds, and compared using Student's t-test.

Results Phenylephrine injected after isoprenaline had a significantly ($p<0.01$) larger mydriatic effect than epinephrine. The mydriatic effect of phenylephrine, however, was significantly ($p<0.05$) smaller than that or epinephrine without the isoprenaline pretreatment. Isoprenaline also exhibited a small mydriatic effect of its own.

Conclusion This study shows that the β-receptor has a role in the dilation of the pupil, here demonstrated with the β-receptor stimulator isoprenaline which augments the mydriatic effect of intracamerally injected phenylephrine. The superior mydriatic effects of a nonspecific adrenergic stimulator such as epinephrine in compare to the specific α1-receptor stimulator phenylephrine may be explained by this β-receptor mediated mydriasis.

• 3123

The discordance between objective signs and giant papillae improvement in patients with vernal keratoconjunctivitis (VKC) participating in a randomized, controlled, clinical trial

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Purpose Resolution of papillae is a desirable objective in the management of tarsal VKC. The effect of Vekacia®, an unpreserved cyclosporine cationic emulsion, was evaluated in children with active VKC presenting with giant papillae and keratitis at enrollment.

Methods 118 VKC patients were randomized to Vekacia® 0.05%, 0.1%, or vehicle QID. The primary criterion was subjective symptom improvement. Objective signs (giant papillae, conjunctival hyperemia, discharge, chemosis, limbal infiltrates and corneal epithelial disease) were assessed as secondary endpoint.

Results At Day 28, patient subjective symptoms improved in all groups without statistically significant difference between groups. Among the objective signs, except for papillae, clinically significant improvements were observed: absence of the sign ranged from 20.5% to 72% in both active groups and from 16.7% to 41.2% for vehicle group, depending of the sign. For papillae, only 4 patients experienced total clearing (2.8%, 2.6% and 6.6% in vehicle, 0.05% and 0.1% CsA groups respectively). Clinically and statistically significant differences in keratitis (CFS mean change) over vehicle were observed at Day 28 in Vekacia® treated patients (0.05%, $p=0.003$; 0.1% $p=0.014$).

Conclusion Corneal involvement in VKC is a sight-threatening complication. Improvement in keratitis, a key element in the management of the active VKC was not associated with complete resolution of the papillae. Therefore, among the signs of the disease, papillae appear to be the least helpful sign to follow VKC improvement.

Commercial interest

• 3124

Azithromycin: intrinsic cytotoxic effects on corneal epithelial cell cultures

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Purpose To compare the cytotoxic effects of preservative free azithromycin versus preservative free netilmycin and levofloxacin upon corneal epithelial cells in vitro.

Methods Corneal epithelial cells in vitro were incubated for 15 min and 6 hours with preservative free netilmycin or levofloxacin and different concentrations of unpreserved azithromycin. Qualitative analysis was performed by using phase contrast optics and examining the morphological aspects of cell cultures. Quantitative analysis was performed by measuring the release of cytoplasmic enzyme lactate dehydrogenase (LDH) into the medium immediately and 24 h after exposure to drugs. We also observed the wound healing rate of mechanically injured corneal epithelial cells cultured in each antibiotic preparation for 24 and 48 hours.

Results The unpreserved preparation of azithromycin up to a concentration of 1.5% showed a low cell toxicity, not significantly different from the other antibiotic preparations ($p>0.05$). Azithromycin did not inhibit the wound healing process after the mechanical injury.

Conclusion Under our experimental conditions, unpreserved azithromycin 1.5 % showed a low cytotoxicity and did not interphere with wound healing process.

• 3125

Assessment of the efficacy of Cationorm® in patients with moderate dry eye compared with Optive® and Emustil® eye drops

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Purpose Dry eye disease (DED), the result of an insufficient tear film, is manifest by symptoms of ocular discomfort and ocular surface damage. An ideal DED therapy would regenerate each deficient tear film layer. Cationorm®, a preservative-free cationic emulsion, augments the aqueous-mucous and lipid layers of the tear film and reduces evaporation. The efficacy of Cationorm® was evaluated.

Methods Adults with moderate DED defined by at least 1 symptom >3 cm on a visual analog scale (VAS) and total corneal fluorescein score ≥3 and tear film break up time (BUT) <7 seconds were enrolled in a 3 month, controlled, randomized, single-masked study. Randomization to qid treatment with Cationorm® (Novagali), Optive® (Allergan) or Emustil® (SIFI) followed a washout period. Efficacy assessments were evaluated at 1 and 3 months.

Results Of 71 patients, 8 (44%) Emustil treated patients discontinued prior to month 3. At month 1, the VAS score in Optive® and Cationorm® patients revealed a statistically significant improvement evident by month 3 for all treatments. Improvements in BUT and reduced fluorescein staining at month 3 were statistically significant for Cationorm® and Optive® but not Emustil®. While Cationorm® and Optive® significantly reduced tear film osmolarity only Cationorm® showed a statistically significant difference compared to Emustil®.

Conclusion In moderate DED patients, Cationorm® was more effective than Emustil®. Although not statistically different, overall improvements were greater in patients treated with Cationorm® than Optive®.

• 3126 / 449

Cationic oil-in-water emulsions protect and restore function of the injured ocular surface

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Purpose Ocular surface damage is a consequence of tear instability arising from numerous inciting events: preserved eye drops, contact lens wear, systemic medications, environment and age. While unpreserved eye drop reduce iatrogenic toxicity they do not restore the deficient tear film which leads to ocular surface injury. Cationic oil-in-water emulsions have been shown to restore and reduce evaporation of the tear film. We studied the effect of cationic emulsions (Cationorm® and Catioprost®) in established animal models of ocular surface injury.

Methods Acute toxicity and local tolerance were evaluated in rabbits. Healing properties were assessed in a rat model of corneal scraping. Abrasions were treated for 5 days, and corneas were evaluated clinically and histologically. Conjunctival function was assessed by goblet cell (GC) count and MUC5 immunostaining. The kinetics of ocular surface healing was assessed in an in vitro scraping assay.

Results Neither Cationorm® nor Catioprost® induced toxicity as evidenced by clinical and confocal microscopy scoring. Catioprost® was well tolerated, with a reduced (-42%) occurrence of hyperemia when compared to Xalatan®. In rats, Catioprost® improved healing, protected GC and maintained normal MUC5 secretion. In vitro, the cationic emulsions improved cell migration and maintained MUC4 expression.

Conclusion Cationic emulsions were well tolerated. In contrast to preserved and unpreserved ophthalmic drops, cationic emulsions promoted healing, restored function of injured ocular surface, and protected against ocular surface injury. The findings suggest that cationic emulsions by augmenting the tear film may benefit patients with ocular surface disease.

Commercial interest

• 3131

Effect of swelling on the ultra structure of camel corneal stroma

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Purpose Previous studies have shown the swelling characteristics of camel cornea. Here we investigate the changes in the architecture of corneal stroma due to swelling.

Methods Six fresh camel corneal buttons (8.5mm) were hydrated separately in deionised water for 24hrs and 48hrs. The change in hydration of corneal stroma was calculated per unit weight. Hydrated corneas were fixed in 2.5% glutaraldehyde containing cuprolinic blue in sodium acetate buffer to analyse the distribution of proteoglycans (PGs). To analyse the collagen fibril diameter and spacing, tissue were fixed in para-formaldehyde (4%) in 0.1M buffer and embedded in LR White.

Results The hydration of corneal stroma after 24hrs and 48hrs was 54 per unit weight and 56 per unit weight respectively. The anterior part of the stroma was less affected by swelling compared to middle and posterior stroma. Stromal lamellae were disorganised with collagen fibrils running in random directions. Most of the keratocytes were disappeared, a small number present showed cell organelles. Throughout the stroma, PGs were rounded in shape instead of normal filaments. The PGs in the pre-Descemet's stroma were larger compared to anterior and middle stroma. The spacing between the collagen fibril had increased significantly, but the diameter was not affected in the anterior stroma.

Conclusion Our study shows that camel cornea has a rather high hydration during the first 24 hrs. After 24hrs, hydration is comparatively low. Hydration of the cornea affects the uniform distribution of collagen fibrils and proteoglycans.

• 3132

Structure of solitary sebaceous glands in the sea lion eyelid – a Meibomian gland equivalent?

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Purpose Pinnipeds stay not only in the sea but also on land and may then require a stable tear film. It was of interest to determine whether sea lions have meibomian glands for a superficial lipid layer that prevents tear evaporation.

Methods Eyelids of a normal sea lion were embedded in paraffin and sections of 10-20 µm thickness stained with H&E.

Results A distinct tarsus was not detectable, the lid consisted mainly of muscular tissue with the lid margin forming a tip. Underneath the epidermis was a whitish granular layer that consisted of hair follicles and sebaceous glands. Bundles of holocrine acini were arranged between hair follicles. Towards the lid margin, the number of hair follicles decreased whereas the relative volume of sebaceous glands increased. At the lid margin, the sebaceous glands formed solitary glands without association to hairs or with only rudimentary hair shafts. The acini drained via short ductules into a straight duct with a four-layered stratified squamous epithelium. The straight ducts opened via a terminal duct onto the outer lid skin.

Conclusion The results show that pinnipeds have solitary sebaceous glands at the eyelid margin that resemble human meibomian glands in structure but are different in orientation and size. It remains to be determined whether the sea lion eyelid sebaceous glands represent an equivalent to human meibomian glands.

• 3133

Characteristics of goblet cells in the conjunctival epithelium of the lid wiper explain the hydrodynamic type of ocular surface lubrication during the blink

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Purpose The lid wiper at the inner aspect of the posterior eyelid border forms an epithelial lip apposed to the globe for distribution the pre-ocular tear film. The present assumption of a squamous may not explain sufficient lubrication in order to avoid friction during the blink movement.

Methods Conjunctival whole-mounts including the lid margins from twelve normal human body donors were investigated by routine histology and semithin plastic sections, using histological stains, histochemistry and immunohistochemistry for MUC5AC.

Results In routine histology the lid wiper showed a conjunctival epithelium with goblet cells, single and in clusters, at the luminal surface and also deep within the epithelium. Semithin sections revealed that the goblet cells at a greater depth were connected to cryptal epithelial infoldings that opened to the surface. Most goblet cells produced mucins of the neutral (PAS) and acidic (Alcian blue) type and also stained positive for the mucin MUC5AC. Surprisingly, MUC5AC negative goblet cells were also observed in the lid wiper.

Conclusion In contrast to conventional assumptions, the lid wiper is a part of the conjunctiva and contains goblet cells & goblet cell crypts that are suitable to provide by a hydrodynamic type of lubrication for sufficient reduction of sheer stress between the lid margin and globe during the blink. This is another strong indication that the lid wiper is the area of the lid margin for the distribution of the thin preocular tear film.

• 3134

Differential effects of various VEGF isoforms on endothelial cells and Tenon fibroblasts

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Purpose We have previously shown that VEGF plays an important role in scar formation after glaucoma surgery. To clarify the differential effects elicited by VEGF isoforms, we compared the biological responses and signaling pathways activated by the various isoforms on endothelial cells and Tenon fibroblasts in vitro.

Methods VEGF-R2 and neuropilin-1 (NRP-1) expression was analyzed on endothelial cells (HUVEC) and Tenon fibroblasts (TF) by RT-PCR. The effect of different VEGF isoforms (VEGF189, VEGF165 and VEGF121) on HUVEC and TF proliferation was determined by WST-1 assay. The extracellular signal-regulated kinase (ERK) pathway was evaluated by TransAM c-Myc assay.

Results HUVEC showed a higher expression of VEGF-R2 and NRP-1 mRNA as compared to TF. VEGF189 only significantly increased the growth of TF, whereas VEGF165 only increased HUVEC proliferation. VEGF165 strongly binds VEGF-R2 and NRP-1. As such, the combined reduced expression of VEGF-R2 and NRP-1 on TF explained why VEGF165 was more potent in inducing proliferation of HUVEC as compared to TF. VEGF121 exerted significant proliferative effects on both cell types by binding VEGF-R2. However, similar concentrations of VEGF121 stimulated HUVEC more than TF, due to the lower expression of VEGF-R2 on TF. All these stimulating effects on proliferation were associated with an activation of the ERK pathway.

Conclusion Our data indicate that VEGF165 and VEGF121 predominantly affect blood vessel growth, whereas VEGF189 may be more important in fibrosis. Selective inhibition of VEGF165 (pegaptanib) may therefore be less effective to reduce ocular scar formation than non-selective VEGF-inhibition (bevacizumab), presumably due to retained action of VEGF121 and VEGF189.

• 3135

Cis-urocanic acid inhibits SAPK/JNK signaling pathway in UV-B exposed human corneal epithelial cells in vitro

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Purpose Urocanic acid (UCA) is a major endogenous UV-absorbing chromophore in the epidermis and it is also an efficacious immunosuppressant. The effects of cis-UCA on UV-B-induced inflammatory and apoptotic responses in HCE-2 cells, focusing on the nuclear factor kappa B (NF-kappaB) and AP-1 signalling pathways were studied.

Methods After exposing HCE-2 cells to UV-B and cis-UCA, the DNA binding of c-Fos, c-Jun and NF-kappaB were measured with ELISA. In addition, the endogenous levels of phosphorylated stress-activated protein kinase/c-Jun N-terminal kinase (phospho-SAPK/JNK and phospho-c-Jun were determined. The proliferative capacity of HCE-2 cells was also quantified, and the cytotoxicity of the cis-UCA and UV-B treatments was monitored by measuring the release of lactate dehydrogenase enzyme in the culture medium.

Results UV-B irradiation induced the binding of transcription factors c-Jun, c-Fos, and NF-kappaB to DNA. Cis-UCA inhibited the binding of c-Jun and c-Fos but not that of NF-κB. Moreover, UV-B increased the levels of phospho-c-Jun and phospho-JNK, and the expression of both was attenuated by cis-UCA. Cis-UCA also alleviated the UV-B-induced apoptosis and proliferative decline in human corneal cells.

Conclusion The results from this study suggest that cis-UCA suppresses JNK signaling pathway, which provides potential for treating UV-B-induced inflammatory defects in human corneal cells.

• 3136

Mesenchymal-like stem cells from human corneal stroma grown in medium containing human serum as the only supplement

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Purpose Besides bone marrow, mesenchymal stem cells (MSCs) can be separated from various tissues including the cornea. We investigated whether human corneal stroma-derived cells resemble MSCs and if they can be grown in animal-materials free medium containing human serum as the only supplement.

Methods Human cornea stromal cells were isolated from cadavers after removal of the epithelial and endothelial layers (approved by the Hungarian Regional Ethical Committee). The cells were grown in DMEM containing human serum as the only supplement. Immunophenotyping with MSC markers, integrins/cell-adhesion-, endothelial- and hematopoietic markers was carried out by FACS analysis. Standard manufacturer protocols were used for differentiating the cells into fat, cartilage or bone.

Results Cells isolated from human corneal stroma grew as monolayers in vitro and could be maintained in culture for more than 10 passages (n=6). They expressed the most important markers for MSCs (CD73, CD90, CD105, CD44, CD147, PDGFRb) and were negative for the hematopoietic markers CD34, CD45, HLA-DR, CD69 and CD133. High per cent of the cells expressed the pluripotency markers CD117, C-kit and CD47, but not the endothelial cell markers CD31, CD105/V-CAM, VEGFR2. One of the hallmarks of human MSCs being capable to differentiate towards adipocytes, chondrocytes and osteocytes could also be demonstrated.

Conclusion Our results indicate the presence of MSC-like cells in the human corneal stroma, which can be grown in human serum-containing medium. This opens the door for studying human keratopathies, as well as corneal tissue engineering and cell-based therapies.

• 3141

Immune modulation in the next decade

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ABSTRACT NOT PROVIDED

• 3142

Roles of human antimicrobial peptides in innate immune defense at the ocular surface: arming and alarming corneal and conjunctival epithelial cells

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Purpose The ocular surface including the lacrimal system and lids have evolved several defence mechanisms to prevent microbial invasion. Included among this armory are several host-defence (so-called antimicrobial) peptides.These multifunctional molecules are being studied not only for their endogenous antimicrobial properties but also for their potential therapeutic effects.

Methods The talk summerizes the current knowledge of antimicrobial peptide (AMP) expression at the ocular surface and lacrimal apparatus focusing on beta-defensins, psoriasin, and a protein of the S100 fused-type namely hornerin.

Results The role of these molecules in ocular surface disease will be discussed with the primary focus being on infectious keratitis and inflammatory conditions including dry eye.

Conclusion Finally the potential of using AMP and their mimetics/derivatives for the treatment and prevention of ocular surface diseases is addressed.

• 3143

Novel therapeutic strategies for the induction of tolerance in corneal transplantation

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Purpose With more than 60,000 procedures per year, the cornea is the most commonly transplanted solid tissue. However, immunologic rejection is still the leading cause of corneal allograft failure, especially in high-risk recipients with a history of previous graft rejection, inflammation or neovascularization. Therefore, novel treatment protocols are desirable.

Methods The genetic engineering of tissues prior to transplantation is an attractive approach to protect the graft from allogeneic rejection. Here the role of lentivirus mediated overexpression of Programmed Death-Ligand 1 (PD-L1) to prevent corneal graft rejection will be discussed. Moreover the injection of regulatory cell populations to modulate immune-mediated rejection will be discussed in this presentation.

Results Overexpression of PD-L1 in ex-vivo cultured corneas prior to transplantation significantly prevents corneal allograft rejection by modulating both innate and adaptive intragraft allo-immune responses. Moreover, injection of regulatory cells is able to prolong corneal allograft survival.

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 graft rejection. 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/B925). TR is supported by a Travel Grant from Millennium Research Funds, National University of Ireland, Galway]

• 3144

Graft survival and cytokine production profile after limbal transplantation in the experimental mouse model

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Purpose To evaluate the immune response in the experimental model of orthotopic limbal allo- and xenotransplantation in the mouse.

Methods Allogeneic (C57BL/6 to BALB/c mouse), xenogeneic (Lewis rat to BALB/c mouse) and syngeneic (BALB/c to BALB/c mouse) limbal transplantations were performed. The rejection of limbal graft was scored according to the corneal opacity. The expression of IL-2, IFN-gamma, IL-4, IL-10 and inducible nitric oxide synthase (iNOS) were detected by Real-time PCR in the graft. The donor cell survival was determined by Real-time PCR after transplantation. The recipients were treated with systemic monoclonal antibodies (mAb) anti-CD4 and anti-CD8 and with saline in the control group.

Results The allografts were rejected in 9.0 ± 1.8 days and xenografts in 6.5 ± 1.1 days after transplantation, syngeneic limbal grafts survived permanently. Distinct pattern of Th1 and Th2 cytokine production and intragraft expression of the iNOS gene were detected during rejection. Limbal grafts were promptly rejected by Th1 (allogeneic group) or by Th2 (xenogeneic group) type of immune response involving CD4+ cells and iNOS expression. The mean survival time of allogeneic and xenogeneic grafts was prolonged by systemic treatment of mAb anti-CD4. Treatment with mAb anti-CD8 did not extend the graft survival.

Conclusion The experimental model of limbal transplantation is useful for testing various immunosuppressive approaches to treat rejection after transplantation. The anti-CD4 mAb treatment presents promising immunosuppressive treatment after limbal transplantation.

• 3145

Anti-apoptotic gene transfer to corneal epithelial grafts modulates immune response and leads to increased graft survival

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Purpose To study whether anti-apoptotic gene transfer to allogeneic corneal epithelial sheets in mice improves graft survival. Transplatation of cultured allogeneic epithelium is a viable therapy for patients bilaterally blind after bilateral limbal stem cell deficiencies, e.g. after chemical burn. Gene therapy to cultured epithelial cell sheets in vitro before engraftment could promote the success in this most demanding ocular surface disease.

Methods Epithelial denuded syngeneic Balb/C corneas were manufactured with syn- or allogeneic epithelium, grafted and compared to epithelial grafts treated with the anti-apoptotic gene p35 (total n=40). Feasibility of gene therapy was determined by examining kinetics of IZsGreen protein expression. Allo-response was studied by delayed type hypersensitivity (DTH).

Results Transfer of IZsGreen was successful obtaining high rated of expression. Interestingly, gene-therapeutically treated allogeneic epithelial grafts showed significantly less opacity and a significantly faster restoration of the epithelial barrier compared to allo-untreated epithelial grafts ($p<0.01$, respectively). In addition, DTH analysis consistently showed significantly reduced T-cell response in the treated group ($p<0.01$).

Conclusion We were able to demonstrate that gene therapy of transplanted cell sheets may be a viable option to improve allogeneneic epithelial graft survival. This might set the stage for future studies of gene therapeutic interventions of epithelial allo-grafts, and its impact on graft survival and immune response.

• 3151
Ocular rigidity: review of measurement methods and its implications in clinical practice

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Ocular rigidity is a parameter that characterizes the biomechanical behavior of the eye. Different measurement techniques have been adopted to quantify this parameter. Invasive measurements in experimental animals have provided initial information on the pressure-volume relation, followed by manometric volumetric and tonographic techniques used in cadaver and living human eyes. Schiotz tonometry with different weights has been employed as a non-invasive method of quantifying ocular rigidity. Other surrogate measures of ocular rigidity have also been used, incorporating fundus pulsation amplitude and choroidal blood volume. In order to approximate the pressure volume relationship, a variety of different mathematical formulations have been employed. Based on available data, ocular volume, age, intraocular pressure, arterial pressure and ocular blood volume have been identified as parameters that affect ocular rigidity. Moreover, there is mounting evidence in the literature that ocular rigidity may be implicated in the pathogenesis of ocular disease. However, its exact role as well as the underlying pathogenetic mechanisms remain to be elucidated.

• 3152
Manometric measurement of the outflow facility in the human eye

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Purpose The intraocular pressure (IOP) is determined by a dynamic equilibrium between the production and the outflow of the aqueous humor. The dependence of outflow facility on IOP may be related to the biomechanical properties of the eye. This study examines the relationship between the outflow facility and IOP for the living human eye using an invasive manometric device.

Methods An intraoperative invasive manometric device was used to measure the IOP of fifty four eyes from fifty four cataract patients. The measurements were performed before cataract surgery. The anterior chamber of the eye was cannulated to a microstepping pump and the pressure was recorded by a pressure transducer through special developed computer software. The IOP was artificially increased to 40 mmHg by infusion of BSS in the anterior chamber of the eye. The IOP decay curve was recorded. A mathematical model was developed to calculate the outflow facility coefficient.

Results The average outflow facility coefficient was 0.328 (SD 0.093) μl/min/mmHg. From the data analysis the outflow facility coefficient was proved to have a non linear correlation with IOP. This non linear behavior of outflow facility was approximated with an exponential mathematical model.

Conclusion The invasive method of measuring in vivo outflow facility coefficient employed in this study, avoiding the errors of tonography may provide accurate data on the dependence of outflow facility coefficient on IOP. These data, in conjunction with ocular rigidity measurements may facilitate our understanding of the relationship between the biomechanical properties of the eye and the anatomical changes in the trabecular area at elevated IOP levels.

• 3153
Ocular pulsatility and intraocular pressure

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Purpose To characterize the effect of intraocular pressure (IOP) on ocular pulsation parameters.

Methods Fifty cataract patients (50 eyes) were enrolled. After cannulation of the anterior chamber, a computer-controlled device for the intraoperative measurement and control of IOP was used to increase the IOP in a stepping procedure from 15 to 40 mm Hg. Recordings of IOP were acquired after each infusion step. Ocular rigidity was computed from the pressure-volume data. Ocular pulse amplitude (OPA), pulse volume (PV), and pulsatile ocular blood flow (POBF) were measured from continuous IOP recordings.

Results The average rigidity coefficient was 0.0224 μL-1 (SD 0.0049). OPA increased by 91%, while PV and POBF decreased by 29% and 30%, respectively, when increasing the IOP from 15 to 40 mm Hg.

Conclusion An increase in IOP is associated with an increased mechanical resistance of the ocular wall, an increase in OPA and decreased POBF.

• 3154
Ocular rigidity assessment in the decision making for glaucoma patients

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Purpose So far there have been controversial reports concerning ocular rigidity in glaucomatous eyes, ranging from reduced values (which may rise following treatment with b-blockers or pilocarpine), to increased values, compared with non-glaucomatous eyes. Ocular rigidity may play an important role in glaucoma pathogenesis, since it determines ocular wall changes in response to pressure changes and thus affects the anatomical course of optic nerve fibers as well as the local vascular autoregulation. Despite the importance of ocular rigidity in glaucoma pathogenesis, its role in the clinical practice has so far been compromised, mainly due to the difficulties in the accurate calculation of a rigidity coefficient in vivo. The traditional approach to ocular rigidity calculation by differential tonometry and insertion of readings into Friedenwald's chart has received criticism, mainly because Friedenwald's nomogram was based on data from cadaveric eyes, which may display significantly altered rigidity values, compared with living eyes.

Methods Related literature review.

Results Recent developments, such as the manometric in vivo calculation of a rigidity coefficient, the determination of ocular elasticity through ultrasound elastography and the differential tonometry between applanation and dynamic contour tonometers may enable a minimally invasive and reliable assessment of ocular rigidity values for living eyes.

Conclusion The possibility to reliably calculate ocular rigidity in vivo using non-invasive or minimally invasive methods could lead to the incorporation of rigidity in the decision making process for glaucoma patients.

• 3155

Ocular rigidity and age-related macular degeneration

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Purpose To compare ocular rigidity in patients with age-related macular degeneration (AMD) and control subjects.

Methods The ocular rigidity coefficient was measured in 32 patients with AMD (16 with neovascular and 16 with nonneovascular AMD) and 44 age-matched control patients (control group) who underwent cataract surgery. The measurement procedure involved injection of microvolumes of a balanced salt solution (in steps of 4.5 microl) through the limbus in the anterior chamber, with continuous monitoring of intraocular pressure with a transducer, up to the limit of 30 mm Hg.

Results There was no difference in age (p = 0.195), gender (p = 0.513) and axial length (p = 0.725) between the groups. Ocular rigidity coefficient was 0.0142 +/- 0.0077 μl-1 in the AMD group and 0.0125 +/- 0.0049 μl-1 in the control group (p = 0.255). In subgroup analysis, the average ocular rigidity was 0.0186 +/- 0.0078 μl-1 in patients with neovascular AMD and 0.0104 +/- 0.0053 μl-1 in patients with nonneovascular AMD. Ocular rigidity was higher in patients with neovascular AMD, compared to patients with nonneovascular AMD (p = 0.004) and controls (p=0.014).

Conclusion Patients with neovascular AMD have increased ocular rigidity measurements compared with patients with nonneovascular AMD and control patients.

• 3161
The physiological role of reactive oxygen species (ROS) in lens and corneal epithelial cells

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Purpose ROS have been shown to mediate growth factor mitogenic function in many cell types. This study is to explore if H2O2 (a stable ROS species) at low levels can promote proliferation in lens epithelial cells, and facilitate adhesion, migration, and wound healing in corneal epithelial cells

Methods Human lens epithelial (HLE) B3 cells were treated with H2O2 (0-50 μM) and analyzed for cell proliferation by thymidine assay. H2O2 (0-70 μM) treated primary rabbit corneal epithelial (RCE) cells were tested for viability by MTT assay, adhesion by centrifugation assay, focal contacts of vinculin and F-actin by immunofluorescence. Activations of Src (pY416), EGF receptor (pY845), vinculin (pY1065), FAK (pY397 and pY576) were examined by immunoblotting. The cell migration was tested by a scratch wound method, while the cornea wound healing in vitro (pig), and in vivo (mouse) was examined by scraping off an area of the epithelial cells, and treated by H2O2 with and without N-acetylcysteine (NAC)

Results Compared with the untreated control, H2O2 at 20 μM stimulated HLEB3 cell proliferation. This level of H2O2 also enhanced RCE cell viability, facilitated adhesion and migration with activations of EGF receptor (Y845), and the downstream Src (pY416), FAK (Y576), and vinculin (Y1065). H2O2-treated RCE cells also showed focal adhesion rich in vinculin, and stress fibers containing F-actin. Low level of H2O2 induced a faster wound healing in cornea both in vitro and in vivo, and the healing was weakened if treated by H2O2 + NAC.

Conclusion H2O2 at low levels can benefit both lens and corneal epithelial cells in growth and wound healing. This novel physiological function of H2O2 confirms the importance of redox balance for the general health of cells and tissues.

• 3162
Oxidative stress in the eye in diabetes

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Purpose The characterize manifestations of oxidative stress in lens and retina in diabetes, and to evaluate the roles for aldose reductase (AR), Na+-H+-exchanger-1 (NHE-1), and poly(ADP-ribose) polymerase-1 (PARP-1) in oxidative stress in both tissues, cataract formation, and retinal apoptosis.

Methods The experiments were performed in streptozotocin-diabetic rats and high glucose-exposed cultured human lens epithelial cells (HLEC) and bovine retinal pericytes and endothelial cells (BRP and BREC). Cataract formation was evaluated by indirect ophthalmoscopy and slit lamp examination, oxidative stress by combination of biochemical and immunohistochemical methods, and retinal apoptosis by TUNEL assay in flat-mounted retinae.

Results Diabetes-induced oxidative-nitrosative stress manifested by accumulation of free lipid peroxidation products, malondialdehyde and 4-hydroxyalkenals, as well as 4-hydroxynonenal protein adducts, and nitrated and poly(ADP-ribosyl)ated proteins, is present in both diabetic lens and retina as well as in high glucose-exposed HLEC and BRP and BREC. Depletion of GSH and ascorbate and changes in the glutathione and ascorbate redox states are present in thre lens only. Activation of AR, NHE-1 and PARP-1 promotes oxidative damage. Inhibition of AR, NHE-1, and PARP-1 prevents diabetes-induced oxidative stress, and prevents or delays cataractogenesis and retinal apoptosis.

Conclusion Ozidative stress is present in lens and retina in diabetes and plays an important role in diabetic ocular comp-lications.

Commercial interest

• 3163
In vitro detection of uv-induced damage of the cornea, lens and rpe

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Purpose UV-A and UV-B radiation from sunlight is a major source of ocular oxidative damage. This paper describes in vitro methods that can be used to detect ocular damage from UV radiation.

Methods Human corneal epithelial cells, lens epithelial cells, and RPE cells were cultured and Ultraviolet A/Ultraviolet B blocking filters and UVB-only blocking filters were placed between the cells and a UV light source. Cells were irradiated with UV radiations at various energy levels, with and without filters. Cell viability after exposure was determined using the metabolic dye alamarBlue and by evaluating changes in nuclei, mitochondria, membrane permeability, and cell membranes using the fluorescent dyes Hoechst 33342, rhodamine 123, calcein AM, ethidium homodimer-1, and annexin V. Images of the cells were taken with a Zeiss 510 confocal laser scanning microscope

Results The alamarBlue assay results of UV-exposed cells without filters showed energy level-dependent decreases in cellular viability. However, UV treated cells with 400 nm LP filter protection showed the equivalent viability to untreated cells at all energy levels. Also, UV irradiated cells with 320 nm LP filter showed lower cell viability than the unexposed control cells, yet higher viability than UV-exposed cells without filters in an energy level-dependent manner. The confocal microscopy results also showed that UV radiation can cause significant dose-dependent degradations of nuclei and mitochondria in ocular cells. The annexin V staining also showed an increased number of apoptotic cells after UV irradiation.

Conclusion UV-induced damage can be evaluated to test the effectiveness of UV-absorbing contact lenses and intraocular lenses with bioassays that measure change in in vitro cells

• 3164
The evidence of oxidation in ultraviolet radiation cataract

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ABSTRACT NOT PROVIDED

• 3165

Mouse models of accelerated lenticular aging by carbonyl and oxidant stress

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Purpose Age-related human cataracts form as a result combined of carbonyl and oxidant stress and other crystallin modifications that destabilize their chaperone function. However, without appropriate models it has been very difficult to demonstrate cause-and effect and implicate protein modifications in the disease process. To test the role of vitamin C oxidation products (carbonyl stress) and protein oxidation in the formation of crystallin aggregates, we have generated two types of mice that exhibit rapid protein damage.

Methods The first model of increased carbonyl stress is the hSVCT2 mouse in which we overexpressed the human vitamin C two transporter under control of the mouse alphaB-crystallin promoter. (Fan et al. PNAS 2006). The second model of increased protein oxidation is the LEGSKO (Lens Glutathione Synthesis Conditional Knockout mouse) in which we conditionally knocked out gamma-glutamyl cysteine ligase (Gclc) in order to mimic the low GSH levels of the old lens nucleus.

Results Gamma glutamyl cysteine ligase mRNA, activity and glutathione (GSH) levels are severely depressed in the lens of the homozygous mouse, but not in the heterozygous mouse. GSSG/GSH ratio, methionine oxidation and protein disulfide formation are increased at 6 mos of age. Nuclear opacities turn into full nuclear cataracts at 6 mos. Protein disulfide formation reveals a shift from intra- to interdisulfide bonds similar to aging human lens. Dramatic upregulation of several candidate transporters is noted.

Conclusion Availability of two mice strains with increased carbonyl and oxidative stress, respectively, will allow us to test the hypothesis that rapid modification of crystallins predisposes to protein aggregation and cataractogenesis when bred together. It will also help us develop drugs that slow down the progression of cataractogenesis and study molecular events that precede cataract formation.

• 3171

From corneal topography to wavefront aberrometry

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In this presentation we will see the how, after more than a century of constant improvements, mapping of the surface curvature of the cornea, progressively evolved into state of the art technologies objectively measuring the quality of vision. We will also discuss how these new tools can help us in our daily refractive surgery practice.

• 3172

Wavefront aberration variations with multifocal intraocular lenses

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University François Rabelais, Hopital Bretonneau, tours

ABSTRACT NOT PROVIDED

• 3173

Professional sportsmen aiming for super vision

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ABSTRACT NOT PROVIDED

• 3174

What are the implications of the straylight domain for the clinician

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Purpose Straylight is an important source of patient complaints. They can be voiced like halos, glare, hazy vision and blinding at night. With visual acuity, contrast sensitivity and slit lamp examination little may be found. Yet increased large angle light scattering in the eye media not detected by common tests, may degrade the image projected on the retina, thus decreasing the quality of vision. Aging changes to the crystalline lens and cataract are the most common causes of increased straylight, but many corneal conditions including laser treatment have been reported to increase straylight as well.

Methods In order to evaluate the importance of straylight for clinical decision making, the quantity in which straylight is expressed must attain a meaningful value. Straylight is expressed logarithmically, as the logarithm of the straylight parameter s, which directly relates straylight to the (outer skirt) of the functional point-spread-function: s = θ^2 PSF. It was found earlier that expressed this way, the straylight value has functionally about equal importance as logMAR. The functional value of straylight was further corroborated by Aspinal et al., finding that straylight was the better predictor of clinical decisions on cataract surgery, as compared to visual acuity.

Results Implications for the clinician include a shift in targeting of patient care. On the basis of straylight elevation treatment can be offered in cases where visual acuity is good. In the case of optical malfunction of the eye, as simple model for functional severity of the condition, the linear average of visual acuity in logMAR and straylight in log(s) is proposed. Data from population study on >5000 eyes show significant retargeting of cataract surgery.

Conclusion Straylight retargets patient care.

Commercial interest

• 3175

An update on adaptive optics and the vision simulator

CHATEAU N
Imagine Eyes, Orsay

ABSTRACT NOT PROVIDED

• 3211

Association of Alzheimer's disease and age-related macular degeneration

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Purpose The pathomechanisms of age-related macular degeneration (AMD) and Alzheimer dementia (AD) show several similarities. Allelic variations of apolipoprotein E (apoE) are associated with both diseases: apoE4 with increased risk of AD, whereas apoE2 with reduced susceptibility of AD, but increased risk of AMD. The AMD associated complement factor H (CFH) gene has also been shown to influence the risk of AD. We investigated, therefore, the occurrence of AMD in AD patients and compared their lipid profile, apoE and CFH polymorphisms.

Methods 96 AMD, 84 AD and 30 control patients were examined (visual acuity, biomicroscopy, fundoscopy). Measurements of triglyceride, total- and HDL cholesterol levels, as well as the analysis of apoE and CFH alleles were performed.

Results The prevalence of the apoE4 isoform in the AMD, AD and control patients was 6%, 34% and 27%, while that of apoE2 was 14%, 11% and 6%, respectively. The occurrence rate of CFH Y402H CC homozygote mutation was 35%, 19% and 16%, respectively. Triglyceride, total- and HDL cholesterol levels were in the reference range. Advanced AMD was found in 13% of the 68 cooperating AD patients, the early and intermediate form was seen in 17%.

Conclusion A higher frequency of apoE2 in AMD, and a higher frequency of apoE4 in Alzheimer's patients have been found. The CFH mutation is associated with AMD, but does not differ significantly between Alzheimer's patients and controls. The frequency of early and intermediate AMD in AD patients was lower than expected from the population-based studies.

• 3212

Evaluating the effectiveness of therapy with prospidin in patiens with age-related macular degeneration

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Purpose The current study was to follow the dynamics of the above medication within a year.

Methods Prospidium directly effects DNA, Ribonucleic acid (RNA), has an anti-inflammatory, anti-modulator, anti-proliferative effects. This medication blocks messenger RNA and damages the synthesis vascular endothelial growth factor. In Kirov Ophthalmology Hospital, patients with wet form of age related macular degeneration were treated with Prospidium. The dose was 30 mg in peribulbar injections every week. 98 patients, 106 eyes were studied. The course of treatment included 5 injections. The age range was 44-82 years. The evaluation included: check-up of visual acuteness, examination of the eye fundus, photography of the eye fundus, fluorescent angiography of the retina, OCT.

Results 3 months later, stability of vision was noted in 56.2%. Visual functions improved in 21.6%. Worsening of visual functions was seen in 12.0%. Repeated decrease of visual acuteness after a one time infusion of Prospidium was noted in 56% of cases on an average 68 days. This fact explains the necessity of the next in-time course of injections.

Conclusion Treatment for the wet form of age related macular degeneration with Prospidium is effective.

• 3213

The effect of intravitreal injections of anti-VEGF on the pigment epithelial detachment (PED) in eyes with the exudative type of age related macular degeneration (AMD)

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Purpose To evaluate the morphological changes of the PED after treatment with intravitreal injections of anti-VEGF in eyes with the exudative type of AMD.

Methods Retrospective chart review of patients with PED and exudative type of AMD treated with anti-VEGF. Alterations of the PED were defined as unchanged if it appeared qualitatively similar to the baseline exam, reduced if it appeared qualitatively smaller, disappeared if no PED could be detected and increased if it appeared qualitatively larger. Changes in BCVA and number of injections were compared to an age similar control group with the exudative type of AMD treated with intravitreal injections of anti-VEGF without PED on the OCT examination.

Results 30 eyes were included in each group. Mean age of the PED group was 75.7 years (SD: ± 5.8 years), while the control group's was 77.7 years (SD: ±6.2 years). Mean follow up period was 19.8 months (SD: ±10.7 months). Changes of the PED morphology were found as follows, unchanged: 9 eyes, reduced: 16, disappeared: 2, increased: 3. The mean paired difference in BCVA comparing the two groups was -0.08 logMAR (p=0.46) and in the number of injections was 2.1 injections (p=0.04).

Conclusion Our study revealed that a substantial number of the studied patients showed reduction of the extent of the PED. The PED group required a greater number of injections compared to the control group.

• 3214

Long-term visual acuity in patients with age-related macular degeneration treated with ranibizumab and persistence of subretinal fluid

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Purpose To analyze the visual acuity (VA) in the long term in patients with age-related macular degeneration (ARMD) treated with ranibizumab with persistent subretinal fluid after induction therapy and / or in the follow-up.

Methods A retrospective study of all patients with ARMD treated with ranibizumab between January 2008 and April 2010 with persistent subretinal fluid for at least one year of follow-up after the induction therapy with ranibizumab. We reviewed the medical records, optical coherence tomography and fluorescein angiography in all patients included in the study.

Results 36 eyes of 34 patients were included in the study of a total of 216 patients analyzed.19 eyes (52.7%) had persistent and 17 (47.2%) recurrent sub-retinal fluid during the follow-up (mean 29.06 ± 9.28 months).The initial mean VA was 0.3 ± 0.2, at 3 months 0.43 ± 0.2 and at the end of the follow-up 0.41 ± 0.22 (p> 0.05).The appearance of bleeding in the relapse was associated with poorer final VA (p = 0.004).There was no significant difference in final VA in the membrane type, lesion size, presence of pigment epithelial detachment or blood before treatment.18 eyes (50%) remain on treatment with ranibizumab,16 eyes (44%) are observed and 2 patients died. We did not find differences in VA and central macular thickness between both groups.

Conclusion The persistence or recurrence of macular subretinal fluid in patients treated with ranibizumab did not significantly lower visual gain obtained after the induction therapy, despite the discontinuation of treatment during the follow-up.

• 3215

Association between hypovitaminosis D and age-related macular degeneration: a case-control study

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Purpose To examine the association of low serum 25-hydroxyvitamin D (25OHD) concentration with age-related macular degeneration (AMD).Based on a case–control study.31 patients with AMD (i.e., early, intermediate and advanced AMD) and 34 control patients without AMD were prospectively recruited.Ophthalmological examination, and funduscopic analysis was performed to determine AMD stage and serum 25OHD concentration was measured for each patient.

Methods Hypovitaminosis D was defined by serum 25OHD concentration < 50nmol/L. Age, gender and season of blood collection were used as potential confounders.

Results Compared to 28 subjects with normal 25OHD status (i.e., ≥50nmol/mL), subjects with hypovitaminosis D (n=37) had more often AMD (P=0.029) all stages confused. Hypovitaminosis D was associated with AMD (unadjusted odds ratio (OR)=3.10 with P=0.031; adjusted OR=3.03 with P=0.041 for full model; adjusted OR=3.10 with P=0.031 for stepwise backward model).

Conclusion Hypovitaminosis D may be associated with AMD.

• 3216

AMD and atherosclerosis coincidence: the role of complement system activation and endothelial dysfunction

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Purpose Age-related Macular Degeneration (AMD) shares several pathological and epidemiological similarities with systemic atherosclerosis (AS). There is considerable evidence implicating endothelial dysfunction in the pathogenesis of both disorders, and complement system (CS) activation appears to be a common denominator underlying those processes. It is widely recognised that both AMD and AS are not only related to local stimulation of the CS, but also result in its systemic activation.

Methods We recruited 77 subjects with clinical diagnosis of AMD and 46 age/sex–matched controls. The concentration of C3a-desArg complement compound,the number of circulating endothelial progenitor cells (EPCs) and circulating endothelial cells (CECs) was measured in the subjects' peripheral blood (PB).

Results We demonstrated increased numbers of CECs in the PB of AMD patients, a finding which reflects a severe vascular disturbance and clearly indicates that there is an endothelial alteration accompanying AMD. We also postulated that EPC enumeration could serve as a novel method for the assessment of AMD-related choroidal neovascularisation and demonstrated significantly elevated EPC counts in the PB of patients with the exudative form of AMD.We found that the levels of C3a-desArg were significantly elevated in plasma of exudative AMD patients compared to the control group. Additionally, the patients and controls with documented AS displayed significantly higher levels of C3a-desArg in PB compared to subjects without AS.

Conclusion We propose a linking hypothesis between CS activation, endothelial dysfunction and the pathogenesis of two common and age-related pathological processes, AS and AMD.(Grant-N N402 172137)

• 3217

Ranibizumab for the treatment of exudative age-related macular degeneration associated with retinal pigment epithelial detachment

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Purpose To evaluate the efficacy of intravitreal ranibizumab in eyes with exudative age-related macular degeneration associated with retinal pigment epithelial detachment.

Methods In this retrospective case series, patients with active exudative age-related macular degeneration associated with retinal pigment epithelial detachment were treated by repeated injections of intravitreal ranibizumab. The outcome measures were best-corrected visual acuity and the signs of lesion activity, as evaluated by optical coherence tomography.

Results Fifteen eyes of 15 patients were followed-up for a median of 6 months (range, 3-12 months). The median number of injections was 3 (range, 1-6). The best-corrected visual acuity improved in 8 eyes (53,4%), remained stable in 5 (33,3%), and decreased in 2 (13,3%).

Conclusion Intravitreal ranibizumab was effective in improving or stabilizing vision and resulting in a quiescent lesion in the majority of patients with exudative age-related macular degeneration associated with retinal pigment epithelial detachment. The functional results were apparently better in eyes without foveal involvement by the retinal pigment epithelial detachment..

• 3221

Looking at the ONH - pros and cons of vascular involvement in glaucoma

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The appearance of the optic nerve head of normal eyes, eyes with vascular optic neuropathies and eyes with glaucoma will be compared and potential hints for the pathogenesis of glaucomatous optic neuropathy will be discussed.

• 3222

Looking into clinical studies - pros and cons of vascular involvement in glaucoma

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Purpose To assess the strength of the evidence for ocular blood flow involvement in glaucoma.

Methods Because of lack of a large number of randomized trials, the assessment of the question must rely on case series and observational studies, and on the replicability of these studies.

Results Currently, evidence that measurement of blood flow can diagnose glaucoma or detect progression of glaucomatous disease is lacking, but several aspects are considered consensual, including low blood pressure association with preponderance and progression of POAG, altered OBF parameters, increased variability of OBF, and insufficient vascular autoregulatory response in glaucoma. It is unclear how much these features are independent from each other. Potential pathogenic keys are endothelial dysregulation and conditions with intermittent hypoxia such a sleep apnea.

Conclusion Designing a proper study may still be failing because of the difficulties in defining the pathogenesis and exact nature of OBF alteration in glaucoma. Nevertheless, the cumulative information makes it unlikely that blood flow has no role in glaucoma. Although evidence that measurement of blood flow supports a specific treatment recommendation for patients with glaucoma is lacking, it is of interest that some antiglaucoma drugs have a potential to protect blood flow in ocular tissues relating to glaucoma, while the effect of surgery remains unclear.

• 3223

Vascular reacitivty in glaucoma

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Today, several lines of evidence indicate that beside the classical risk factors such as increased intraocular pressure or family history, decreased ocular perfusion may contribute to the pathogenesis of the disease. In particular, a decrease in ocular blood flow may lead to ischemic events, which in turn may trigger ganglion cell loss and subsequent detoriation of visual field. Recent studies have indicated that instabilities of perfusion rather than a continuous decline of ocular perfusion may be an important factor in the pathogenesis of the disease. In healthy subjects, changes in ocular perfusion pressure are compensated for by an autoregulatory response of the ocular vasculature, in order to keep blood flow constant. This mechanism may be impaired in patients with glaucoma. Indeed several studies indicate that glaucoma patients showreduced vascular reactivity as induced for example by changes in ocular perfusion pressure or by increased metabolic demands. This talk aims to summarize different techniques to test vascular reactivity in humans and the data currently available for patients with glaucoma. In addition, possible pathomechanisms of impaired vascular reactivity will be discussed.

• 3224

The vascular aspect of glaucoma - what should we look at?

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Purpose Glaucoma is an optic neuropathy of unknown origin. Increased intraocular pressure is the most important risk factor for the disease. In addition, reduced ocular perfusion pressure has been identified as a risk factor for glaucomatous optic neuropathy.

Methods In a variety of studies we have focused on the complex interaction between intraocular pressure, mean arterial blood pressure, ocular perfusion pressure and ocular blood flow. In these studies various strategies were used to manipulate intraocular pressure, mean arterial blood pressure and ocular perfusion pressure and choroidal and optic nerve head blood flow were measured.

Results In vivo the capacity of choroidal and optic nerve head blood flow to regulate its vascular tone during changes in ocular perfusion pressure strongly depends on the way how perfusion pressure is manipulated. Generally ocular vascular beds regulate better during changes in blood pressure than during changes in intraocular pressure.

Conclusion With the improved understanding of ocular blood flow regulation in humans our understanding of perfusion abnormalities in glaucoma has also increased. Most importantly these studies show that any reduction in intraocular pressure has a strong impact on ocular blood flow regulation.

• 3231
Biomarkers and proteomics in corneal cell biology

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(3) Ophthalmology, NUS, Singapore

Purpose Developing a basis for personalized medicine requires instrumentation that has a high throughput and appropriate senstivity. To discover proteomic biomarkers of ocular surface diseases using quantitative mass spectrometry for discovery of molecular representatives within the tear film that can be used for clinical application and pharmacological development. Additionally, proteomics carried out by mass spectrometry provides a ready tool for use with quantitative biomarkers.

Methods Tear samples can be collected by several means, our lab usually uses type I Schirmer's test from patients and has been used successfully with patients with dry eye, pterygium or on anti-glaucoma medications as well as age-matched healthy unmedicated controls. Tear proteins are analyzed using iTRAQ (Isobaric tags for relative and absolute quantification) based quantitative proteomics or SELDI mass spectrometry. ELISA is used for confirmation of proteomic findings.

Results In dry eye patients, over 200 tear proteins have been identified. Potential biomarkers include up-regulated proteins, alpha-enolase, alpha-1-acid glycoprotein 1, S100 A8, S100 A9, S100 A4 and S100. In chronic glaucoma patients, 128 tear proteins were identified with 99% confidence. We found 5 proteins whose iTRAQ ratios showed significant changes ($p < 0.05$) when comparing non-medicated control group and medicated group. Levels of 4 tear proteins (S100 A8, S100 A9, mammaglobin B and 14-3-3 z/d protein) were elevated.

Conclusion Proteomic biomarkers provide new insights into the disease process as with the inflammatory S100 proteins found here and they are measurable end points for drug development, diagnosis and response to treatment. A biomarker panel for dry eye has been developed for patient use.

• 3232
Corneal epithelium in ocular pharmacology

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Purpose Corneal epithelium is the main barrier of ocular drug absorption form the tear fluid to the anterior chamber. The aim was to generate corneal epithelial cell culture model for drug permeability testing.

Methods Human corneal epithelial cell line was used and cultured on filters to build the model. The model was characterised in terms of permeability, electrical resistance, intercellular space, and gene expression of drug transporters and 11,000 other genes. Human corneal epithelium and rabbit cornea were used as positive controls.

Results The results indicate that the corneal epithelial model has similar morphology and permeability characteristics and intercellular space as the normal corneal epithelium. However, significant differences were seen in the gene expression patterns.

Conclusion Even though tight corneal epithelial organotypic culture model can achieve some features of the corneal epithelium, it deviates from the in vivo counterpart substantially. Thus the model has only limited utility.

• 3233
Replacement of corneal epithelium

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(2) Department of Eye, Ear and Oral Diseases, Tampere University Hospital, Tampere
(3) SILK, University of Tampere, Medical School, Tampere

Purpose Ocular surface reconstruction with cultivated oral mucosal epithelial transplantation technique has potential in the treatment of patients with severe ocular surface injuries. Currently, this technique is mainly based on utilization of xenogenic/allogenic components such as murine feeders, serum and amniotic membrane. The use of animal-derived materials possesses risk of pathogen transmission, immune reactions and graft rejection.

Methods The formation of stratified sheets by human oral mucosal epithelial cells under serum-free culture environment both in the absence and presence of fibroblast-conditioned culture medium and elevated epidermal growth factor concentration was examined. The integrity of the epithelium was measured by transepithelial electrical resistance. The tissue-engineered cell sheets were also studied for histology and immunohistochemical markers for epithelial keratins (K), cell proliferation and cell adhesion.

Results In all examined culture conditions, the cultivated oral epithelial cells formed a stratified tissue positive for keratins K3/12, K4, and K13. The tissue-engineered oral epithelia also expressed proliferation and progenitor markers Ki67 and p63 in the basal layer. The cultures presented expression of tight junction proteins ZO-1 and occludin and high transepithelial electrical resistance values.

Conclusion Tight multi-layered epithelium with proliferative potential can be produced from human oral mucosal epithelial cells under defined culture conditions and without the use of serum.

• 3251
An introduction to binocular vision & stereopsis. why 2 eyes are better than 1!

BARRETT BT
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Purpose In visual normals, covering one eye does not markedly alter central vision. However, having two eyes confers at least 2 advantages. 1. Binocular Summation: performance is generally better on tasks when both eyes are open; and 2. Stereopsis: the recovery of information about depth that results from disparity in the retinal images in the right & left eyes. Indeed stereopsis is usually considered to be the ultimate in binocular co-operation.

Methods The precise value of stereopsis remains somewhat controversial. Good stereopsis is highly valued by those who enjoy it and its loss due to trauma/pathology has a major negative impact. However, a significant minority of the population (>5%, many of whom have strabismus and/or amblyopia) have never had clinically measurable stereopsis and they appear to behave little different from visual normals in everyday tasks. If stereopsis is so valuable, why does its absence seemingly have so few consequences?

Results Here we examine the many facets of this conundrum, highlighting how, for example, many of those apparently without stereopsis when tested with standard clinical tests may in fact be capable of extracting depth-from-disparity information in lab-based testing. It also emerges that those with reduced/absent stereopsis do exhibit differences relative to normals on fine motor tasks. And, when asked, these individuals often report avoidance of, or poor performance in, tasks relying upon good stereopsis.

Conclusion As well as introducing the symposium presentations, this talk will summarise the recent research literature on the importance of binocular vision & stereopsis. This shows that, as in visual normals, 2 eyes are better than 1 in seemingly stereo-deficient individuals, but the binocular advantage is reduced.

• 3252
Development of binocular vision and implications for clinical testing

MCGRAW P
Nottingham

Purpose It is now clear that newborn infants are not a tabula rasa as once thought. Instead, they are born with the cortical circuitry required to process rudimentary visual information already in place. Early in life, these circuits are shaped by experience-dependent plasticity and a range of new visual abilities are brought on-line. Any disruption to normal sensory input can, and often does, result in marked functional impairment of binocular vision. A comprehensive understanding of the neurodynamics of binocular visual development is critical to determining how and why certain functions deviate from the developmental plan and the most appropriate ages at which these problems can be detected.

Methods The essential components of binocular vision are simultaneous perception of monocular images, fusion, oculomotor control and stereopsis. Each of these aspects has a distinct developmental trajectory and sensory and motor function must develop in concert to provide the neural basis for normal binocular experience.

Results Early in life, infants superimpose dichoptic images rather than alternating perception between eyes. Stereopsis has a sudden onset around 3-5 months of age and fusion develops at around the same time. Following the onset of stereopsis, disparity thresholds improve rapidly over a period of several weeks while at the same time inter-ocular differences in acuity decline.

Conclusion This talk will summarise research relating to binocular vision in early life, with an emphasis on the methods used to assess visual function and the factors that constrain the development of normal binocular vision. The implications for clinical testing in children will also be discussed.

• 3253
Assessment of BV & the more common anomalies of binocular vision

VAKROU C
D.Vakros Eye Clinic, Athens

Purpose Binocular vision is the co-ordination and integration of what is received from the two eyes separately into a single binocular percept. Simultaneous macular perception is the most elementary type of binocularity and represents simple sensory fusion. It occurs when the visual cortex processes separate stimuli from the two eyes at the same time and perceives them as a single image. However, true fusion occurs when both two images are fused, and some effort is made to maintain this fusion by adding a motor response. Finally these fused images of the two eyes are blended to produce a stereoscopic effect. Thus stereopsis involves a perceptual synthesis at a higher level.

Methods When investigating binocular vision we should aim at assessing the presence or absence of 1) simultaneous perception, 2) fusion with some amplitude and 3) stereopsis.

Results Here we examine the mechanisms of these conditions and how they reflect increasing levels of binocularity. Additionally, we will discuss the different clinical tests available to assess these conditions and what is observed when abnormal binocular vision is present.

Conclusion Understanding binocular vision and how there are different levels of processing is of great importance. This talk will try to assist on the understanding of the mechanisms of binocular vision and stereopsis so we can be in better position to understand the clinical findings of our patients and what they mean in terms of cortical processing.

• 3254
The impact of binocular vision disorders on 3D display viewing

STRANG NC
Vision Sciences, Glasgow

Purpose Recent advances in display technology have led to 3D display viewing becoming a commonplace activity. This exciting development has a number of implications for the vision science community. From a scientific point of view 3D displays allow us the opportunity to develop new types of tests to examine binocular function, while clinically a number of issues arise relating to visual symptoms and treatment.

Methods Here we review the range of methods employed to create a 3D viewing environment and discuss the advantages and disadvantages of these technologies from a binocular vision perspective.

Results We will summarise the recent research findings relating to the influence of 3D viewing on visual measures such as the AC/A and CA/C ratio and discuss how these changes may induce visual symptoms in certain patient groups. The impact of 3D viewing upon the visual system during the earlier stages of visual development will also be considered.

Conclusion Findings suggest that in the mature visual system 3D display technology may induce visual symptoms in patients with normally insignificant binocular anomalies. In the immature binocular vision system, consideration should be given to the possibility of developmental problems arising from prolonged 3D display viewing. However, continued advances in 3D display technology also offer great potential for the assessment and restoration of binocular vision in patients with binocular vision anomalies such as amblyopia and strabismus.

• 3255

Clinical assessment of binocular vision with the "ZEISS Polatest"®

KRESS C
Carl Zeiss Vision, Aalen

Purpose The "ZEISS Polatest", introduced in 1958, was the first instrument to allow a complete and precise assessment of binocular vision, including heterophoria. In this talk we give an overview about the history of for binocular vision testing using Polatest and its clinical application.We will highlight how binocular vision testing can be incorporated into the routine visual acuity measurement for every patient. The information gained allows us to provide better eye care for our patients in their day-to-day vision needs.

Methods The ZEISS Polatest uses polarized light to separate the information sent to the right and the left eye. In this way, binocular fusion can be controlled and the rest position of each eye can be determined precisely.We will review the technology used in the ZEISS Polatest for binocular vision testing and its evolution in the last 50 years. We will also present a review of the clinical literature related.

Results Modern binocular vision testing based on polarisation separation provides a superior and eficient way to screen and measure binocular vision deficiencies.

Conclusion With the widespread use of 3D entertainment many patients become aware of their binocular vision deficiencies which may have been asymptomatic before. This is leading to a renewed interest in binocular vision testing in clinical practice. Incorporating binocular vision screening into the regular screening protocol increases the quality of vision care for our patients.

Commercial interest

• 3261
Radiation induced optic neuropathy. Clinical presentation and treatment

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ABSTRACT NOT PROVIDED

• 3262
Irradiation induced maculopathy and retinopathy. Diagnosis and treatment

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Purpose To describe the pathology and clinical features of radiation-induced maculopathy and retinopathy and to discuss treatment.

Methods Direct maculopathy occurs when the macula has received a high dose of radiation whereas indirect maculopathy occurs as a result of exudation from the irradiated tumour. Investigations include: fluorescein angiography, optical coherence tomography and visual acuity testing. Treatments include: photoablation of leaking retinal vessels as well as transpupillary thermotherapy or photodynamic therapy, endoresection or exoresection of the exudative tumour.

Results Direct radiation-induced maculopathy is essentially untreatable but it is often possible to reverse visual loss occurring as a result of exudation from the 'toxic tumour.'

Conclusion It is important to differentiate direct from indirect radiation-induced maculopathy so that the appropriate treatment can be administered.

• 3263
Neovascular glaucoma anti-VEGF treatment

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Purpose To present the anti-VEGF treatment in neovascular glaucoma following proton beam irradiation in uveal melanomas.

Methods Prospective evaluation on 69 cases of iris neovascularisation and neovascular glaucoma treated with anti-VEGF intraocular injections.

Results Iris neovascularisation was classified as pupillary 26%, sectorial 16%, tuffts 15% and diffused 43%. A sectorial iris ischemia related to proton beam irradiation was present in 64% of the cases.Following an observation period of 6 months to 3 years a normalisation of the intraocular pressure (less than 20 mm Hg) was obtained in 84% of the cases. Regression of iris tortuosity was observed in 77% of the cases. Regression of the iris neovascularisation in 68 % of the cases and reduction of diffusion of the dye in 67% of the cases. A remodelling of the iris ischemia was observed in 32% of the cases.

Conclusion The intraocular injections of anti-VEGF drugs in selected cases is a promising therapeutic approach for the treatment of iris neovascularisation and neovascular glaucoma related to proton beam irradiation of uveal melanomas.

• 3264
Inflamation and scleral defect following ocular radiotherapy. Therapeutic approach

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(2) Radiotherapy, Paris
(3) Biostatistics, Paris

Purpose to describe inflammation and scleral necrosis following irradiation for uveal melanoma, their risk factors and their therapeutic approach.

Methods retrospective review of patients treated in Curie Institute; all the data concerning the initial tumor, the treatment and the follow up are registered in the data base .Statistical analysis has been performed.

Results Twenty-three patients treated with a single plaque therapy (cobalt-60 (Co(60)) or iodine-125 (I(125)) (1.5% of treated patients) or proton beam radiotherapy (0.45% of treated patients) for choroidal or ciliary body melanoma, presented scleral necrosis as a post-radiation complication .In a retrospective series of 2413 patients treated with proton beam with a median follow up of 98 months 21% of patients have had inflammation and 3,3% of them have active inflammation. Risks factors were essentially tumour related and were correlated with larger lesions (height > 5 mm, diameter > 12 mm, volume > 0.4 cm Multivariate analysis identified initial tumour height and irradiation of a large volume of the eye as the two most important risk factors.

Conclusion Treatment options: Scleral necrosis usually requires only observation Ocular inflammation often consisted of mild anterior uveitis, resolving rapidly after topical steroids and cycloplegics. Nevertheless for large tumors, inflammation can be associated with neovascular glaucoma and can be more severe. The use of anti VEGF is useful to obtain regression of iris néovascularíastion. Preventive endorésection of the tumor scar if possible gives the best results.

• 3265

The preservation of ocular surface following complete irradiation of the anterior segment

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Purpose Diffuse iris or ciliary body ('ring') melanoma is still considered an indication for enucleation. We perform proton beam irradiation of the whole anterior segment as an alternative, conservative treatment for these eyes with often good vision.

Methods Since 1992 we treated more than 70 patients with total anterior segment irradiation, 60 of whom presented primary diffuse iris and/or ring melanoma. We studied local tumor control, eye retention probability, final visual acuity, radiation induced side effects and their management.

Results Local tumour control was 100%. Three eye were enucleated. Vision was influenced by tumor and radiation induced side effects such as cataract, intraocular hypertension and ocular surface toxicity. Their management consisted of phacoemulsification, trabeculectomy, deep sclerectomy or tube surgery and preventive limbus deposition and reposition (LDR).

Conclusion Proton beam irradiation of the whole anterior segment is a safe alternative to enucleation in diffuse iris or ring melanoma. Management of actinic cataract, glaucoma and ocular surface toxicity through modern techniques is essential for maintaining the eye and a useful vision.

• 3271

Conjunctival autografts: indications and techniques

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In conjunctival autograft an autologous free conjunctival graft is obtained from the superior bulbar conjunctiva. It is then sutured to the sclera bed. This technique is widely used in pterygium surgery. In this case the graft is obtained from the same eye. It may also be obtained from an healthy fellow eye if previous surgery, limbal stem cell deficiency or scarring is present. With this common procedure, a very low rate of recurrence is observed in the treatment of pterygium. However a lack of understanding of the basic principles of this surgery can result in a poor outcome and frequent recurrences. In this presentation we will review together all the important steps required for a successful conjunctival autograft.

• 3272

Corneal epithelial limbal stem cell transplantation for ocular surface reconstruction

DUA H
Queens Medical Centre,, Nottingham

ABSTRACT NOT PROVIDED

• 3273

Corneal collagen cross linking: traditional vs transepithelial results with histopathological analysis

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Purpose To evaluate the effects of transepithelial corneal crosslinking (TE-CXL) on epithelium and stroma in human corneas

Methods Fifteen corneal buttons were examined. Ten were from patients with keratoconus submitted to penetrating keratoplasty (PKP). Five of them were treated with TE-CXL 2 hours before PKP, five of them were treated with TE-CXL 3 months before PKP. Five normal corneal buttons from healthy donors were used as controls. TE-CXL was performed with two different time of imbibition: 30 minutes and 2 hours.All samples were prepared for the detection of keratocyte apoptosis by TUNEL assay and for the morphological evaluation of epithelium and stroma by immunohistochemical analysis (Connexin 43, CD34).

Results Normal corneas exhibited no TUNEL positive keratocytes while keratoconus and crosslinked samples showed moderate apoptotic cells in the anterior part of the stroma. Moreover, the samples treated with TE-CXL 2 hours before PKP showed also an almost completely deteriorated epithelium with TUNEL positive cells. The epithelial positivity for connexin43 (transmembrane protein that forms gap junction channels) was similar in the control and in the corneas with crosslinking 3 months before PKP, while seemed more scattered in the keratoconus. In the samples treated with TE-CXL 2 hours before PKP the positivity was patchy in the few remained epithelial cells.

Conclusion The treatment with TE-CXL leads to epithelial damage and a reduction of keratocytes in the sub-epithelial region in the corneas treated 2 hours before PKP. In the samples treated with TE-CXL 3 months before PKP the positivity of both CD34 keratocytes and connexin-43 epithelial cells is similar to control.

• 3274

Amniotic membrane transplantation

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Purpose Aim of this presentation is to indicate current applications of amniotic membrane transplantation in corneal diseases and to describe, by means of in vivo imaging techniques, postoperative modifications of corneal tissue.

Methods Different indications for Amniotic Membrane Transplantation will be presented as clinical cases and literature review including corneal ulcers and perforations, persistent epithelial defect, bullous keratopathy. Surgical techniques and adverse events will be described and morphological changes of transplanted tissue and corneal profile will be analyzes by means of anterior segment OCT and in vivo confocal microscopy.

Results Amniotic membrane transplantation allows to obtain epithelial restoring, corneal sealing and stromal thickness recovery together with an antinflammatory effect on corneal tissue and reduction of pain. Transplanted tissue may be differently oriented and composed to obtain different effects on recipient cornea.

Conclusion Amniotic membrane transplantation is an useful surgical technique for managing of ulcerative corneal pathologies with or without perforation and epithelial defects. In vivo imaging diagnostic devices enable to visualize postoperative effects of transplanted tissue on recipient cornea in terms of morphology and tissutal modifications.

• 3275

New trends in endothelial transplantation: DSAEK vs DMEK

SCORCIA V
University of Catanzaro

ABSTRACT NOT PROVIDED

• 3276

Refractive and therapeutic applications of femtosecond laser corneal surgery

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Purpose Femtosecond laser (FSL) devices, based on the physical phenomena of ultrashort laser pulses in the sub-picosecond range of duration, have gained significant interest in ophthalmology thanks to their potential for high-precision microsurgery, particularly in applications involving the transparent tissue of the cornea that take the greatest advantage of these attributes. The potential advantages and limits in using FSL in the field of refractive corneal surgery and keratoplasty are presented.

Methods FSL is applied in performing LASIK flap, femtosecond laser lenticule extraction, deep lamellar (DALK), and DSEK lenticule preparation. Clinical and histological analysis was performed.

Results FSL LASIK procedures produced excellent clinical and morphological results, with great precision achieved in flap thickness and morphology. FSL refractive lenticule extraction enables the treatment of myopia and astigmatism without the use of the excimer laser. FSL technology enables multiple cut configurations and customized-shaped lamellar keratoplasty techniques. Transmission electron microscopy revealed precise geometry and good quality of the cuts.

Conclusion Femtosecond laser technology may offer further promising approaches towards all-FSL refractive surgery, and dissection procedures in the field of corneal transplantation

• 3311
Isolation and structural studies of native RPE and BM fluorophores

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Purpose To determine the chemical structure, fluorescence spectra and lifetimes and spatial distribution of the major retinal lipofuscin and Bruch's membrane fluorophores and to correlate their relative amounts with disease.

Methods Human RPE lipofuscin granules and Bruch's membrane explants were isolated from donor globes (Midwest Eye Banks and Transplantation Centers). The organic soluble portion was obtained by extraction with equal amounts of CHCl3:CH3OH:H2O, and the extract was analyzed by LC-MS (Thermo Finnigan, LCQ Advantage, Surveyor; Surveyor LC with fluorescence and PDA detectors, quadrupole ion trap mass analyzer, electrospray ion source). Fluorescence lifetimes were measured with a PTI Timemaster Lifetime analyzer. MALDI spatial distribution maps were imaged with an Applied Biosystems Voyager-DE Biospectrometry workstation.

Results Several derivatives, including higher molecular weight condensation products, of A2E have been isolated and structurally and spectroscopically characterized. A Bruch's membrane specific biomarker, nitro-A2E, has also been characterized and found to increase in concentration with both age and progression of AMD. These materials have unique fluorescence emission maxima and lifetimes and can be used with non-invasive diagnostic methods. The spatial distribution of these molecules yields information as to their origin.

Conclusion Knowledge of the fluorescence maxima and lifetimes of identified retinal fluorophores may allow for a more detailed interpretation of fundus autofluorescence. Of particular importance are the trends in concentration as a function of disease state.

• 3312
Spectral properties of the anterior segment of primates

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(2) Ophthalmology (Columbia University), New York

Purpose To determine the age related spectral properties of the anterior segment such as transmission and fluorescence and relate those changes to aging mechanisms and retinal imaging

Methods A simple method has been developed to determine the optical properties of the anterior segment of the intact eye. This consists of a probe which is inserted into the posterior sclera and detects light passing through the anterior segment. The probe is connected to a CCD spectrophotometer via a fiber optic bundle. Using this the absorptive properties of primate cadaver eyes were determined

Results A young primate anterior segment has a maximum absorption of 365 nm due to the beta-glucoside of 3-hydroxykynurenine (3-HKG) in the lens. This has a small transmission window to the retina centered at 320 nm, which closes up at around puberty. There is also a steep increase in transmission at wavelengths longer than 400 nm. With aging there is an increase in absorption throughout the visible (up to 550 nm) such that by the 6th decade only 20% of blue light is transmitted to the retina compared to the young primate eye. The increase in absorption is paralleled by an increase in fluorescence.

Conclusion Yellowing of the lens seems to be related to reactions of 3-HKG. The window of transmission at 320 nm in the young primate may explain the early increased rate of production of lipofuscin in the retina. The rate of lenticular yellowing is similar to the rate of lipofuscin formation in the retina from 20-70 years, suggesting that the amount of light absorbed by lipofuscin is constant over that span. The role of age related lenticular changes in retinal imaging will be discussed.

• 3313
Time resolved autofluorescence - a new diagnostic tool in ophthalmology

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Experimental Ophthalmology, Jena

Purpose The metabolic state can be characterized by endogenous fluorophores. Excitation- and emission spectra as well as the decay of fluorescence intensity after pulse excitation characterize endogenous fluorophores and can be used for determination of fluorophores.

Methods Based on measurements on pure fluorophores and on isolated anatomical structures of porcine eyes, a laser scanner ophthalmoscope was developed for detection of time-resolved auto-fluorescence in two spectral ranges (490-560 nm and 560 – 700 nm). The 3-exponential fit approximates optimally the decay of fluorescence intensity.

Results Sections in OCT and in lifetime images show good correspondences between retinal pigment epithelium and the component with the shortest decay (1=60-80 ps) and between the neuronal retina and the component with the mean decay time (2=450-500ps). The component with the longest decay time (3= 2.5-3 ns) is determined by the fluorescence of the crystalline lens and of connective tissue. In early AMD, arterial branch occlusion, and in diabetes, when no signs are visible for diabetic retinopathy, most significant alterations are detectable for 2 in the spectral range 490-560 nm. Comparing histograms of 2 for healthy subjects and well controlled diabetic patients, a lack of a fluorophore with decay time of 380 ps is present in diabetes. Free NADH has such a lifetime. Furthermore, an accumulation of advanced glycation end-products is detectable in the crystalline lens of diabetic patients.

Conclusion Fluorescence lifetime enables functional metabolic diagnostics at cellular level.

• 3314
Quantitative autofluorescence measurements

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Demarest

Purpose Technology for quantitative measurement of fundus autofluorescence (AF).

Methods Scanning laser ophthalmoscopes (SLO's, HRA2 and Spectralis, Heidelberg Eng.) were modified by insertion of an internal AF reference to account for variable laser power and detector sensitivity. 30° images (mean of 9 without histogram stretching) were acquired from normal test subjects (10-60 y/o) after a 20 s bleaching period,.. Quantified AF (qAF) was calculated from the reference gray level (GL), the zero GL, the media and the magnification (refractive error). The linearity of the system, field uniformity, effect of refractive error, and reproducibility were tested. qAF measurements were then done on 22 patients with Stargardt disease (STGD) and 11 patients with retinitis pigmentosa (RP).

Results The linear detection range extended to 175 GL. Field uniformity was better than 5% in a central 20°-diameter circle. The recorded AF and the square of the image magnification were inversely related. Different day reproducibility was 4.1 % at the fovea. Median inter-instrument reproducibility (Spectralis and the HRA2) was 7.4 %. Normals. qAF highly correlated with age (central qAF = 8.8+3.5*Age, p<0.00001). STGD. Background levels of qAF were elevated up to 4 times age-matched controls; fleck levels were twice background. RP. HyperAF rings had significantly higher levels than controls and correlated with inner segment/outer segment junction loss.

Conclusion Modified SLO instrumentation and analytic methods that account for optical media density and refractive error allow non-invasive, in vivo quantitative AF measurements (total lipofuscin fluorescence) relative to a fixed internal standard in normal subjects and patients with retinal degenerations to monitor disease progression and response to therapy.

• 3315
Dual-wavelength "color" autofluorescence

HAMMER M
Jena

Purpose To distinguish fluorophores at the human ocular fundus by their different emission spectra.

Methods Autofluorescence images were taken from 62 eyes (78.3±6.3 years) with age-related macular degeneration (AMD), 65 eyes (71.2±8.4 years) with diabetic retinopathy (RD), and 19 eyes (60.7±18.3 years) without any ophthalmic or systemic pathology (control group) by a fundus camera. All eyes were pseudophacic. A 3-chip color CCD camera was used as detector, recording the fluorescence in two separate spectral bands: Upon excitation at 475-515 nm, fluorescence was observed at 530-570 nm and 570-675 nm. For a global estimation of the fluorescence characteristics, the ratio of the green vs. the red emission (g/r) was calculated in a 70 by 70 pixel area temporal to the macula and apart from pathologic lesions and retinal vessels. Local changes of fluorescence emission spectra were assessed.

Results An orange fluorescence was found in the control group. Compared to that group (g/r=0.869±0.073), the global fundus fluorescence of AMD-patients (g/r=0.906±0.105) and diabetics (g/r=0.974±0.119) was green-shifted. This shift was statistically significant (t-test, p=0.001) for the RD and the control group. The optic disc, hypo-fluorescent atrophic areas (geographic atrophy, laser scars), hyper-fluorescent drusen, and lipid exudates appeared greenish.

Conclusion The ocular fundus autofluorescence is dominated by the orange fluorescence of lipofuscin. The green-shift of the fluorescence in AMD and RD may indicate protein glycation since advanced glycation end products show green fluorescence. Greenish fluorescence of drusen and exudates reveal non-lipofuscin fluorescence which needs further clarification. Color autofluorescence visualizes different fluorophores and, thus, may be of diagnostic merit.

• 3316
Differences in fundus autofluorescence in clinical practice

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(2) Coumbia University, New York
(3) New York University, New York

Purpose Fundus autofluorescence (AF) has become a standard imaging test for evaluating retinal disorders such as age-related macular degeneration, hereditary, and inflammatory conditions. Little attention has been given to the influence of technical specifications of individual imaging devices and their potential influence on the studies obtained.

Methods AF was recorded using a Heidelberg confocal scanning laser ophthalmoscope (cSLO) with 488 nm laser exciter (488 nm-AF), and a conventional Topcon fundus camera with halogen lamp exciter and 580 nm band-pass filter (580 nm-AF). Images of patients with various macular conditions were obtained and compared.

Results The autofluorescent signal is largely believed to derive from lipofuscein in the retinal pigment epithelium (RPE) and to represent a correlate of cellular metabolic activity. However, while images of geographic atrophy appeared to be rather comparable, significant differences were noted in patients with central serous chorioretinopathy, rip of the RPE and cystoids macular edema. It has been hypothesized that macular pigments (MPs) and more precisely changes of MPs density account in part for the differences, as MPs block 488nm-AF more intensely than 580nm-AF.

Conclusion Fundus autofluorescence images obtained with different imaging systems may not be interchangeable depending on the exciter and band-pass filters used. Caution has to be taken when comparing diagnostic or therapeutic findings on AF from imaging devices with different specifications

• 3321

Dhea analogue neuroprotection in an experimental model of retinal detachment

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Purpose To evaluate the neuroprotective activity of a new synthetic analogue of Dehydroepiandrosterone (DHEA) in an experimental model of retinal detachment (RD).

Methods Sprague Dawley rats underwent a retinal detachment in their right eye under deep anesthesia while the left eye was served as a control. Animals were dived into three groups and injected with the synthetic DHEA analogue. The analogue can be detected in the rat retina after intraperitoneal injection. Animals received intraperitonealy 10 mg of the analogue diluted in 70 ul of ethanol in a total volume of 1 ml WFI per animal. In the first group the injections were administered after RD while in the other two groups (group 2 and 3) a pretreatment was utilized starting 7 days before RD (every day and every second day, respectively). The animals were sacrificed three days after RD, the eyes were enucleated and prepared for TUNEL labeling and confocal microscopy.

Results Morphological analysis revealed that the phenotype is rescued when the administration of the analogue begins before retinal detachment, with only a few cells labeled positive after TUNEL staining in groups 2 and 3. Administration of the drug only after the retinal detachment (group 1) seemed to have less anti-apoptotic effect.

Conclusion Our results suggest that this molecule may prove to be anti-apoptotic in retinal detachment induced apoptosis. Further investigation is required for the most efficient treatment and drug dosage in several time points of the apoptotic process.

• 3322

Retinal bioavailability of a DHEA synthetic analog after intraperitoneal administration in the Sprague Dawley rat

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Purpose To evaluate the retinal bioavailability of a synthetic Dehydroepiandrosterone (DHEA) analog, a molecule with potential anti-apoptotic action, after systemic administration.

Methods 25 Sprague Dawley rats were injected intraperitoneally with 10 mg of the analog in1 ml of an ethanol/Water For Injection (WFI) solution. The synthetic neurosteroid was injected in 3-5 rats at each time point at the same concentration every time. The animals were euthanized at 15, 30 min and 1, 2, 4, 6 & 24 hrs. The eyes were enucleated and the retina was isolated from the eye cup with an eye sponge with suitable handling. After appropriate preparation, the samples were measured with HPLC LC/MS.

Results The recovery of the method was 91.4%. The Limit Of Quantification (LOQ) was 0,05 ng/mg. The substance was detected at 30, 60, 120 and 240 min in mean concentrations of 0.10 ng/mg, 0.42 ng/mg, 0.91 ng/mg & 0.17 ng/mg respectively. No substance was detected with this method at 15 min, 6 & 24 hrs. No substance was detected in all blind samples

Conclusion The synthetic DHEA analog was successfully detected in the rat retina with an LC/MS HPLC method. The molecule seems to reach the retina in thirty minutes after systemic administration and is still detected there after four hours. Further investigation is obligatory for complete data of the pharmacokinetics of the substance in the rat retina.

• 3323

Topical application of AMA0076, a locally acting rho kinase (ROCK) inhibitor, results in a robust IOP control in a hypertensive rabbit model

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Purpose To elucidate the IOP lowering effect of the local ROCK inhibitor, AMA0076, in the rabbit eye.

Methods An ocular hypertensive rabbit model, based on the intracameral injection of visco-elastic material, has been developed to determine the IOP lowering effect of compounds acting to improve aqueous humor outflow. Using this model, the IOP lowering effect of AMA0076 was tested and compared to Y-39983, Latanoprost and Bimatoprost (5 rabbits/compound).

Results Topical administration (TID) of AMA0076 prevented the IOP rise induced by the injection of visco-elastics in a dose dependent manner (overall $P<0.0001$). Treatment with AMA0076 0.3% completely prevented the rise in IOP (overall $P<0.0001$). Administration of Y-39983 0.3% significantly reduced (but did not completely abolish) IOP rise in the hypertensive model compared to the control eye (overall $P<0.0001$). A more subtle IOP decrease was also observed in the control eye with this non-local ROCK inhibitor, presumably due to the systemic absorption of Y-39983. AMA0076 was significantly more potent in blocking the IOP elevation in the hypertensive model compared to Latanoprost and Bimatoprost (respectively overall $P=0.0004$; $P=0.0003$).

Conclusion The local ROCK inhibitor AMA0076 lowers IOP in an efficient manner in an acute rabbit model for ocular hypertension, with a potency exceeding that of the non-local ROCK inhibitor Y-39983, as well as the prostaglandin analogues Latanoprost and Bimatoprost. In summary, the present data indicate that this new class of ROCK inhibitors has potential therapeutic value for the treatment of glaucoma through a novel IOP lowering strategy.

• 3324

Effect of anti-VEGF drugs and steroids on the inner blood-retinal barrier, after experimental BRVO in rats: preliminary results

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Purpose To evaluate the effect of anti-VEGF drugs and steroids on the inner blood-retinal barrier (BRB) function after experimental branch retinal vein occlusion (BRVO) in rats. The integrity of the barrier is related to the expression of occludins by retinal endothelial cells.

Methods Laser photocoagulation was applied to retinal veins of the right eye of 4 Long-Evans rats, to induce BRVO. The left eye was used as control. One day after the occlusion, the right eye of each animal was injected intravitreally with either bevacizumab (n=2) or triamcinolone (n=2). The animals were sacrificed 7 days later; all retinas were harvested and prepared for indirect immunohistochemistry, using an anti- occluding primary antibody. The specimens were examined using a confocal microscope and images were acquired.

Results In normal retinas, occludins appeared as a dense, well-organised, fluorescent reticulum along the vascular wall. In eyes with BRVO, the structure of occludins was disrupted; irregular linear fluorescence appeared along occluded veins, while absence of fluorescence suggested down-regulation of occludin expression. Occludin distribution was improved in animals having received treatment post BRVO.

Conclusion The administration of bevacizumab and triamcinolone post BRVO seems to improve the function of the inner BRB. This could explain macular edema reduction after the use of these drugs. These preliminary results are part of an ongoing experiment, which will include the use of combination therapy in the management of BRVO.

• 3325

Cytoarchitectonic and apoptotic consequences after intravitreal octreotide injection in an oxygen induced retinopathy mouse model

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Purpose To evaluate the cytoarchitectonic and apoptotic consequences after intravitreal Octreotide acetate (OA) injection in different concentrations in an oxygen induced retinopathy (OIR) mouse model.

Methods A total of 26 of C57BL/J6 mice were exposed to 75±2% oxygen from postnatal day 7- 12. On day 12, 12 mice (group-C) were injected with 0.1microg intravitreal Octreotide acetate (IVOA), 14 mice (group-D) were injected with 0.05microg IVOA in right eye. The contralateral eyes were injected with isotonic saline (control group, group-B). Four age-matched mice, maintained in room air, were used as negative controls (group-A). Neovascularization was quantified by counting the number of retinal vascular endothelial cell nuclei anterior to the inner limiting membrane. Cytoarchitectonic changes were examined by light and electron microscopy. Apoptosis was investigated using TUNEL technique.

Results Endothelial cell nuclei count was lower in groups C ($p<0.0001$) and D ($p<0.0001$) compared with group-B. Light microscopy showed no retinal toxicity in any group. Electron microscopic cytoarchitectonic evaluation revealed mitochondrial damage in the inner segment of the photoreceptors in OIR mouse model without increasing in IVOA injected groups. There was no significant increasing apoptotic cell death in the IVOA injected groups.

Conclusion Intravitreal injection of OA may be a potential treatment of proliferative retinopathies.

• 3326

Ghrelin and obestatin decreases the IOP in a acute glaucoma model

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Purpose The aim of this study is to evaluate the effect of the pro-ghrelin derived peptides in the intra-ocular pressure in animal models of acute glaucoma.

Methods The first part of the experimental protocol was the calibration of the Tonovet® used to measure the IOP. In the second part of the protocol we studied, in a rabbit model of acute glaucoma, the effects of ghrelin (10-4M, n=6), des-acyl-ghrelin (10-4M, n=7) and obestatin (10-4M, n=7), as well as the subcellular pathways involved. This model was achieved with an intra-vitreal injection of 20% NaCl. Then, one of the three peptides was sub-conjunctivally injected. Concerning the subcellular pathways, keterolac (a COX inhibitor; 30mg/ml; 500microl; n=7) and L-NAME (a NO synthase inhibitor; 150mg/Kg; 500 microl; n=11) were sub-conjunctivally injected previously to both NaCl and ghrelin injection. All the results were compared to a control group which did not receive ghrelin, des-acyl-ghrelin or obestatin.

Results There is a linear correlation between the IOP measured by the Tonovet (Y) and its real value (X), being that underestimated ($Y= -0,331 + 0,750X$). Our results show that the NaCl injection increases the IOP from 9.9 ± 1.9 to 44.9 ± 4.1. After that ghrelin promotes a decrease of 20,8 ± 5,0 mmHg (decrease of 47,9 ± 11,6%); obestatin promotes a maximal decrease of 15,8 ± 3,9 mmHg (decrease of 37,5 ± 9,4%), while des-acyl-ghrelin does not significantly change IOP. When keterolac or L-NAME are added, ghrelin's effect is completely blunted.

Conclusion Ghrelin showed to promote a decrease of the intra-ocular pressure, independently from GHSR-1a and dependently on NO and prostaglandins. Obestatin also promotes a decrease in the IOP.

• 3331

SOCS1 gene overexpression in the retinal pigment epithelium during experimental autoimmune uveitis

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Purpose Autoimmune uveitis is a non-infectious, inflammatory intraocular disease affecting predominantly patients in the working age group. Actually available treatment including corticosteroids and/or immunomodulating agents, often leads to serious side effects. In order to explore new therapeutic attitudes, we propose a project to investigate both in vitro and in vivo a potential beneficial role of Suppressors of Cytokine Signalling (SOCS1) overexpression in controlling autoimmune uveitis.

Methods In the in vitro part, using stable transfection, we will test the effect of SOCS1 overexpression on the activation of on the retinal pigment epithelium (RPE) by different cytokines important in experimental autoimmune uveitis (EAU) development: IFN gamma, TNF alpha, IL-17 and IL-22. In the in vivo part, intraocular injections will be used to deliver adeno-associated viruses (AAV) vectors containing or not a SOCS gene to the subretinal space. The aim of the in vivo part is to study the effect of SOCS1 overexpression in RPE cells on the development of uveitis. Three experimental autoimmune uveitis (EAU) models will be tested: classical EAU, adoptive transfer of non-manipulated autoreactive T lymphocytes and adoptive transfer of Th1/Th17 polarised autoreactive lymphocytes.

• 3332

Glaucoma from eye to brain: are MMP-2 and MMP-14 involved?

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Purpose 1) To visualize the timescale of pathological changes from eye to cortex in a mouse glaucoma model.2) To investigate the involvement of MMP-2 and MMP-14 in the pathophysiology of glaucoma throughout the mouse visual system.

Methods Mice will be subjected to experimentally induced glaucoma through monocular injection of microbeads. A detailed characterization of this model will be performed via histological analysis of the visual system, and the survival of RGCs will be analyzed by stereotactic tracer injections. We will examine the retina and its target structures for changes in macro- and/or microglial reactivity using specific cellular markers, and changes in neuronal activity in the brain will be charted via evaluation of the expression of the activity reporter gene Zif268.Second, the spatiotemporal expression pattern of MMP-2 and MMP-14 in the retina and its target structures in the brain will be determined after the induction of glaucoma, by means ofRT-PCR, Western blotting, activity assays, immunohistochemistry and zymography. The in vivo involvement of MMP-2 and MMP-14 in the pathophysiology of glaucoma, will be evaluated in wild type and MMP deficient glaucomatous mice. In addition, their in vivo function will be studied via intravitreal injections with specific MMP inhibitors/ antibodies.

Conclusion Glaucoma is increasingly recognized as a disease with effects beyond the eye/retina. Therefore, unraveling the influence of chronic hypertension on the neuronal circuitry from eye to cortex will contribute to a better understanding of glaucoma as a disorder of 'visual neurons' within the eye and brain and may encourage comprehensive treatment strategies to prevent vision loss.Moreover, we will define the potential roles of MMP-2 and MMP-14 during glaucoma disease progression.

• 3333

Regulation of adhesion molecules in EAU

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Purpose Auto-immune uveitis are a group of diseases characterized by the accumulation of immune cells in the eye tissues. These diseases are one of the main cause of blindness in developed countries. The toxicity and the weak specificity of the usual therapy have led to intensive research in the field of immunotherapy. These new therapies target whether effector cells of uveitis or cytokine produced by these cells or adhesion molecules which allow their penetration in eye tissues. Indeed, no cells can reach intraocular tissues without adhesion molecules. At the physiological state, the eye is isolated by a blood-retinal barrier which separates the systemic circulation of the neuroretina. Inflammatory signals lead to the expression of adhesion molecules on BRB cells. The adhesion molecules allow immune cells recruitment and thus play a crucial role in the breaking of the BRB and auto-immune uveitis development.

Methods In order to study the role of adhesion molecules in uveitis we want to first characterize the retinal expression of adhesion molecules during EAU. EAU will be classically induced in C57BL6 mice, and the expression of ICAM1, ICAM2, VCAM1, and selectine molecules studied by immunofluorescence. The respective roles of Th1 and Th17 lymphocytes on the induction of adhesion molecules on the surface of the BRB will be next addressed by adoptive transfer of retinal specific autoreactive lymphocytes Th1 and Th17 cell lines. Cell lines will be first characterized by their cytokine production, transcription factor and adhesion molecules expression. Those T cells will be next transferred in naïves mice, uveitis induction analyzed by clinical grading and histological scores and expression of adhesion molecule evaluated by immunofluorescence.

• 3334

Evaluation of Cyclosporine ocular dosage forms in an in vivo mouse model

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Ocular delivery of Cyclosporine A (CyA), used in the treatment of dry eye syndrome, requires new concepts in order to optimize the bioavailability and its therapeutic effect. In our laboratory, CyA was formulated in positively charged nanoparticles, using chitosan or Eudragit®, in order to increase the residence time of the carriers in the cul-de-sac. These nanoparticles will be added to muco/bioadhesive films in order to facilitate their administration. The aim of the project is to investigate films as delivery system for nanoparticle preparations. In vitro drug release, swelling properties, film flexibility and the effects of gamma-sterilization on the drug delivery systems characteristics will be studied and a selection of films with required properties will be carried out. The influence of the preparation conditions of the drug delivery systems on the biological activity of CyA will be evaluated by performing in-vitro experiments on Concanavalin A stimulated Jurkat T cells with IL-2 secretion as biological read-out. The most suitable preparations will be selected for an in vivo study using a mouse model that has been described by Lin et al (2011, Mol Vis 17: 257-264) where a 0.2% benzalkoniumchloride solution is instilled twice a day in the eye of mice for 7 consecutive days. Tear production and epithelial damage will be monitored by cotton thread test and corneal fluorescein staining and/or rose bengal respectively. Assessment of inflammatory cytokines in tear fluid will be performed using cytometric bead assay. The films selected should decrease the amount of inflammatory cytokines in tears as well as decrease signs of epithelial damage.

• 3335

The role of local rock-inhibition in the pathogenesis of age-related macular degeneration

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Purpose Age-related macular degeneration (AMD) is the leading cause of visual loss in the elderly. ROCK inhibition may be a new way to treat angiogenesis-related disorders, such as AMD correlated with choroidal neovascularization (CNV). The use of the ROCK-inhibition might have a therapeutic potential to inhibit angiogenesis, fibrosis and inflammation without causing severe side effects. This project will investigate the anti-angiogenic, anti-inflammatory and anti-fibrotic efficacy of ROCK-inhibition in a mouse model of CNV.

Methods Three laser spots of 50µm will be placed with a 532nm green laser around the optic disc of C57BL/6J mice. Mice will be divided into two major experimental groups. In one group the ROCK-inhibitor will be compared to a control solution (vehicle); in the other group one eye will be injected with the murine anti-VEGF Ab and the other eye with an irrelevant mouse Ab. All solutions will be injected intravitreally on day 0, 4 and 10. Mice will be sacrificed on different time points after lasering. The effects of the ROCK-inhibitors will be checked on day 5 (inflammation), day 14 (angiogenesis) and day 35 (fibrosis). Expression of ROCK and VEGF in choroid and retina will be determined using quantitative real-time RT PCR. Expression of ROCK-1 and ROCK-2 at the protein level will be confirmed by Western Blot.

Conclusion AMD is the major cause of irreversible blindness worldwide. It is already known that ROCK is associated with VEGF-driven angiogenesis. Therefore, the aim of our project is first to investigate the therapeutic potential of ROCK-inhibitors with a local mode of action in the pathogenesis of CNV.

• 3341
Management of thyroid dysfunction in Graves' orbitopathy

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Graves'Orbitopathy (GO), generally associated with hyperthyroidism, may develop also before or after the onset of hyperthyroidism, or even in hypothyroid Hashimoto's patients. The course and treatment modalities/outcomes of the thyroid disease may alter GO expression and severity. Restoration of euthyroidism with antithyroid drug (ATD) usually improves ocular conditions. However, recurrence of hyperthyroidism after ATD withdrawal, may favour GO progression. Therefore, radical treatment with radioiodine (RAI) or thyroidectomy, should be considered in relapsing patients with GO.RAI leads to a progression of GO in 15-37% of patients. Several factors are predictive: a) pre-existing 'active' GO, b) severity of hyperthyroidism, c) high serum TSH-R Ab levels, d) cigarette smoking and e) occurrence of uncorrected post-radioiodine hypothyroidism with elevated serum TSH. Progression of GO can be prevented by glucocorticoid (GC) therapy, 0.5 mg/Kg BW initially gradually withdrawn over 10-12 weeks. In patients with inactive GO nor other risk factors, GC coverage is not necessary. In patients with 'moderate-severe and active GO,' if radical treatment with RAI is indicated, GO should be treated concomitantly with iv GC and/or orbital radiotherapy.Thyroidectomy is 'neutral' for GO. Total thyroid ablation (total thyroidectomy + RAI) might even be beneficial for GO. Iatrogenic hypothyroidism, whatever the treatment, is a significant risk factor of occurrence or progression of GO which warrants close control, and prompt correction, of thyroid function during ATD or after radical treatment.In conclusion, learned treatment strategy and close management of thyroid function are mandatory in Graves' disease patients. In patients with GO, the combined endocrinological-ophthalmological approach is the prerequisite for efficient global management.

• 3342
Management of mild and moderate Graves' orbitopathy

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Purpose Management of Graves orbitopathy (GO) varies according to the level of its activity and its severity.For the activity evaluation, although no method is both specific and completely reliable, a simple office-based tool is the Clinical Activity Score, which reflects the presence or absence of symptoms and signs that indicate inflammation. In addition, the severity of disease should be assessed by measuring exophthalmos, lid width, evaluating soft-tissue involvement and extra-ocular muscle function, and assessing corneal involvement and optic-nerve involvement. Features of mild and moderate to severe GO will be presented.

Results Specific treatments for GO vary depending on the severity of the disease.Mild GO usually does not require any treatment except for local measures (ex lubrificants, ointments, dark lenses, and prisms to to reduce diplopia).However, in some patient quality of life is so impaired that treatment such as that for more severe GO might be suggested. Regular follow-up every 3-6 months is recommended, since progression of GO is observed in about 25% of the pats.Patients with moderate to severe with active disease (CAS>/=3) should be treated with immunosuppressive treatment modalities, while those with inactive GO may benefit from rehabilitative surgery.

Conclusion The treatment of choice for moderate to severe GO is IV glucocorticoids +/- orbital radiation therapy, if GO is inactive, surgery as orbital decompression and /or squint surgery and/or eyelid surgery

• 3343
Dysthyroid optic neuropathy: diagnosis and treatment

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Optic neuropathy is a rare complication of dysthyroid orbitopathy (incidence < 5%). Its onset is often insidious and progression is frequently slow. However it is mandatory to recognize it early as it is a potentially blinding but treatable condition.At the end of the presentation, participants will be able to recognize the various clinical features of dysthyroid optic neuropathy, decide which diagnostic procedures is necessary to establish the diagnosis, understand the underlying physiopathologic mechanisms, and choose amongst the therapeutic options.

• 3344
Radiologic features of inflammatory versus tumooural orbital diseases

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To propose guidelines for analysis and interpretation of orbital imaging studies (CT and MRI) in order to help the ophtlamologist in the differential radiological approach between oncologic versus inflammatory orbital disorders.

• 3345

Clinical cases

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Clinical cases will be presented.

Commercial interest

• 3351

Glaucoma of the brain: a disease model for the study of transsynaptic neural degeneration

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ABSTRACT NOT PROVIDED

• 3352

Abnormal retinal vascular function and cognitive loss in Alzheimer's disease patients

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Purpose To identify signs of abnormal retinal vascular function and their relationship to cognition deficits in newly diagnosed mild AD patients

Methods Retinal arterial and venous reaction times to flickering light were assessed in 10 AD patients and 28 age-matched healthy individuals by means of Dynamic Vessels Analysis (DVA). Minimental state examination (MMSE) and Addenbrooke's Cognitive Examination-Revised (ACE-R), as well as blood pressure measurements and blood analyses for lipid metabolism markers were also performed in patients and controls.

Results AD patients demonstrated differences in their vascular reaction times to repeated cycles of flicker exposure at the retinal arterial level compared with healthy controls, which correlated with the degree of the patients' cognitive impairment at the time of the test

Conclusion It proposed that a simple screening of the retinal vascular function could offer valuable information about risk for future vascular complications as well as progressive cognitive decline in newly diagnosed patients suffering from mild AD.

• 3353

Quantitative assessment of the visual pathway by MRI-DTI

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ABSTRACT NOT PROVIDED

• 3354

Impairment of 4th neuron axons correlates with retinal nerve fiber loss in glaucoma

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Purpose In glaucoma damage of retinal ganglion cells may continue to the linked optic radiations (OR). This damage may concern the axonal integrity as well as demyelination or glia cell impairment. This study investigated measures of axonal demyelination, i.e. radial diffusivity (RD), in the optic radiation of glaucoma patients. The results were correlated with the homonymous retinal nerve fiber layer thickness (RNFL).

Methods Fourteen control subjects (mean age, 52.0±11.7 years) were age-adjusted to 12 patients with normal tension glaucoma (NTG, mean age, 58.3±9.5 years; p=0.157) and 18 patients with primary open angle glaucoma (POAG, mean age, 55.7±7.3 years; p=0.296). The control subjects had eye diseases without neuronal participation. All subjects underwent magnetic resonance (MR) tomography-based diffusion tensor imaging (DTI) of the optic radiation and eye examination by the Spectralis optical coherence tomography. MR images did not show cerebral space occupying lesions along the visual pathway. The optic radiations in the DTI were outlined semi-automatically and the mean values of FA and RD of both OR's were measured. The homonymous RNFL thickness corresponding to the respective OR was calculated.

Results If corrected for age, gender, and diagnosis groups (control, NTG, POAG) partial correlation analysis disclosed a correlation between RD and the RNFL thickness (right OR: r=-0.350, p=0.025; left OR: r=-0.478, p=0.002).

Conclusion In glaucoma DTI-derived parameters of axonal integrity and demyelination of the optic radiation (4th neuron) are suggested to change with decreasing retinal nerve fiber layer thickness (3rd neuron), i.e. with increasing glaucoma severity.

• 3355

Retinotopic organisation of primary visual cortex in glaucoma: a fMRI study

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ABSTRACT NOT PROVIDED

• 3356

Neuroprotection of the visual pathway in glaucoma - is there a future role?

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ABSTRACT NOT PROVIDED

• 3361

Proteomic analysis of aqueous humor in retinoblastoma: a preliminary approach

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Purpose Compare the basic protein composition of the aqueous humor from retinoblastoma (RTB) patients with aqueous humor from patients with cataract who served as controls.

Methods The study was carried out on 18 hospitalized RTB patients, who had undergone ocular enucleation (Reese-Ellsworth stage V or ABC classification group E RB), and 10 cataract patients. Five out of 18 RTB patients presented with associated secondary glaucoma and 5 out of 13 with no secondary glaucoma received chemotherapeutical treatment with Melphalan. The total protein concentration and electrophoresis pattern (SDS PAGE) of the aqueous humor was analysed.

Results The aqueous humor from RTB patients had significantly higher total protein concentrations than controls ($p<0.01$); patients with secondary glaucoma presented with the highest total protein concentrations, and they were significantly different from controls ($p<0.05$), while those treated with Melphalan presented a 70% decreasing in protein concentration and, in respect to all non-treated patients, were significantly different ($p<0.01$). Besides, the protein content of controls was not significantly different from treated patients. The SDS PAGE pattern of RTB patients was very different from controls; yet, after chemotherapeutical treatment, patterns were similar.

Conclusion This study represents a preliminary step towards a more accurate 2DE pattern, which will be combined with mass spectrometry analysis to clarify the potential role of specific proteins in tumor development and progression; although this results suggest that aqueous humor protein pattern in RTB is characteristic, several aspects of the study are still under investigation.

• 3362

ERK activation and monosomy 3 are associated with Src expression in uveal melanoma and may serve as biomarkers for dasatinib treatment

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Purpose Uveal melanoma (UM) leads to metastasis in up to 50% of the patients. Patients at risk are readily identified using an array of prognostic markers but an effective treatment is lacking. We recently identified Src as an important tyrosine kinase that conveys MAPK activation in UM. GNAQ/GNA11 mutations are the common denominators of oncogene signalling in UM and Src is a likely downstream kinase. We describe the preclinical analysis of Dasatinib, a known inhibitor or Src kinase, in UM.

Methods Eight tumours were removed, cultured and exposed to Dasatinib treatment. proliferation and MAPK signalling were evaluated. Additionally, 36 UM samples were analyzed for Src/ERK signalling, GNAQ/GNA11 mutation status, chromosome 3 and known histological prognostic parameters.

Results Growth arrest was observed in 5 of 8 UM cultures and molecular analysis indicated that Dasatinib inhibited MAPK via Src. Treatment efficacy associated with MAPK and Src kinase activity as UM cells with the highest Src activity and MAPK activation displayed the strongest growth inhibition. Furthermore, treatment responses tended to be better in UM cultures with monosomy 3. In the cohort of primary UM, Src expression was highly correlated with MAPK activation and monosomy 3.

Conclusion We identified the Src family kinase inhibitor, Dasatinib, as a treatment option for UM. Dasatinib inhibits UM proliferation and may also inhibit UM progression as an association between Src and monosomy 3 was revealed. Consequently, monosomy 3 analysis in tumour tissue may suffice both the prognosis and choice of treatment.

• 3363

C-met signaling and preclinical analysis of crizotinib in uveal melanoma

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Purpose Uveal melanoma (UM) is the most common intra-ocular tumor in adults that often leads to metastases for which no effective treatment is available. The aim of this study was to analyze molecular mechanisms in UM in order to reveal treatment targets.

Methods Efficacy of kinase inhibitors and molecular mechanisms are analyzed in preclinical models of UM. Focus in this study was on the kinases and pathways that are associated with metastasis.

Results Based on c-Met expression in UM with a bad prognosis (monosomy 3) and activation of c-Met in all metastasis cell lines c-Met was chosen as treatment target and Crizotinib was chosen as candidate drug. Crizotinib is a dual kinase inhibitor that inhibits both ALK and c-Met. Molecular analysis revealed that Crizotinib was able to inhibit c-Met in UM effectively at nano-molar range. Proliferation was however not affected by Crizotinib treatment when cells were grown attached to culture dishes. To achieve growth inhibition with Crizotinib cells had to be grown non-attached. Moreover, only tumor cells that contained activated c-Met were affected by Crizotinib while c-Met negative cells continued to grow in the presence of the drug. Molecular analysis furthermore revealed that focal adhesion kinase (FAK) is a downstream target that was also inactivated in response to Crizotinib treatment. FAK is involved in tumor cell motility and tumor cell extravasation that are both crucial processes in metastasis.

Conclusion We propose Crizotinib as a possible treatment option for metastasizing UM. As c-Met expression is highly correlated with monosomy 3, both c-Met and monosomy 3 may be evaluated as biomarker for Crizotinib treatment.

• 3364

Immunosuppressive inflammation is an inherent characteristic of prognostically bad uveal melanoma

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Purpose The presence of infiltrating immune cells in uveal melanoma is associated with poor prognosis. An analysis of the different functional phenotypes of the tumor-infiltrating leukocytes (TIL) may help to gain insight in the role of these infiltrating immune cells.

Methods The density of CD8+ (CD3+CD8+ T cells) and CD4+ (CD3+CD8– T cells) T lymphocytes, CD4+ regulatory T cells (Tregs; CD3+CD8-Foxp3+ cells), CD68+ and CD68+CD163+ macrophages was evaluated by immunofluorescence histochemistry in 43 cases of uveal melanoma. The correlations between different parameters were analyzed and their presence compared to known morphologic, immunologic, cytogenetic and molecular prognostic variables.

Results The presence of increased numbers of all T cell subsets was associated with an epithelioid cell type, monosomy 3, and the class 2 gene expression profile (GEP). The presence of TIL was very variable, but strong correlations were observed between the different types of TIL. The presence of Tregs was correlated with the presence of M2 macrophages.

Conclusion Uveal melanoma with more malignant characteristics such as monosomy 3 and the class 2 GEP contained more TILs, which included Tregs. These data suggest that tumor-intrinsic factors distinguishing bad from good melanoma probably control the initiation of inflammation, which involves infiltration of tumors by different lymphocytic and myeloid immune cell subtypes, and support the notion that immunosuppressive inflammation contributes to increased malignancy in high risk uveal melanoma cases.

• 3365
Inflammation in primarily and secondarily enucleated eyes with uveal melanoma

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Purpose Uveal melanoma with a bad prognosis contain high numbers of infiltrating macrophages, especially of the M2 phenotype, and different subsets of lymphocytes. The aim of this study is to determine the presence of inflammatory cells in uveal melanoma-containing eyes enucleated after different types of irradiation, i.e. ruthenium-106 brachytherapy, sandwich therapy, or proton beam irradiation.

Methods We analyzed 46 eyes enucleated due to tumor recurrence, non-responsiveness, or complications after irradiation. Immunofluorescence staining was performed to determine the presence of CD68+ and CD68+CD163+macrophages, CD3+, CD8+ and Foxp3+ regulatory T lymphocytes. Outcomes were compared with known clinical and histological prognostic parameters.

Results Numbers of CD68+ and CD68+CD163+ macrophages in secondarily-enucleated eyes varied widely, but was not related to the reason for enucleation. The median of CD3, CD8, FoxP3+ lymphocyte counts was 55, 99 and 9 cells/mm2, respectively. When compared to primarily-enucleated eyes, the lymphocytic infiltration was significantly ($p<.02$) higher in irradiated eyes.

Conclusion Numbers of T-lymphocytes and macrophages varied widely. Irradiation has no clear effect on the number and type of macrophages in uveal melanoma. However, there were higher numbers of lymphocytes in previously irradiated uveal melanoma.

• 3366 / 433
Mutations in the BAP1 gene in uveal melanoma

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Purpose Uveal melanoma (UM) is the most frequently occurring intraocular malignancy in adults. UM has a strong tendency to metastasize to the liver. There are no effective therapies for metastatic disease resulting in a tumour-related death in about 45% of UM patients within 15 years after the initial diagnosis. Monosomy of chromosome 3 is the most frequent found chromosomal aberration in UM and is predominantly found in metastasizing tumours. Chromosome 3 losses can be detected by karyotyping, FISH or DNA based techniques as QPCR/MLPA and Array CGH. We use a combination of FISH and SNP arrays to select patients for a dendritic cell therapy trial.Recently, inactivating somatic mutations were identified in the gene encoding BRCA1-associated protein 1 (BAP1) on chromosome 3p21.1 in metastasizing tumours. In a retrospective series of UMs we will determine the sensitivity and specificity of mutations in BAP1 and compare these with the currently used predictive standard of monosomy.

Methods We will use targeted multiplexed Next Generation Sequencing to determine mutations in the BAP1 gene.

Results Our results will follow shortly.

Conclusion Conclusions will be drawn when all the results are known.

• 3367 / 434
Preclinical study of a glycoengineered anti-human CD20 antibody in murine models of primary cerebral and intraocular B-cell lymphomas

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Purpose Primary cerebral lymphomas (PCL) and primary intraocular lymphomas (PIOL), related to the systemic diffuse large B-cell lymphoma family, are highly aggressive tumors, with poor prognosis and any specific therapy. Despite good results obtained with chemotherapy, many patients relapse and new therapeutic strategies are needed. PCL and PIOL are characterized by the presence of CD20+ lymphomatous B-cells and as such are eligible for therapy with anti human CD20 antibodies.

Methods In this study, we evaluated the efficiency of LFB-R603, a promising glycoengineered anti-hCD20 monoclonal antibody that displays a high affinity for FcgRIIIa (CD16) receptors, when injected intumoraly. We used a murine lymphomatous B cell line transfected with the human CD20 gene to generate two syngeneic murine models of PCL and PIOL

Results After a single therapeutic injection of LFB-R603 mAb, a strong anti-tumor response was noted against the PCL and a less pronounced response in the PIOL model. This was linked to an inhibition of tumor growth and infiltration with CD8+ T-cells in both models. Interestingly, therapeutic effects were much better than those obtained with the Rituximab used as a reference.

Conclusion These in vivo results confirm the potential of the LFB-R603 mAb as an innovative therapeutic approach for the treatment of PCNSL tumors.

• 3371

Autologous and allogeneic limbal stem cell therapy - where are the limits?

DUA H
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ABSTRACT NOT PROVIDED

• 3372

Keratin films for ocular surface reconstruction

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Purpose Keratins are a group of cysteine-rich structural proteins formed in the epithelial cells of higher vertebrates. Keratin from hair or wool has been proposed as an appropriate biomaterial for producing films or cell cultivation scaffolds. This study was performed to develop transparent, stable and transferable human hair keratin films that support cellular adhesion and proliferation.

Methods The films were engineered by a multi-step procedure including reductive keratin extraction, aqueous dialysis, casting on hydrophobic membrane, drying and a final curing process. The influence of various process parameters on the ultrastructure, biomechanical properties, light transmission and cell growth behavior of corneal epithelial cells on keratin film in comparison to amniotic membrane (AM) were tested. Keratin films were investigated by SDS-PAGE, SEM and X-ray analyses. Furthermore, the tensile strength and light transmission of the films were studied. Finally, the growth behavior of human corneal epithelial cells on the keratin films and AM was estimated.

Results The film-forming process resulted in transparent films composed of nanoparticulate keratin structures. The film characteristics could be varied by changing the protein composition, adding softening agent (glycerol) or varying the curing temperature and duration. Based on these findings, an optimized protocol was developed. The films showed improved light transmission and biomechanical strength in comparison to AM. Furthermore, cell behavior on the films was similar to that found on AM.

Conclusion Biopolymer films based on human hair keratin may represent a new, promising alternative for corneal surface reconstruction. Further investigations will have to describe the clinical usefulness in animals and humans.

• 3373

Nanoparticle-mediated transfer of therapeutics to corneal cells

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Purpose Calcium phosphate nanoparticles (CaP-NPs) are biodegradable and biocompatible as they dissolve in the cell in calcium and phosphate. Therefore they are an ideal tool for transfection with DNA or RNA. It has been demonstrated that the impact on intracellular levels of Ca2+ is low and therefore does not affect cell vitality. In this study, we determine the most efficient type of CaP-NPs for transfer of DNA into in corneal endothelial cells (EC).

Methods CaP-NPs with triple-shell pcDNA3-EGFP in different concentrations or coated by dispersions of polyethylenimine (PEI) were manufactured. Polyfect®-pcDNA3-EGFP served as positive control. Human and murine EC (suspensions and donor tissue) were transfected using various concentrations of CaP-NPs and different times of transfection. Transfection efficacy was determined by measuring EGFP-expression (flow cytometry, fluorescence microscopy). To evaluate toxicity, apoptosis was studied by TUNEL and propidium iodide staining.

Results The transfection efficacy of triple shell CaP-NPs (EGFP expression up to 50% after transfection with triple shell CaP-NPs) was significantly increased after coating with PEI. Cell viability in corneal tissue was not significantly impaired after treatment. As EC possess minimal proliferative capacity, there was no significant change of EGFP expression.

Conclusion CaP-NPs seem to be an alternative to viral vectors and safe for application in patients. Therefore CaP-NP may be a new and suitable tool for DNA transfer into EC. Further studies are necessary to carefully evaluate functional application and biosafety.

• 3374

Corneal stromal mesenchymal stem cells for corneal stroma reconstruction

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Purpose To date, corneal epithelial reconstruction has been very successful. However, in a number of cases of injury or disease, the stromal layer is affected. Our goal is to develop biomaterials that will enable the regeneration of the corneal stroma. In this study, we compare endogenous vs exogenous stem cell courses for corneal stromal regeneration.

Methods We have previously developed collagen-based corneal stromal extracellular matrix substitutes based on EDC crosslinked collagen, and have shown that they promote ingrowth of stromal cells from the host cornea (Merrett et al. 2009; Fagerholm et al. 2010). For cases where stromal progenitors are depleted, we developed a non-toxic collagen-based hydrogel system where a macromolecular photoinitiator (Dex-BBA)was used to form the hydrogel around cells. The feasibility of Dex-BBA as a photoinitiator to initiate the gelation of aminoethylmethacylate-modified collagen (Coll-AEMA) was examined with or without the presence of stroma cells.

Results The Dex-BBA crosslinked hydrogels were weaker than the EDC crosslinked constructs. However, they were fairly robust and no apparent toxicity of the hydrogel system to mesenchymal stroma (or stem) cells (MSCs)were observed during the culture of 7 days, which indicated that Dex-BBA based macrophotoinitiator and our collagen-based hydrogel system may have potential in corneal stromal regeneration applications.

Conclusion We show that corneal stromal regeneration can be achieved by endogenous stimulation of existing corneal progenitor cells. Where the host cells may be depleted, our results show that hydrogel encapsulated stem cells may be used in the future.

Commercial interest

• 3421
The role of oxygen in ocular blood flow regulation

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The normal function of the retina is crucially dependent on an adequate perfusion and oxygenation of the tissue. Thus, it does not come as a surprise that ocular blood flow is very well autoregulated. It is known for a long time that the retinal circulation, and to some extent also the chorodial circulation can compensate for changes in ocular perfusion pressure in order to keep blood flow constant. This is usually referred to as an autoregulatory response of these vascular beds. However, the ocular circulation also responds to changes in oxygen tension. For example, breathing of pure oxygen leads to a pronounced vasoconstriction of the retinal vessel, indicating that the ocular circulation also adapts to changes in oxygen tension. This talk aims to summarize our current evidence of the role of oxygen in ocular blood flow regulation and how this may relate to ocular pathologies such as glaucoma or diabetic retinopathy.

• 3422
Neurovascular coupling and retinal oxygenation

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Purpose Luminance flicker stimulation of the photoreceptors is known to increase retinal blood flow. Oxygen supply may be the target of blood flow regulation. Thus, we investigated the oxygen saturation in retinal arterioles and venules along with their diameters in healthy as well as diabetic subjects.

Methods 18 patients with non-proliferative diabetic retinopathy (mean age: 62.2±8.3 years, diabetes type I/II: 4/14, HbA1c: 7.7±0.92, duration of diabetes: 24.1±9.3 years) and 20 healthy controls (71.2±7.5 years) were included. Dual – wavelength (548 nm and 610 nm) fundus images were taken before and during monochromatic (567 – 587 nm) luminance flicker stimulation (12.5 Hz, modulation depth: 1:20) for 90 s. Diameters (central retinal arterial and venous equivalents – CRAE and CRVE) and oxygen saturation (SO2, dual – wavelength optical oximetry) were determined and averaged for all arterioles and venules in an annular area centered at the optic disk ("ARIC" – grid). Changes of these parameters by the flicker were considered for statistical analysis.

Results Flicker light increased CRAE, CRVE, and venous SO2 by 1.42%±3.72%, 2.80%*±2.70%, and 2.03%*±2.43% in the patients as well as 4.98%*±6.23%, 8.94%*±5.26%, and 4.20%*±3.71% in the controls (*: $p<0.05$). This increase was significantly higher in the controls vs. patients for all parameters (t-test, $p<0.05$). The arterial SO2 remained unchanged in both groups. After adjustment for the subject's age, the increase of the venous SO2 correlated significantly ($p=0.035$) with that of the CRAE in the controls but not in the diabetics.

Conclusion Our data demonstrate a coupling of retinal neuronal activity and hemoglobin oxygenation addressing the need of oxygen by the outer retina. Blood flow regulation and oxygen supply seem to be impaired in diabetes.

Commercial interest

• 3423
Retinal vessel oximetry in glaucoma

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Purpose We undertook retinal vessel oximetry, using spectral imaging, with both sequential and snapshot cameras. We have validated the values obtained using a model eye. We have explored the propagation of light through the retina using Monte Carlo modelling. Clinical retinal oximetry results are presented from normal volunteers, and glaucoma patients.

Methods The sequential spectral camera employs a liquid-crystal tunable filter. Images were captured using a cooled CCD camera, at wavelengths between 550nm and 680nm. The snapshot camera captures multiple spectral images simultaneously. We used the spectral images from these devices to calculate retinal vessel oximetric values, with the output displayed as a retinal oximetric 'map'. We obtained oximetric maps from normal volunteers, and compared these with the oximetric maps from glaucoma patients with a range of visual field loss.

Results There were significant differences between oxygen saturation in the retinal venules of the most severely affected glaucoma patients, compared with the normals: the glaucoma patients had higher values of venous saturation, with a correlation between visual field mean deviation (MD) and venous saturation. There were no significant differences in ateriolar oxygen saturation between normals and glaucoma patients.

Conclusion We have demonstrated retinal vessel oximetry using two types of spectral imager. We have attempted to validate our cameras using a model eye. We found higher venular oxygen saturation in glaucoma patients versus normals: these findings might suggest reduced inner retinal oxygen consumption in glaucoma. The venular oxygen saturation might represent an objective, clinically useful, measure of ganglion cell health.

• 3424
The effect of intravitreal ranibizumab on retinal oxygenation in central retinal vein occlusion

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Purpose To investigate the effect of intravitreal anti-VEGF on retinal oxygenation in patients with central retinal vein occlusion.Intravitreal anti-VEGF injections have recently become an approved method of treatment for retinal vein occlusions, as several studies have shown a beneficial effect on visual acuity and retinal thickness. However, there are indications that intravitreal anti-VEGF may cause constrictions of the retinal vessels, leading to a reduction in retinal blood flow.

Methods Retinal oxygen saturation in patients with CRVO was analysed, using the Oxymap Retinal Oximeter P3, before and during 6 months of treatment with intravitreal injections of ranibizumab.

Results Our preliminary results indicate that retinal oxygen saturation is not decreased by intravitreal anti-VEGF injections.

Commercial interest

• 3431

Expression and role of aquaorines in proliferative vitreoretinopathy

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Purpose Proliferative vitreoretinopathy (PVR) is the major cause of failure of retinal detachment surgery. PVR is characterized by the proliferation and migration of different cell type which will form contracting membranes. Abnormal RPE cell differentiation has been well described during PVR including epithelial-mesenchymal transition (EMT) where RPE lose retinal differentiation and acquires myofibroblastic and mesenchymal cells markers. Aquaporines (AQPs) are proteins that allow transcellular passage of water and have recently been involved in cellular migration and proliferation. Our group have found AQP1 expression by SMA-positive cells in human PVR, which are classically described as dedifferentiated RPE cells. Thus, we have postulated that AQP1 expression by RPE cell was cell differentiation dependent and involved in RPE cell migration. In this project we would like to 1/Confirm the expression of AQP1 in PVR 2/Precise the cell type expressing AQP1 3/Investigate if AQP1 expression is dependent of cell differentiation in RPE cells 4/Study if AQP1 is involved in RPE cell migration or proliferation

Methods We will perform PCR and immunofluorescence using other cell type markers. ARPE-19 and primary human RPE cells will be cultured in different protocols to obtain differentiated and undifferentiated cells. The expression of AQPs, RPE cell differentiation and EMT markers will be analyzed by RT-PCR and Western Blot. AQPs expression will be induced or knock down in primary culture and ARPE cells. Cell proliferation and migration will be respectively analysed by BRDU incorporation and Boyden chamber assay

Conclusion This project will help to determine the role and implication of AQPs in PVR and the effect of cell differentiation on AQPs expression in RPE cells

• 3432

A Th2-inducing dendritic cell vaccine targeting amyloid-β as found in drusen of patients with age-related macular degeneration

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Purpose According to the results of several studies, amyloid-β (Aβ) plays a significant role in both the bio-and pathogenesis of AMD. Since other groups have demonstrated that T helper 2 (Th2) responses are most effective in degrading Aβ, we want to develop a Th2 inducing dendritic cell (DC) vaccine against amyloid-β (Aβ). The aim is to make a vaccine that may be used in a later step for local application in patients presenting early signs of AMD, e.g. the soft drusen stage of the disease.

Methods From peripheral blood of healthy volunteers and AMD patients, peripheral blood mononuclear cells (PBMC) will be isolated by Ficoll density gradient centrifugation. Next, dendritic cells (DC) are generated starting from CD14+ monocytes which are isolated by magnetic bead selection. Two different culture protocols will be compared: (i) we will obtain conventional DC triggering a T helper 1 (Th1) immune response on the one hand; (ii) on the other hand we aim to develop DC which are capable of inducing an effective T helper 2 (Th2) immune response.Phenotype and cytokine expression profile of different DC subtypes will be analyzed in vitro using flow cytometry and cytometric bead array, respectively. In addition, Th1/Th2 stimulatory capacity of DC will be determined in DC/T cell co-cultures by means of IFN-γ and IL-5 ELISPOT, respectively.

Results The results will consist in showing the progress in the development of Th2-inducing DC from CD14+ monocytes, targeting the Aβ antigen.

• 3433

The effect of local rock-inhibition on wound healing after glaucoma filtration surgery

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Purpose Glaucoma is a neurodegenerative disease that is the second most important cause of irreversible blindness. This disease is characterized by a raised intra-ocular pressure (IOP) and by progressive retinal ganglion cell apoptosis, resulting in irreversible visual field loss. Current treatment is directed towards the reduction of IOP, which is the main risk factor for glaucoma. Filtration surgery (trabeculectomy) remains the most effective therapy to reduce IOP. However, in 30% of the cases this surgery fails due to subconjunctival wound healing. We will test whether administration of local ROCK-inhibitors (Amakem NV) could lead to a better maintenance of the constructed channel, and thus improve surgical outcome.

Methods We will test the in vitro role of ROCK-inhibition on HUVEC and TF. Cells will be pre-incubated with different concentrations of ROCK-inhibitors (Amakem NV) and cell proliferation will be assessed using the WST-1 Cell Proliferation Assay System. Next we will investigate the in vivo effects of ROCK-inhibition in a rabbit model for glaucoma filtration surgery. One eye will be treated with the ROCK-inhibitor and the other eye will be used as a control (vehicle). TGF-β levels in the aqueous humour will be analysed using ELISA. Different (immuno)stainings will show us the blood vessel density, inflammation and fibrosis on different time points after surgery.

Conclusion This research project will elucidate the potential role of local ROCK-inhibition in the improvement of filtration surgery outcome, and will highlight any angiostatic, anti-inflammatory, and/or anti-fibrotic effects.

• 3434

Local rock-inhibition as a novel therapeutic approach for neuroprotection of retinal ganglion cells

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Purpose Glaucoma is characterized by progressive retinal ganglion cell (RGCs) apoptosis, resulting in visual field loss. Current treatment of this disease is directed towards the reduction of intraocular pressure (IOP), which is the main -but not only- risk factor of glaucoma. Besides IOP lowering, there is no effective neuroprotective therapy. So, there is a need for the development of new strategies preventing or inhibiting neuronal damage in glaucoma. Therefore, we want to investigate the neuroprotective effects of a local ROCK-inhibitor (AMA0076; Amakem NV) in different models of neurodegeneration.

Methods First, the in vitro role of AMA0076 will be tested on cultured RGCs subjected to hypoxia. At different time-points after administration, cell survival and apoptosis will be assessed. Secondly, the in vivo neuroprotective effect of AMA0076 will be investigated in different mouse models for neurodegeneration. Mice will be subjected to the optic nerve crush model and a chronic laser-induced glaucoma model to induce IOP-increase and RGCs damage. Immediately after the injury, AMA0076 will be injected into the vitreous. On different time-points the number of RGCs will be determined on retinal flat mounts and different immunostainings will identify apoptosis, axon degeneration and microglial activation.

Conclusion Therapy focusing solely on IOP lowering is not sufficient to halt visual deterioration in glaucoma patients. Indeed, patients can continue losing vision despite a successful IOP-control. Therefore, new therapies concentrating on neuroprotection to prevent, hinder or even reverse RGCs death might be as important as IOP-lowering strategies. This study on the neuroprotective role of ROCK-inhibition in glaucoma will potentially shed new light on future possibilities for neuroprotection in glaucomatous nerve damage.

• 3435

Local Rock inhibition as a novel IOP lowering strategy in the treatment of glaucoma

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Purpose 1) To check the effect of AMA0076 on the behavior of trabecular meshwork (TM) cells (in vitro). 2) To further elucidate the IOP lowering effect of AMA0076 (in vivo).

Methods To investigate the effect of ROCK inhibition on the morphology of TM cells, confluent cultures of HTM and RTM cells will be incubated with various concentrations of AMA0076 (Amakem) or vehicle. Any morphological changes will be observed and photographed by using a phase-contrast microscope. Filamentous actin and focal adhesion will be stained using FITC conjugated-phalloidin and anti-vinculin, respectively. Fluorescence will be visualized using a confocal laser scanning microscope. Secondly, we will further investigate the in vivo IOP lowering efficacy of AMA0076 in normotensive and hypertensive rabbits. Dose-response experiments will be carried out to determine the optimal dose. The optimal dosing frequency will be determined, and if necessary, the drug formulation will be optimized to extend the duration of action and/or lower the concentration of the drug. In vivo ocular toxicology of AMA0076 will be evaluated using slit lamp examination, fluorescein test, red phenol test, impression cytology and in vivo confocal microscopy.

Results A pilot study, preformed by our lab, with normotensive New-Zealand white rabbits already confirmed the potential IOP lowering effect of AMA0076. Repeated administration (TID) of 0.3% AMA0076 resulted in a significant lowering of IOP in normotensive rabbits (average reduction in IOP 14%, $p<0.05$, N=15).

Conclusion In summary, our proposed research project will determine the potential role of the local ROCK inhibitor, AMA0076, as a novel IOP lowering strategy in the treatment of glaucoma.

• 3441

Immune modulation in the next decade

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

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

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

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

Commercial interest

• 3442

Immune modulation in uveitis:biologicals - “golden calf” or “gold standard”?

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Uveitis is a sight-threatening auto-immune condition. Most of the cases require corticosteroids and conventional immunosuppressors. Until recently, safety issues limited the use of new therapeutic strategies such as biological agents. Anti-TNF alpha and interferon alpha are the two major drugs, used for more than 12 years with well-defined results and side-effects. Behçet’s disease is the principal indication of biologicals with a dramatic improvement of uveitis and a long-lasting remission. Dosing and duration remain controversial. Anti-TNF alpha are used in severe cases with a direct visual threat. The intravitreal use of the drug seems to be inefficient. Interestingly, other molecules such as anti-IL1 molecules did not show a significant control of uveitis in a randomized multicentre clinical trial. Refractory cases of JIA-associated uveitis are another indication of anti-TNF alpha drugs. Even though, etanercept is highly effective on the rheumatological component of the disease, it is ineffective on uveitis. On the other hand, adalimumab is effective on uveitis but less commonly on arthritis. In the future, we will probably welcome new types of biologicals agents in the field of uveitis. However, it seems paramount to determine the best route and rhythm of administration, dosages and duration of therapy. Side effects are also important to consider before any further conclusions, especially in children.

• 3443

Immune modulation in ocular allergy: update and future directions

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Purpose In the presence of active severe allergic reaction, steroids are preferred over anti-allegic drugs since the former is more effective in inhibiting rapidly the inflammatory component of corneal damage, i.e., eosinophil- and neutrophil- liberated epithelial toxic mediators. However, one often finds steroid-resistant forms of VKC and AKC that necessitate an alternative therapy.

Methods In poor responders, or when only prolonged steroids are effective, topical cyclosporine 0.5% to 2% ameliorates the signs and symptoms of severe VKC and AKC without significant side effects. New formulations of topical cyclosporine at 0.05% may be further available for the treatment of severe VKC and AKC.

Results Topical cyclosporine A (CsA) 1% or 2% emulsion in castor or olive oil has been considered for years the primary alternative to steroids for treatment of severe VKC and AKC. CsA 1% was reported to be the minimum effective concentration in the treatment of vernal shield ulcer, with recurrence observed at lower concentrations. Lower concentrations of CsA have been suggested as a steroid sparing agent with moderate to good effectiveness.

Conclusion Newer alternatives to the use of topical mast cell stabilizing drugs, topical steroids and topical cyclosporine are other immunosuppressive drugs and biological agents that are able to specifically target different elements of the immune response.

• 3444

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

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ABSTRACT NOT PROVIDED

• 3445

Immune modulation in optic neuritis: "good news?"

LAGREZE W
Universität Freiburg

ABSTRACT NOT PROVIDED

• 3451
Intraocular tumours and glaucomas

DE POTTER P
Brussels

Anterior segment and posterior segment intraocular tumors and their treatments may induce secondary glaucomas. Their mechanisms and therapeutic approaches will be review in this presentation

• 3452
Thyroid and ocular hypertension

BOSCHI A
Neuro-ophthalmology, Brussels

Purpose To present and discuss the association between thyroid disorders and the development of glaucoma. Several population-based cross-sectional sample studies support the hypothesis that thyroid disorders may increase the risk of glaucoma. However, because the self-report studies, data on specific type of glaucoma and / or thyroid disorders as well as severity and duration are not available. In Graves orbitopathy (GO), different mechanisms leading to intraocular pressure (IOP) increase are: eyeball compression by enlarged extra-ocular muscles, and episcleral venous pressure elevation secondary to intraorbital content and pressure increase. But, the prevalence of glaucoma in GO patient doesn't seem to be increased compared to the general population. However, most of the studies were retrospective and with a short-term follow-up.

Methods Clinical features of GO and risk factors associated with high IOP and glaucoma in GO pat will be discuss, as well as management recommendations

• 3453
Glaucoma after vitreoretinal surgery

DETRY-MOREL M
Brussels

With the important advances in the microsurgical techniques during the past three decades, various and complex eye diseases involving retina and vitreous are currently accessible to vitreoretinal surgery. Most current vitreoretinal surgical procedures have major relationships with glaucoma and potential devastating consequences on the optic nerve head. In a pre-existing glaucoma patient having history of filtering surgery, maintenance of the patency of the filtering bleb requires a vitreoretinal approach for conjunctival preservation with techniques (pneumatic retinopexy or small gauge vitrectomy). Whether coming after intravitreal triamcinolone acetonide injection or associated with panretinal photocoagulation, scleral buckling, pars plana vitrectomy, intraocular gases or silicone oil tamponade, transient or sustained elevation of intraocular pressure and open- or closed-angle secondary glaucomas of a multifactorial nature are a common occurrence following vitreoretinal surgery. Adequate and successful therapeutic intervention should be tailored to the individual patient based on the early identification of the underlying mechanism of the pressure elevation. Patients with or suspect for glaucoma or those who may at risk to develop postoperative ocular hypertension and secondary glaucoma should be carefully screened before any vitreoretinal procedure. This presentation will focus on the different mechanisms, frequency, risk factors, clinical diagnosis and prognosis of ocular hypertension and glaucoma resulting from the different vitreoretinal procedures with their respective available therapeutical options.

• 3454
Secondary glaucoma associated with congenital corneal abnormalities

CLAERHOUT I
Ophthalmology, Ghent University Hospital, Ghent

Purpose To present an overview of developmental glaucomas associated with congenital corneal abnormalities.

Results This overview will discuss the different underlying congenital abnormalities causing secondary glaucoma including aniridia, Peters anomaly, Axenfeld-Rieger syndrome and micro and megalocornea.

• 3455

Management of secondary glaucoma

LIM KS
Ophthalmology, ST Thomas' Hospital, London

Purpose To summarised the current medical and surgical treatment options for patients with secondary glaucoma.

Methods Identify causes of the secondary glaucoma. Understand the mechanism of raised intraocular pressure.Option 1: Medical/drops treatment; Option 2:Laser Trabeculoplasty; Option 3: Trabeculectomy; Option 4: Non-penetrating surgery; Option 4: Diode laser; Option 5: Tube surgery

Results Pros and cons for each option will be discussed.

Conclusion Depending on the underlying cause of the raised intraocular pressure and the status of the conjunctival, surgical option may be best in preserving long term vision for patient.

• 3461

Definition, clinical aspects and new imaging of small melanocytic lesions of the choroid

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Hopital de la Salpétrière, Paris

ABSTRACT NOT PROVIDED

• 3462

Genetic findings in small melanocytic lesions

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(2) University of Liverpool, Ocular Oncology Service, Liverpool

Purpose The management of patients with small melanocytic choroidal tumour is controversial. The aim of this presentation is to inform the current debate on patient care by reporting on histological grade of malignancy and genetic type of such tumours.

Methods We reviewed our database and selected patients with: a melanocytic tumour having dimensions conforming to the TNM size category 1 (i.e., 'small'); tumour involving choroid; and clinical and/or histological features of malignancy. Patients with such a 'small choroidal melanoma' were excluded if not resident in the British Isles, if the tumour was not treated at our centre between 1993 and 2010 or if they had bilateral uveal melanoma.

Results 3132 patients with a choroidal melanoma were identified, of which 1001 (32.2%) were 'small.' Chromosome 3 status was known in 102 of such small choroidal melanomas. Chromosome 3 loss was detected in 40% of these. Approximately 63% of tumours with chromosome 3 loss showed chromosome 8q gain (cf. 85% of tumours of TNM size category 4). Approximately 70% (i.e., 16 tumours) of small choroidal melanomas with both these genetic abnormalities also showed epithelioid cells. Metastatic death occurred in 4 patients, all of whom had a tumour with chromosome 3 loss, chromosome 8q gain and epithelioid cells.

Conclusion Our data suggest that uveal melanomas show 'crescendo malignancy' with cumulative genetic abnormalities ultimately resulting in a lethal 'double-hit' of chromosome 3 loss and chromosome 8q gain. We hypothesize that treatment of small choroidal melanomas showing either chromosome 3 loss or chromosome 8q gain prevents such a lethal double hit and hence the onset of metastatic spread. Delayed treatment of small choroidal melanomas may therefore be dangerous. Prognostication is greatly enhanced by multivariate analysis combining TNM staging with histological grading and genetic typing also taking account of the patient's age and sex. There would seem to be scope for greater use of biopsy so as to provide better counselling of patients and plans for systemic screening and other aspects of care.

• 3463

Metastasis from small melanocytic lesions: OOG experience and review of the literature

KIVELÄ T
Helsinki

Purpose To summarise current knowledge regarding the risk of metastasis from small melanocytic lesions.

Methods Review of Ophthalmic Oncology Group experience and relevant literature.

Results Studies have not specifically addressed the threshold size, if any, beyond which uveal melanomas gain the capacity to metastasise. Anecdotal data from series of small uveal melanomas indicate that at least tumours around 5-6 mm in diameter have killed patients. Theoretical calculations based on average published doubling times of primary uveal melanomas and empirically estimated doubling times of metastatic uveal melanoma suggest that the primary could be 3 mm in diameter and 1.5 mm thick when metastasis starts. A pilot survey within the Ophthalmic Oncology Group uncovered lethal uveal melanomas that ranged 3.2-6.0 mm in diameter. A collaborative study will address this question in more detail. Finally, in the new Tumor, Node, Metastasis (TNM) classification a small melanoma (T1, stage I) refers to tumours less than 9 mm in diameter when less than 6 mm in height and less than 12 mm in diameter when less than 3 mm in height. The 10-year melanoma-related mortality of T1 melanomas was 10%.

Conclusion Theoretical and clinical evidence suggest that uveal melanomas are able to metastasize when larger than 3 mm by diameter, but the risk of metastasis remains at 10% when the diameter is less than 9 mm or even 12 mm when the tumour is shallow.

• 3464

Practical management of small melanocytic lesions

ZOGRAFOS L
Jules-Gonin Eye Hospital, Lausanne

Purpose To present the spectrum of various therapeutic options in the practical management of small melanocytic tumors

Methods The therapeutic decision is influenced by:

- The cumulative risk factors
- The presence or absence of documented tumor growth.
- The localisation and the volume of the tumor.
- The personal data of the patient.
- The expected functional results following a conservative management.

Results The predictions established by the statistical evaluation of the various risk factors, in the majority of the cases are confirmed by the therapeutic outcome. However, an unpredictable evolution which may occur in selected cases has to be taken in account in global therapeutic strategies which are used for the management of small melanocytic tumors.

Conclusion Successful management of small melanocytic tumors depends on a correct interpretation of risk factors and careful observation of all individual cases.

• 3465
Practical management of small melanocytic lesions

DAMATO BE, HEIMANN H
Ocular Oncology Service, Liverpool

Purpose The purpose of this presentation is to describe the authors' current approach to the treatment of small melanocytic uveal tumours of indeterminate malignancy.

Methods The tumours are assessed by binocular ophthalmoscopy, ultrasonography, ocular coherence tomography and autofluorescence imaging, according to the location of the tumour. Patients are advised on the likelihood of malignancy and the risk of metastasis. They are given the choice between observation, treatment and biopsy.

Results In most patients it is possible to distinguish small melanoma from large naevus. When the diagnosis remains uncertain, the management is decided by the size and location of the tumour, the chances of visual loss following treatment and the patient's attitude to risk.

Conclusion The practical management of small melanocytic tumours is based on the size and location of the tumour and the patient's fears and wishes.

• 3466
Practical management of small melanocytic lesions

DESJARDINS L
Institut Curie, Paris

Purpose In 2009 we have performed a retrospective study of 368 small uveal melanoma (diameter less than 12 thickness less than 3 mm) Overall survival at 5 years was 92%and at 10 years 78% survival without metastasis at 5 years was 96% and at 10 years 93%. According to our data the smallest tumor associated with metastatic death was 5mm in diameter and 1,5 mm in thickness and 14 of the tumors had a diameter of less than 10 mm developed. Half of the metastatic patients developed metastasis 5 years or more after treatment.

Methods According to the study performed by Gass and Shields the risk factors for growth of small melanocytic lesions are the presence of symptoms, subretinal fluid,proximity of ON , orange pigment , thickness of more than 2mm and diameter of more than 7 mm. Performing genetic test on small melanocytic lesions is not always usefull , as it has been shown that a good prognosis lesion can grow and change in a bad prognosis.

Results Ophthalmologists are always trying to preserve vision as a rule. Nevertheless with possibly malignant lesions, the metastatic risk has to be considered before a therapeutic approach is decided. Factors like age of the patient, number of risk factors for growth and location of the tumor should be taken in account. Thus the practician should advise the patient and discuss and explain the decision.

Conclusion We usually recommend treatment if there are at least two risk factors and if the patient is young and the lesion away from the posterior pole.In all different situations we usually recommend close follow up for suspicious lesions and treatment in case of documented growth.

• 3471

Limitations of 'hard' keratoprosthesis in clinical practice - can 'soft' kps lead the way out?

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Brighton

Two winners have emerged among dozens of keratoprostheses (KPros) which have come and gone. The Osteo-odonto-keratoprosthesis is the device of choice for end stage inflammatory ocular surface disease associated with a dry eye, such as Stevens Johnson syndrome and ocular cicatricial pemphigoid. The Boston Type 1 keratoprosthesis is successful for wet blinking eyes and can be considered as an alternative to high risk keratoplasty in highly vascularised corneae or in multiple previous graft failure. The main advantage of these "hard" KPros is optical clarity. Whilst the field of view may be somewhat limited, there is no astigmatism and the optical surface is usually bare and clear. Hard KPros depend mostly on bio-inertness as opposed to biointegration. Soft KPros have the theoretical advantages of the possibility of having the same mechanical moduli as the host tissue thus reducing stress at the interface when the eye is subjected to minor trauma, intraocular pressure measurement by applanation, and drug penetration. However, much effort has to be directed towards adequate integration (healing), and either total and smooth epithelialisation or no epithelialisation whatsoever. Partial epithelialisation, tear meniscus, and buckling of a soft optic contribute to poor optical performance and thus poor vision.

• 3472

Autologous versus allogeneic limbal stem cell therapy - challenges and pitfalls

DUA H
Queens Medical Centre, Nottingham

ABSTRACT NOT PROVIDED

• 3473

From lab to limbus and back to the lab!

AHMADI-LARI S
United Kingdom

ABSTRACT NOT PROVIDED

• 3474

Corneal cell and nerve regeneration promoted by biosynthetic implants

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Purpose To assess cell, nerve, and stromal regeneration in a biosynthetic material 3 years after implantation into human corneas, and compare results to human donor corneas.

Methods 10 patients received biosynthetic implants, and 10 received human donor corneas. At 12, 24, and 36 months postoperatively, slit lamp, anterior segment optical coherence tomography (ASOCT), contact esthesiometry, and in vivo confocal microscopy (IVCM) examinations were performed.

Results Thickness remained stable in biosynthetic corneas, while swelling was observed in donor material. Reduced transparency was apparent at graft borders in all corneas, while clear central corneas were observed in all donor corneas and in some biosynthetic corneas at 3 years. At the cellular level, biosynthetic material was incompletely populated by keratocytes after 3 years, while human tissue contained keratocytes and features indicative of stromal cell death, not seen in biosynthetic implants. Only partial touch sensitivity was restored in both groups after three years, corresponding to slow subbasal nerve recovery. Nerve regeneration into the central cornea was apparently impeded by peripheral interface scar tissue in all corneas. The epithelial-to-stromal transition was uneven in biosynthetic implants, while epithelium overlying human donor tissue often contained dendritic inflammatory cells.

Conclusion No cornea resembled a native cornea at 3 years. Nerve and sensitivity restoration were incomplete, and scar tissue was stable over the long term. Keratocytes slowly populated the biomaterial, and keratocyte death was common in human donor tissue. Only human donor corneas exhibited signs of an immune response at the microscopic level.

• 3475

Mesechymal stem cell properties in the endothelium - bioengineered ec for lamellar keratoplasty?

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(2) Institute of Anatomy, Essen University Hospital, Essen

Purpose Corneal endothelium (EC) is crucial to maintain corneal transparency. Loss of EC finally results in blindness with the need of corneal transplantation. As lamellar grafting is globally spreading, engineering EC sheets are rational. However, in-depth knowledge of precursor or stem cell-like properties in EC and the precise anatomical locations are not yet clearly identified. These progenitor cells might serve as basis for tissue engineering. This study aims to identify the distribution and localization of EC with mesenchymal stem-cell (MSC) and progenitor characteristics.

Methods To study the distribution of putative MSC in the cornea and in the anterior chamber, typical MSC markers (CD44, CD73, CD90, CD105,stro-1) were studied by immunohisto- and immunocytochemistry in sections of eyes, corneas and whole mount staining (Balb/C and C57BL6 mice, human tissue).

Results CD44 expression was identified in the periphery of the lens epithelium, in single cells located in the peripheral parts of EC and in the limbus, but not in central parts of cornea. Moreover, CD44 was detected on cell borders of specific cell clusters throughout the endothelium (7%).

Conclusion To our knowledge, we identified for the first time CD44+ cells with potential stem cell properties in the cornea. This was localized in the peripheral part of the EC and the limbus. Therefore, the peripheral cornea might be a potential source for future tissue engineering approaches for corneal endothelium.

• 4111
Adaptive optics imaging in age-related macular degeneration

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(2) Imagine-Eyes, Orsay

Purpose To document cases of drusen and age-related geographic atrophy(GA) at the microscopic scale using adaptive optics(AO).

Methods Four cases of age-related drusens, 2 cases of familial drusen and 7 patients of GA underwent en face retinal imaging by AO retinal camera(rtx1, Imagine Eyes, Orsay, France). AO images were confronted to high-resolution spectral-domain optical coherence tomography(OCT) and scanning laser ophthalmoscopy(SLO) examinations.

Results In AO images, most drusen appeared as doughnut-shaped highly reflective zones, and were better delineated than by color fundus photograph. The overlying cone mosaic could be detected over most of them, including their top. Between drusen, the cone photoreceptor mosaic appeared normal. In GA cases, AO images revealed irregular patches of multiple cone-like bright spots as well as larger dark disks in atrophic areas.

Conclusion AO provided images of microscopic structures in various types of AMD, including GA. Local losses in cone contrast at the drusen slopes confirmed a strong relation between cone visibility and their orientation. There was no evidence of cone loss in association to drusen. In GA patients, our findings suggest that photoreceptors with shortened outer segments may survive within atrophic areas, which may lead to the development of novel therapeutic strategies aimed at restoring the function of surviving cones. These results demonstrate that AO retinal camera can detect isolated residual photoreceptors, and hence that it will be a powerful tool for quantifying spontaneous or therapeutic changes in AMD patients.Supported by ANR through Tecsan Program (project iPhot n° ANR-09-TECS-009)

• 4112
The effect of anti-VEGF treatment and triamcinolone in experimental retinal vein occlusion

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Purpose We investigated the effect of intravitreal injection of anti-VEGF antibodies and triamcinolone acetonide (TA) in a rat model of central retinal vein occlusion (CRVO).

Methods In one eye of adult Brown Norway rats (n=81) CRVO was induced with laser photocoagulation. Animals were divided into 3 groups (each n=27): 1. CRVO only without any treatment; 2. CRVO with anti-VEGF antibodies; and 3. CRVO with TA. The injection of anti-VEGF antibodies or TA was performed 15 minutes after CRVO induction. The gene expression was investigated using RT-PCR in the neural retina 1, 3 and 7 days after CRVO. We analyzed the expression of VEGF-A, VEGF-B, PEDF; of channels implicated in retinal osmohomeostasis (Kir4.1, AQP4, AQP1), and of inflammatory factors IL-1ß and IL-6.

Results CRVO induced a rapid transient upregulation of Vegfa, and a delayed upregulation of Pedf. Further strong, downregulation of Kir4.1, Aqp4, and Aqp1, and striking rapid upregulation of Il1ß and Il6 was observed. Anti-VEGF antibodies fully prevented the upregulation of Vegfa and of Pedf, and decreased the upregulation of Il1ß. This treatment had no effect on the expression of Kir4.1, Aqp4, Aqp1, and Il6. Intravitreal TA reversed the downregulation of Kir4.1 and accelerated the normalization of the upregulated expression of Il1ß and Il6, but had no significant effect on the expression of Vegfa.

Conclusion The anti-VEGF treatment inhibits strongly the upregulation of Vegfa but influences only marginally the water channels or inflammatory factors. TA inhibits the expression of IL-1ß and IL-6, and has neuroprotective effects via improvement of retinal potassium homeostasis.

• 4113
Technical and topographical variability in automatic retinal oximetry

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Purpose To assess if retinal vessel oxygen saturation measurements are affected by (1) which eye is measured (2) photographic flashes (3) image angle (4) location within the retina (quadrant).

Methods The Oxymap retinal oximeter simultaneously acquires fundus images at 570nm and 600nm and calculates relative oxygen saturation in retinal vessels. Oximetry images were obtained from 26 healthy individuals, 18-30 years. Images were taken of one eye at different angles and at the same angle with at least two photographic flashes in between. In addition, one image from the other eye was obtained. Retinal vessel oxygen saturation was measured with the Oxymap analysis software.

Results (1) No difference was found between the left and right eyes (n=24, p>0.68). (2) Saturation increased by 0.5±1.0%, (p=0.028, mean±SD, hemoglobin saturation percentage) in arterioles and 0.9±1.9% (p=0.020) in venules after three or more photographic flashes. (3) Saturation was higher in both arterioles (1.3±1.7%, p=0.0004) and venules (1.9±2.4%, p=0.0007) when the subject gazed down than when looking straight. (4) Significant topographical variations were found within the retina, up to -3.1±2.4% difference from average saturation in arterioles and -5.4±4.0% in venules.

Conclusion The left and right eye are comparable in retinal vessel oxygen saturation measurements. A few photographic flashes have a small effect on the measurement. The difference in saturation by angle is significant when the subject is looking down and the topographical difference in saturation is notable between quadrants. It is important to standardise image acquistion and analysis.

Commercial interest

• 4114
Daily skills performed by previously blind RP patients with subretinal electronic implant Alpha IMS

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(2) Retina Implant AG, Reutlingen
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(5) STZ Eyetrial, Tuebingen

Purpose To investigate visual perception of previously blind retinitis pigmentosa (RP) patients using electronic subretinal implants.

Methods The new Alpha IMS chip (Retina Implant AG) with its 1500 photodiodes, amplifiers and electrodes powered wirelessly via a subdermal coil was implanted subretinally in 7 retinitis pigmentosa patients for indoor and outdoor use.

Results VA was up to 21/1000 within a field of 11° by 11° (see previous pilot study http://rspb.royalsocietypublishing.org/content/early/2010/11/01/rspb.2010.1747).A) Near vision: Localizing, cutlery and tableware, plates and content in 4AFC mode and in restaurants, facial characteristics of persons, items on working desk. B) Far vision: Recognizing clouds, clothes of people, borders of cars by metallic reflections, discerning smaller from larger persons.C) Spatial resolution: Position of clock hands, stripe patterns up to approx. 0.33 – 0.44 cpd, reading letters 4 to 8 cm high, localization and recognition of square, round or rectangular objects .D) Contrast: Differentiation of 7 to 10 shades of grey; increased sensitivity for infrared radiation.E) Motion: Hand movement, walking direction of a goose, circumvention of obstacles.F) Eye-hand coordination: Pointing at objects and moving them.

Conclusion Subretinal Alpha IMS implants allow RP- patients within few days of exercising to localize objects and to perform visuomotor tasks for improved orientation and mobility. This device thereby can provide considerable support to blind RP patients in mastering tasks of daily life, indoor and outdoor, as shown in an ongoing clinical study.

Commercial interest

• 4115
Blood-retinal barrier function status from OCT data

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Purpose To demonstrate the presence of blood-retinal barrier (BRB) function information within OCT data.

Methods It was recently suggested that OCT data embeds functional information on BRB status.In this work a different approach was followed resorting to the use of support vector machines (SVM) to discriminate between healthy (N=31), ETDRS level 10 diabetic retinopathy (DR) (N=31) and diabetic macular edema (DME) eyes (N=31).Healthy volunteers and diabetic patients underwent Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, USA) using both the 512x128 and the 200x200 Macular Cube Protocols.Data was exported and the intensity distributions were computed for each eye, taking into consideration only the retina (between the inner limiting membrane ILM and the retinal pigment epithelium RPE), both on the logarithmic and linear spaces.A total of 43 parameters per eye were computed and labeled accordingly (healthy, DR and DME).A publicly available SVM toolbox (LIBSVM) was applied to assess the possibility of discriminating between each of these groups using a radial basis function (RBF) kernel and the leave-one-out approach for validation.

Results Achieved results allow to conclude on the possibility of discriminating between healthy and DR eyes (level 10 ETDRS and DME eyes).Of added value is the fact the system is able to discriminate between healthy and ETDRS level 10 DR eyes. This suggests that optical properties of the retina are modified and that this change cannot be currently detected using any other available technique.

Conclusion In this work, it was demonstrated the presence of early changes in the optical properties of the human retina related to diabetes, and that this information is embedded in OCT data.Support: FCT/PTDC/SAU-BEB/103151/2008

• 4116
Calculation of central retinal artery diameters in patients with type 1 diabetes using non-invasive measurements

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Purpose To compare the diameter of the central retinal artery between patients with type 1 diabetes and healthy control subjects in vivo. Central retinal artery diameters were calculated from results of non-invasive measurements of ocular hemodynamics.

Methods 16 patients with type 1 diabetes with no or mild diabetic retinopathy and 16 age-matched healthy controls were participated in this study. Total retinal blood flow was assessed by the use of laser Doppler velocimetry and measurement of retinal vessel diameters in all veins entering the optic disc using a Dynamic Vessel Analyzer. In addition blood flow velocity in the retrobulbar central retinal artery was measured using color Doppler imaging. The diameter of the central retinal artery was then calculated individually for each subject using the obtained ocular hemodynamic data.

Results Calculated central retinal artery diameters were significantly larger in patients with diabetes (180 ± 13 µm) compared to healthy controls (166 ± 10 µm, $p = 0.001$). There were no significant differences in retinal blood flow, retinal vessel diameters or mean flow velocity in the central retinal artery between the two groups.

Conclusion The present results indicate a dilation of the central retinal artery in patients with type 1 diabetes, whereas total retinal blood flow is unaltered compared to healthy controls. Results from blood flow velocity measurements using color Doppler imaging in retrobulbar vessels do not include information about vessel diameters and need to be interpreted with caution in terms of retinal blood flow.

• 4117
Retinal vascular profiles

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Purpose It is our aim to study the retinal arterial and venous vascular profiles, in health and in arterial hypertension and glaucoma

Methods The temporal arteries and veins were studied, from the optical disk margin to the first bifurcation,Their trajectory was pinpointed in a digital platform, and their coordinates in the two dimensional plane were noted.A polynomial function was found that was graphically equal to the profile, To compare polynomials, a Pearson correlation was used. The variables to be compared were the coefficients and the squares of x. The intercept of the regression line (on the y axis) made the distinction between arteries and veins, and between pathological entities studied. We used the t test, with $P < .05$ to analyze groups.

Results NORMAL: 3 for the arteries and 2, 7 for the veins. HIPERTENSION: 4, 4 for the arteries and 4,6 for the veins. GLAUCOMA: eighteen eyes, all with primary open angle, two with pseudo exfoliation. We divided them in two groups: A with a stabilized clinical control and B with a degrading ophthalmological situation. The P values between intercepts of the arteries and the veins of the two groups were respectively 0,037 (<0, 05) and 0, 11

Conclusion The correlation between the coefficients and the squares seems to be characteristic for arterial hypertensive patients. For glaucoma patients, the low values of the arterial intercepts are characteristic of the group with worse response to medical and surgical therapy. Those with normal values stabilized their clinical glaucomatous condition with medical therapy.

• 4121

Comparison of optic nerve head and choroidal blood flow regulation during isometric exercise

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Purpose In the recent years the response of choroidal blood flow (ChBF) to isometric exercise has been characterized in some details. Generally, the degree of blood flow increase is lower than the degree of ocular perfusion pressure (OPP) increase indicating for some regulatory capacity of the choroid during these conditions. In the present study we compared the response of optic nerve head (ONH) blood flow and ChBF in response to isometric exercise.

Methods Two study days were performed in 48 healthy young subjects. 24 subjects participated in the choroidal studies and 24 subjects in the ONH studies. The effect of a 6 minutes squatting period on ChBF and ONH blood flow was studied. ChBF and ONH blood flow were measured using laser Doppler flowmetry. OPP was calculated as 2/3*mean arterial pressure-intraocular pressure.

Results ChBF and ONH blood flow increased during isometric exercise ($p < 0.001$ each). The increase was, however, in both vascular beds less pronounced than the increase in OPP indicating for some degree of blood flow regulation. The pressure/flow curves revealed that ChBF was constant until OPP of about 60% above baseline, whereas ONH blood flow was constant until OPP of about 40% above baseline.

Conclusion During isometric exercise ChBF regulates better than ONH blood flow. In some subjects an interesting phenomenon was found in the ONH blood flow experiments. During isometric exercise blood pressure temporarily decreased slightly, when subjects were exhausted from squatting. These periods were sometimes associated with a pronounced decrease in ONH blood flow (up to 30% below baseline values) although the OPP was still much higher than at baseline. The significance of this observation is unknown.

• 4122

Measurement of retinal oxygen saturation in patients with chronic obstructive pulmonary disease

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Purpose In the recent years several systems for the measurement of retinal oxygen saturation became commercially available. These systems rely on spectral analysis of the light reflected and scattered at the fundus. To measure the validity of the obtained results is difficult, because no gold standard method for the measurement of retinal oxygen saturation exists. We measured oxygen saturation in patients with reduced arterial oxygen saturation due to chronic obstructive pulmonary disease (COPD) and correlated data obtained in retinal arteries with systemic oxygen saturation values.

Methods Eleven patients with COPD were included in this study and two identical study days were scheduled. The patients were in need of long term oxygen therapy to reach normal values for the oxygen saturation. Retinal arterial oxygen saturation was studied using spectral analysis of fundus photos using the Retinal Vessel Analyzer (Imedos®). Systemic oxygen saturation was studied with a pulse oximeter. The measurements were repeated 20 minutes after the oxygen therapy was paused.

Results On day one systemic oxygen saturation in patients with COPD was 93 ± 4% and 86 ± 6% with and without oxygen therapy, respectively. Retinal arterial oxygen saturation was 91 ± 5% and 87 ± 6%, respectively (similar findings on day two). The correlation between systemic and retinal oxygen saturation was high (Day 1: r=0.68, p=0.023; Day 2: r=0.91,b p=0.001). In addition we found a high correlation coefficient of the change in oxygen saturation values (Day 1: r=0.88, p=<0.001; Day 2: r=0.67, p=0.047).

Conclusion Our data indicate that measurements of arterial retinal oxygen saturation using the Retinal Vessel Analyzer show adequate validity.

• 4123

Effects of increased neutrophile count on ET1 – induced changes in erythrocyte and leukocyte movements

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Purpose It is known that granulocyte-colony stimulating factor (G-CSF) increases white blood cell (WBC) count. There is evidence from other vascular beds that an increase in WBC count impairs blood flow regulation in the microcirculation. Whether this also holds true for the ocular circulation is yet unknown. In the following trial we investigated whether an increase in WBC count alters the endothelin-1 (ET-1) induced vasoconstriction.

Methods 24 healthy male subjects entered this randomized, placebo-controlled, double masked, two-way cross over study. 300µg G-CSF or placebo were applied intravenously to increase WBC count on two study days. Thereafter, ET-1 (5ng/kg/min) was infused for 30 minutes. Ocular hemodynamic variables were measured before and after G-CSF treatment and during the last 10 minutes of ET-1 infusion. Measurements of retinal WBC flux were performed with the blue-field entoptic technique, blood flow (BF) velocity using a laser Doppler velocimeter and retinal vessel diameter using a Retinal Vessel Analyzer.

Results Neither G-CSF nor ET-1 had any consistent effect on blood pressure, pulse rate or IOP. G-CSF induced an increase in retinal WBC density ($p<.01$). As expected ET-1 lowered choroidal BF ($p<.01$), retinal BF ($p<.01$)and WBC velocity ($p=.01$). Changes in choroidal BF and WBC velocity in response to ET-1 were not altered by pre-treatment with G-CSF. Contrary, the decrease in retinal BF was more pronounced during leukocytosis ($p=.02$) as compared to placebo.

Conclusion During vasoconstriction, induced by ET-1, vascular regulation can be altered by the number of circulating leukocytes. Whether this is caused by an interaction of red and white blood cells or by another mechanism is yet unknown.

• 4124

Complex regulation of optic nerve head blood flow during combined isometric exercise and elevation of intraocular pressure

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Purpose For a long time it was assumed that ocular vascular beds are characterized by one specific pressure/flow curve. Recently we have, however, shown that this behavior is much more complex in the choroid, because alterations in arterial and venous pressure lead to different regulatory behaviors. In the present study we tested the hypothesis that this is also the case in the optic nerve head.

Methods Two study days were performed in 40 healthy subjects. On the 1st day the effect of isometric exercise and an elevation of IOP on optic nerve head blood flow (ONHBF) were studied separately. On the 2nd day the effect of combined IOP and mean arterial pressure (MAP) increase was investigated. IOP was increased in a stepwise way using the suction cup method. ONHBF was measured using laser Doppler flowmetry. For correlation analysis all values from all subjects were pooled according to IOP and MAP values.

Results When data were grouped according to MAP values a highly significant correlation was found between ONHBF and IOP ($p<0.001$). The regression lines at different MAP levels were almost equal. When data were pooled according to IOP levels a significant correlation was found between MAP and ONHBF for IOP values up to 25 mmHg ($p<0.05$) and the correlation lines were almost identical. At higher IOP values, however, no correlation between ONHBF and MAP was found.

Conclusion Our data are in agreement with previously published studies that ONHBF shows some autoregulatory capacity. The autoregulatory behavior appears to be complex and dependent on the site of perfusion pressure regulation (arterial vs venous). Compared to the choroid the ONH adapts its perfusion better to an increase in IOP

• 4125

A randomized, placebo-controlled study investigating the effects of moxaverine on ocular blood flow after oral administration in healthy subjects

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Purpose We know that several eye diseases such as glaucoma, diabetic retinopathy and AMD are associated with ocular perfusion abnormalities. In recent studies we have shown that intravenous administration of moxaverine is capable of increasing ocular blood flow in healthy subjects compared to placebo as well as in elderly people with healthy eyes and in patients with eye diseases associated with hypoperfusion. In the present study we hypothesized that oral moxaverine may increase ocular blood flow.

Methods In this placebo-controlled, two-way crossover study 16 healthy subjects received 900 mg moxaverine-hydrochloride, administrated per os in 3 equal doses, and placebo. Outcome variables were measured at BL and 5 hours after first drug administration. Choroidal and optic nerve head blood flow (ONHBF) were assessed with laser Doppler flowmetry and blood velocities in the retrobulbar vessels were measured with color Doppler imaging.

Results No parameter showed any difference between moxaverine and placebo. The p-values of ANOVA testing between moxaverine and placebo were as follows: Choroidal blood flow (p=0.52), ONHBF (p=0.54), peak systolic velocity (PSV) in the ophthalmic artery (p=0.33), end diastolic velocity (EDV) in the ophthalmic artery (p=0.58), PSV in the posterior ciliary arteries (p=0.38), EDV in the posterior ciliary arteries (p=0.26), PSV in the central retinal artery (p=0.35), EDV in the central retinal artery (p=0.51).

Conclusion Our results indicate that oral moxaverine, in contrast to systemic moxaverine, does not increase ocular blood flow. This may be related to the relatively low bioavailability of moxaverine after oral administration.

• 4126

Characterization of retinal blood flow in healthy subjects

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Purpose Here we present by far the largest study in healthy subjects in an effort to characterize the physiology of retinal blood flow.

Methods In the present study 64 healthy subjects aged between 18 and 45 years were included. Bi-directional laser Doppler velocimetry (Oculix, Arbaz, Switzerland) was used to measure retinal blood velocities. Venous vessel diameters were measured using the Retinal Vessel Analyzer (Imedos, Jena, Germany). Retinal blood flow was calculated by measuring all visible veins entering the optic nerve head. The perfusion values in the 4 quadrants were evaluated. In addition, the correlation between vessel diameters and red blood cell velocities was studied.

Results Total retinal blood flow was 46.2 ± 6.4 µl/min. The range of total retinal blood flow values was very high (29.0 – 70.8 µl/min). Blood flow was highest in the temporal inferior quadrant (17.9 ± 6.1 µl/min), followed by the temporal superior quadrant (12.2 ± 6.0 µl/min), the nasal inferior quadrant (7.3 ± 2.0 µl/min) and the nasal superior quadrant (6.5 ± 2.2 µl/min). In all four quadrants a highly significant linear correlation was found between blood velocities and vessel diameters (r-values between 0.55 and 0.89). The regression line was, however, considerably steeper in superior than in inferior vessels. Whereas, within the confidence limits, the regression line included the point 0,0 in the velocity-diameter graph in inferior veins, this was not the case in superior veins.

Conclusion The present data indicate that retinal blood flow shows a wide range in healthy subjects. In addition, differences were seen between the flow characteristics of the vessels in the inferior and the superior parts of the retina. The reason for these differences is hitherto unknown.

• 4131

Technical principles of optical coherence tomography and basic differences among time-domain, spectral-domain and swept-source OCT

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ABSTRACT NOT PROVIDED

• 4132

Important factors determining reliability and reproducibility of OCT scans: advantages and disadvantages of commercially available OCT devices

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ABSTRACT NOT PROVIDED

• 4133

Lamellar and penetrating keratoplasties

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ABSTRACT NOT PROVIDED

• 4134

Corneal dystrophies and hereditary anterior eye segment disorders

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ABSTRACT NOT PROVIDED

• 4135

Cataract, refractive and glaucoma surgery

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ABSTRACT NOT PROVIDED

• 4136

Ocular injuries

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ABSTRACT NOT PROVIDED

• 4141
Risk factors in JIA associated uveitis

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Purpose To show from different studies from the literature (including published and new data from a German population based registry (Heiligenhaus et al Rheumatology 2007)) which are the special traits and risk factors in patients with juvenile idiopathic arthritis (JIA) associated uveitis.

Methods Literature review and risk factor analysis. Comparison of different populations. Analysing predictors of longterm outcome.

Results Young age of JIA onset, ANA positivity and the oligoarthritis subtype are risk factors for the development of uveitis. Patients with complications at first visit fare worse in terms of visual acuity than those without. Especially cataract development is of concern in this age group prone to amblyopia. Screening intervals of every three months in the first year after arthritis diagnosis may be insufficient. Patients with uveitis that stays active into adulthood frequently showed complications at time of first uveitis detection as cataract, glaucoma and synechiae.

Conclusion Ophthalmological screening is of utmost importance in patients with JIA and should be initiated as early as possible after the diagnosis and repeated regularly, the timing of intervals has to be further investigated. Complications present at first uveitis diagnosis may predict longterm uveitis activity into adulthood.

• 4142
Living with juvenile idiopathic arthritis

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Purpose The purpose of the current study was to get a deeper insight into adolescents' experience of life with juvenile idiopathic arthritis (JIA) in the transition process from childhood to adult life, as described by young adults with JIA.

Methods The method used was individual qualitative interview, and 15 young adults were interviewed. The interviews were tape recorded and transcribed. Data were analysed using a qualitative content analysis approach.

Results From childhood into adult life, living with JIA involves struggle and adjustment to an insecure everyday life and an unpredictable life course. The informants' experiences emerged as dicotomies on a continuum describing the dynamics in life experiences individually and over time. The categories include bodily experiences of limitations or freedom, being acknowledged or set aside in interpersonal relationships, and intrapersonal experiences of insecurity or confidence. The findings indicate a change to greater acceptance and adjustment to the disease over time. However, the perception of being weak and different continued, and in adult life concerns about future health and life were more pronounced.

Conclusion The impact of JIA on life in a time of transition from childhood to adult life involves complex challenges on coping strategies and adjustment processes. Understanding this complexity is urgent for health professionals in order to contribute to both normal developmental task achievements and overall well-being for young people with JIA.

• 4143
Outcome measures in JIA associated uveitis

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Purpose Uveitis associated to juvenile idiopathic arthritis (JIA) is still the most frequent cause of blindness in the western world. It is an orphan disease and there are up till now no controlled trials for the treatment. Our multidisciplenary group is focusing on the further development of outcome measures of the SUN group (1) ,which could be used for prospective controlled studies. To develop outcome measures for JIA associated uveitis, which enable us to score the disease activity and complications of uveitis.

Methods We established our group based on special interest in this topic, and had two face to face group meetings to develop a proposed outcome measure domains and items.

Results We reached consensus in the group in the face to face meeting and definedspecific domains to assess the activity of JIA associated uveitis and defined items to assess the domains.

Conclusion This proposed domain and items will be discussed with a larger group of specialist and after that prospectively tested on consecutive patients for validation. It is aimed to develop outcome criteria according the OMERACT procedure.

• 4144
Long-term follow-up of patients with uveitis associated with juvenile idiopathic arthritis: a cohort study of three centers

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ABSTRACT NOT PROVIDED

• 4151

Outcomes of trabeculectomy with transconjunctival application of mitomycin C

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Purpose To assess outcomes of trabeculectomy surgery augmented with Mitomycin C (MMC) applied trans-conjunctivally.

Methods An MMC applicator (Duckworth and Kent, UK) was developed for drug delivery. Fornix-based conjunctival flap dissection was performed in each trabeculectomy case after trans-consjunctival MMC application for 3 min. A retrospective, case-note study was conducted. Records of patients who underwent the procedure over a one-year period, were analysed. Duration of follow-up, intraocular pressure (IOP) at last follow-up, and complications were noted.

Results 33 eyes of 28 patients were included. 23 eyes had primary open angle glaucoma, 5 had chronic narrow angle glaucoma, 2 had ocular hypertension and 3 had secondary open angle glaucoma. Mean follow-up duration was 8.4 months (range 3-15 months). Mean IOP at last follow-up was 11.9 mm Hg (range 2 to 21). Proportions of patients achieving IOPs at last follow-up of less than or equal to 12, 15, 18 and 21 mm Hg were 66.7%, 72.7%, 93.9% and 100% respectively. Two eyes (6.1%) had an IOP of 6 or below at last follow-up. Eight eyes (25%) required further needling or antimetabolite injection (2 of these underwent bleb revision). Other complications included choroidal effusions (4 eyes, 12.1%), transient bleb leakage (2 eyes, 6.1%) and corneal decompensation (1 eye, 3.0%).

Conclusion IOP outcomes in this preliminary study of trans-conjunctival MMC application are comparable to those reported using the more conventional subconjunctival application of MMC (WuDunn et al. Am J Ophthalmol. 2002;134:521-8; Wilkins et al. Cochrane Database Syst Rev. 2005;4:CD002897). Thus trans-conjunctival application may be a viable alternative. A larger study is underway comparing the two methods.

• 4152

Patients with advanced glaucoma with controlled intraocular pressure and visually significant cataract: phacoemulcification vs combined surgery

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Purpose Cataract surgery alone may have a beneficial effect in glaucoma patients by mildly lowering the intraocular pressure but loss of intraocular pressure (IOP) control may occur after cataract operation. It has also been suggested that patients presenting with more advanced glaucoma may have better outcomes with surgery than medical treatment. The purpose of the study is to investigate the postoperative results of two surgical alternatives: phaco only versus combined phaco trab operation in eyes with advanced glaucoma and controlled IOP.

Methods Prospective study of 78 patients with advanced open angle glaucoma (MD≥12 dB) with IOP≤21mmHg on topical medication and visually significant cataract (VA ranging from Hand Movements to 4/10). All patients were randomized to have either combined surgery (phaco-trab, two-sites, using adjustable sutures) (Group A, 39 eyes) or phaco only (clear cornea temporal approach) (Group B, 39 eyes). Follow up for 6 months. VA, IOP and VF were measured regularly with appropriate IOP control. Postoperative complications were recorded.

Results Phaco group showed faster visual recovery, higher peak IOP, greater IOP fluctuations and less MD difference than phaco_trab group, with the latter performing worse. Final VA didn't differ significantly between groups. Major complications: 9 choroidal detachments and 1 hyphema in Group A.

Conclusion For the first 6mo postoperatibvely higher IOPs in phaco only patients do not seem to worsen glaucoma lesions given strict IOP control. Even more, phaco_only eyes show faster visual improvement and need less prolonged intensive postoperative monitoring than phaco_trab eyes.

• 4153

Glaucoma and retinal detachment surgery

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Purpose Secondary transient or permanent elevation of intraocular pressure (IOP) is a quite common complication following vitreoretinal procedures.

Methods This presentation will focus on different mechanisms, clinical diagnosis and management of the secondary glaucoma after scleral buckling, vitrectomy with or without gas or silicone oil tamponade, and application of steroids.

Results In pre-existing operated glaucoma with filtering surgery, maintenance of the bleb requires an approach for conjunctiva preservation with techniques such as small gauge vitrectomy. Secondary hypertension can occur after scleral buckling because of congestion and anterior rotation of the ciliary body. Medical therapy is usually successful in controlling IOP, however surgical intervention could also be needed. Intravitreal injection of gases (SF6, C3F8) may produce secondary angle-closure glaucoma with or without pupillary block. Intraocular gas removal may be indicated. Secondary glaucoma can also develop after intravitreal injection of silicone oil due to pupillary block, inflammation, synechial angle closure, or migration of emulsified or nonemulsified silicone oil into the anterior chamber. Patients with medically uncontrolled glaucoma after silicone oil tamponade, with an open inferior iridectomy, may require oil removal with or without concurrent glaucoma surgery.

Conclusion Diode laser transcleral cyclophotocoagulation and drainage implants constitute approved methods for long-term IOP regulation. The underlying cause of secondary glaucoma after vitreoretinal surgery is often multifactorial. Cooperation between vitreoretinal and glaucoma specialists may be helpful in successful treatment.

• 4154

Lens phacoemulsification in treatment primary angle closure glaucoma with block induced lens after laser peripheral iridotomy

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Purpose To investigate the features of iridocilliary zone in patients with primary angle closure glaucoma (PACG) in cases of anterior chamber angle (ACA) block induced by lens after laser iridotomy and subsequent lens phacoemulsification with foldable IOL implantation.

Methods 45 patients (54 eyes) with PACG have been selected for this investigation. Parameters of iridocilliary structures were measured using ultrasound biomicroscopy (UBM) model «Humphrey-840».

Results UBM allowed to determine the features of block induced by lens at PACG. In these cases there was the displacement of lens-iris diaphragm forward independent of lens thickness with ACA block. The iris had a convex profile. The posterior chamber lost correct triangle configuration with decrease in section area by 1.3 times as compared to the norm. Most cases had a short-term hypotensive effect after laser iridotomy with only segmental opening of ACA. The extreme anterior position of the lens-iris diaphragm and small posterior chamber area persist at all cases. Configuration of the iris saved its convex. Subsequent phacoemulsiaicftion with foldable IOL implantation decreased the intraocular pressure (IOP) and eliminated block induced by lens with opening of the ACA. The restore of iris profile and posterior chamber configuration have been observed in all cases.

Conclusion Laser iridotomy creates optimal conditions for lens phacoemulsiaicftion by removing angular block and decreasing IOP from preoperative level. Phacoemulsiaicftion is pathogenic operation in cases of PACG with ACA block induced by lens.

• 4155 / 221

Evaluation of the efficacy of patterned laser trabeculoplasty: pilot study

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Purpose To evaluate the efficacy of Pascal Laser Trabeculoplasty (PLT) employing reduced energy levels in patients with OHT or POAG.

Methods Prospective, pilot study including 12 patients with OHT or POAG. Pascal laser trabeculoplasty was performed on the inferior 180° of the treated eye after titrating the energy for each patient. The IOP was measured with Goldmann applanation tonometer (GAT) on laser treatment day (D0), 1 week post laser (D7) and 1 month post laser (D30). Anova for repeated measurements was used for the statistical analysis.

Results The mean IOP on D0 was 25.2 ± 1.4 mmHg (range: 22 to 28.4 mmHg), mean IOP on D7 was 23.1 ± 1.5 mmHg (range: 19.8 to 26.4 mmHg) and mean IOP on D30 was 20.6 ± 1.1 mmHg (range: 18 to 23.1 mmHg). There was no significant difference between the D0 IOP and D7 IOP (p= 0.43) but between D0 IOP and D30 IOP (p= 0.001)

Conclusion Patterned laser trabeculoplasty causes significant IOP decrease after 1 month. In this pilot study The IOP drops by 20% after 1 month.

• 4156 / 217

Outcome of trabeculectomy in uveitis patients with secondary glaucoma

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Purpose To review the clinical outcome of our series of patients with uveitis and secondary glaucoma in which a trabeculectomy has been performed.

Methods Each patient was classified according to clinical presentation, pre and postoperative IOP, visual acuity and number of antiglaucoma drops needed. The outcome of trabeculectomy was classified in 3 categories: absolute success defined as IOP controlled (< 21 mmHg) without other treatment, relative success defined as IOP controlled with hypotensive drops and failed when IOP was not controlled or required hypotensive drops and oral acetazolamide. Success ratio with and without perioperative mitomycin were compared.

Results Mean visual acuity, IOP and number of drop used decreased at 3 month and at last follow-up. The mean follow-up was 19.3 months (2.9 – 67.1 months). At 3 month, we found 80% of overall success (53,33% of relative success and 26,67% of absolute success) and 20% of failure. At final follow-up, we also found 80% of overall success(56,67% of relative success and 23,33% of absolute success) and 20% of failure. Patients in whom perioperative mitomycin were used where more likely to have a favorable outcome (last follow-up: 83.33% vs 75%) but this difference between the two groups was not statistically significant.

Conclusion Our data are in accordance with the rest of the literature which shows that trabeculectomy with antimetabolite agents allows IOP control in the majority of patients. However, many of them will still need topical hypotensive drugs.

• 4161

Photodynamic therapy for symptomatic high risk choroidal melanocytic lesions

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Purpose To evaluate the role of photodynamic therapy (PDT) for symptomatic high risk choroidal melanocytic (HRCM) lesions with subretinal fluid extending to the fovea.

Methods Retrospective review of the medical records of all patients who underwent PDT for a HRCM lesion.

Results Seventeen patients were included in the study. The mean initial visual acuity was 20/80 (range CF-20/20). The mean initial tumor thickness was 1.23 mm (range 0.66-1.93). All tumors presented at least 2 risk factors for growing. The mean number of PDT sessions was 1.41 (range 1-3). The mean final visual acuity improved to 20/60 (range CF- 20/20). Subretinal fluid was reduced in all (100%) eyes and had completely disappeared in 9 (53%) eyes after PDT. The mean final tumor thickness increased to 1.24 mm (range 0.66 to 2.01) at a mean follow-up of 22.47 months (range 6-60). Tumor thickness increased in 3 (18%) eyes, remained unchanged in 13 (76%) eyes, and 1 (6%) lesion shrank down to a flat chorioretinal scar.

Conclusion PDT prevents vision loss with improvement of choroidal leakage in HRCM lesions with serous macular detachment, but doesn´t allow a good local tumor control. Longer follow-up is required to determine its value in these patients.

• 4162 / 435

Juvenile xanthogranuloma of the iris treated with proton beam radiotherapy.

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Purpose To report a case of juvenile xanthogranuloma of the iris treated with proton beam radiotherapy.

Methods An 18-year-old male presented in October 2010 with blurred vision of the left eye. Clinical examination showed a hyphaema. A yellow-pink tumour was noted in the temporal aspect of the iris. Ultrasonography showed the tumour to have a low internal reflectivity, measuring 7.8mm by 6.4mm in basal diameter with a thickness of 1.4mm. The lesion was noted to be extending to the pars plana. Incisional biopsy showed the tumour confirmed a diagnosis of juvenile xanthogranulomatosis. Treatment with topical steroids was unsuccessful. The patient was therefore treated with proton beam radiotherapy, comprising 18 Gy delivered in four fractions, penetrating to 4mm. Margins of 8mm around the lesion were also treated.

Results The patient was followed up in March 2011 where significant tumour shrinkage was observed on slitlamp examination. The response to treatment was confirmed on ultrasound. There were no new lesions and no evidence of anterior chamber activity. The patient remains under review.

Conclusion Proton beam therapy is an effective alternative local treatment for this condition.

• 4163

Supraselective intraarterial melphalan as the primary treatment for advanced retinoblastoma in older children

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Purpose To report 4 late retinoblastoma cases treated with supraselective injection of intraarterial melphalan as the primary treatment. In advanced retinoblastoma in older children enucleation remains the most common treatment option although some eyes can be salvaged with combinations of systemic chemotherapy, focal techniques and external beam radiotherapy. Direct infusion of chemotherapy into the ophthalmic artery has be attempted to achieve tumor control and avoid enucleation.

Methods The authors prospectively collected data of all retinoblastoma cases treated with selective intra-ophthalmic melphalan at the Referral Center for Retinoblastoma of Siena, Italy, from 2008 to 2011. Four out of 43 cases (4 eyes out of 49 eyes) of late unilateral advanced retinoblastoma received intraarterial melphalan infusion therapy as the primary treatment.

Results Complete remission was obtained in 1 out of 4 cases.

Conclusion The role of intraarterial chemotherapy as primary treatment for advanced retinoblastoma in older children remains to be elucidated.

• 4164 / 436

Superselective intra-arterial chemotherapy complications in advanced retinoblastoma

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Purpose The purpose of this study is to report the complications of superselective intra-arterial chemotherapy with melphalan in children undergoing treatment for advanced intraocular retinoblastoma.

Methods 49 eyes of 43 children with advanced intraocular retinoblastoma (Reese-Ellsworth Group Vb or International Classification Group D) were treated with superselective intra-ophthalmic artery infusion of melphalan. 22 eyes of 43 children were first diagnosis. 27 eyes of 43 children had previously failed traditional management with systemic chemotherapy and focal therapies and underwent intra-ophthalmic artery infusion of melphalan as an alternative option to enucleation. Serial complications RETCAM images were collected.

Results Ophthalmic artery cannulation was successfully performed in 49 eyes of 43 patients. 9 eyes out of 43 (20.9%) patients were enucleated. 4 eyes out of 43 (9.3%) patients were lost to follow-up. No severe systemic side effects occurred. Grade III neutropenia was seen in 3 patients (0.6%). No transfusions were required. 25 (58.1%) patients developed eyelid hyperaemia, 10 (23.2%) frontal region skin rash, 12 (27.9%) emiptosis, 6 (13.9%) eyelid edema, 2 (4.6%) frontal alopecia, 2 (4.6%) eyelashes loss, 2 (4.6%) chorioretinal atrophy, 1 (2.3%) acute ischemic optic neuropathy, all resolved spontaneously. 1 case (2.3%) with permanent ptosis underwent surgery. 1 case (2.3%) presented Roth's spots.

Conclusion Ophthalmic intra-arterial infusion with melphalan is a promising globe-conserving treatment option in advanced retinoblastoma cases with minimal systemic side effects.

• 4165
Follicular lymphoma of the ocular adnexal region in Denmark

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Purpose To characterize the clinicopathological features of follicular lymphoma of the ocular adnexal region.

Methods The present nation-based series of orbital and adnexal follicular lymphoma was collected between 1980 and 2009. Histological specimens were re-evaluated using a panel of monoclonal antibodies. Clinical files from all patients with confirmed follicular lymphoma were collected.

Results A total of 24 patients with follicular lymphoma of the ocular adnexal region were identified. Fourteen of the patients were females. The patients had a median age of 63 years (range 42 to 96 years). Eighty-eight percent of the patients had unilateral ocular adnexal region involvement, and the most frequently affected sites were: the conjunctiva (35%), the orbit (29%), and the lacrimal gland (21%).Fifteen patients (63%) presented with Stage I lymphoma. Three patients (12%) had Stage II, one patient (4%) had Stage III, and five patients (21%) presented with Stage IV lymphoma. Patients were treated with: radiotherapy (58%), chemotherapy (37%), and surgery alone (5%). Complete remission was observed in 79% of the patients. However, seven (37%) of these had a relapse, and were treated with local radiotherapy prior to setback. The 5-year and 10-year overall survival rate for the whole study group was 89% and 66%.

Conclusion Follicular lymphoma of the ocular adnexal region is mainly prevalent in elderly patients. The conjunctiva is the most commonly affected location. The majority of patients present with Stage I/II lymphoma, and the overall prognosis is relatively good. However, relapse or disease progression is frequently seen in this patients group.

• 4166 / 437
Anterior segment OCT and histopathologic data in conjunctival, limbal and subconjunctival tumours

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Purpose To show the use of anterior segment optical coherence tomography (AS-OCT) in conjunctival, limbal, subconjunctival tumors and to compare the data with histopathologic specimens.

Methods 15 patients (15 eyes) with conjunctival, limbal and subconjunctival lesions were examined using AS-OCT (Visante OCT 2.0, Carl Zeiss Meditec, Dublin, CA). Eyes were scanned using Anterior Segment Single, High Resolution Corneal and Raw Image modes. Gray-scale, OCT Color and Rainbow Color images were analyzed using built-in software. All tumors were excised and histopathologicaly examined.

Results In all small tumor cases AS-OCT allowed to see the deeper lesion structure with complete penetration. In conjunctival melanoma, papilloma, subepithelial naevus and pterygia cases AS-OCT showed tumor structure, layers and extension clearly. Underlying cornea was also visible. In larger and solid tumors (squamous cell carcinoma, fibroma and lipoma) anterior surfaces were hyper-reflective, but the deeper structures of the lesions were incompletely penetrated. However, in all cases it was possible to differentiate cystic lesions from solid lesions. Histopathologic examination revealed the diagnosis and in small tumors confirmed the AS-OCT data showing tumor epithelium and underling layers.

Conclusion AS-OCT may be a useful non-invasive diagnostic tool for the evaluation of ocular surface tumors in selective cases. AS-OCT may give useful information before planning the surgery.

• 4167 / 438
Squamous cell carcinoma (SCC) of the caruncle, with clinical presentation of an inflammatory mass.

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Purpose The presentation of 2 cases with a very rare adenoidlike SCC of the lacrimal caruncle, clinical referred with a inflammation mass apparent as an abscess.

Methods The tissue of a lacrimal caruncle is arising as well as from skin as mucous and adnexal structures, where in most of the patients only benign laesions could be developed. In our cases inflammation and malignant tumours were found. The diagnosis were made clinical, by imaging methods, (as coherence tomography scan (CT), and ultrasound) and histological analyses. In both cases good differentiated squamous cell carcinomas of the right caruncle were characterized

Results Although in the literature very rarely found, the adenoid type of SCC is described as a less malignant type but in our cases with inflammation a more aggressive behaviour was demonstrated during the follow-up. Both patients refused orbital exenteration and radiotherapy was performed. However in the second patient, at a later stage, an exenteration was done for a recurrence and extension to the nose and sinus, she died several months later.

Conclusion The very rarely published adenoid caruncle SCC , which first was presented in two cases as an

• 4168 / 439
Adenocarcinoma of the retinal pigment epithelium: clinicopathological case report

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Purpose Adenocarcinomas of the retinal pigment epithelium (RPE) are rare adult tumors, treated with enucleation or surgical excision. We present a child with an adenocarcinoma of RPE, treated with protontherapy.

Methods A 10-year-old girl with loss of vision had a pigmented macular tumor, diagnosed as hamartoma. Five years later, tumor growth led to a transvitreal incisional biopsy.

Results Histopathology and immunohistochemistry were compatible with an adenocarcinoma of the RPE. The tumor was irradiated. After 5 years of follow-up, the tumor is under control and the patient presents no distant metastases.

Conclusion Adenocarcinomas of the RPE can simulate a combined hamartoma of the retina and RPE. Diagnosis can only be established after biopsy. Protontherapy is a valid therapeutic alternative.

• 4169 / 440

Unexpected ectopic thyroid tissue in the orbit: a clinical case report

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Purpose To present clinical case report of the benign ectopic thyroid tissue in the orbit.

Methods 75-year-old woman with a slowly growing, painless, elastic tumor in the left inferior –lateral part of the orbit complained about diplopia, eye globe protrusion and dislocation medialy-superiorly. Symptoms were progressing for two years. Head magnetic resonance imaging (MRI), tumor excision and histopathological examination of the obtained specimen were performed.

Results Head MRI showed 18x14 mm in size, non-homogenic, contrast accumulating mass with well defined margins in the inferior –lateral part of the orbit. Gross examination of the excised mass revealed grey color, round tumor, covered by connective tissue. Histologicaly tumor was well circumscribed, composed of micro-/ macrofolicules with colloid. Folicular epithelium had no atypical changes. These criteria support diagnosis of ectopic thyroid tissue with slight signs of goiter. In the National Pathology Registre it was found that one year before patient had thyroidectomy and histological diagnosis of nodular thyroid hyperplasia and follicular adenoma was established. Possibility of follicular carcinoma metastasis to the orbit was rejected reviewing both cases by three pathologists and only usual Hematoxylin/Eosin method was used for staining.

Conclusion There are rear case reports of ectopic thyroid tissue. To our knowledge this is the first description of thyroid tissue with signs of goiter in the orbit.

• 4171 / 401

Ocular surface evaluation in children presenting ongoing ocular allergy

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Purpose to evaluate in a retrospective study ocular surface impairment and tear osmolarity in children presenting ongoing ocular allergy. Tears are necessary for continued health of ocular surface and tear osmolarity is considered a key point for tear film impairment and ocular surface damage.

Methods Our retrospective study included 20 children (mean age 11 yo, range 6 to 17 yo) of two groups that presented at ocular consultation of our hospital. Group a, 10 children with ongoing ocular allergy, group b 10 control children who had been tested but finally did not present any sign of allergy or dry eye. All the children underwent a tear osmolarity measure prior to complete ocular consultation to be aware of influencing results by the examination. The tear osmolarity measure was obtained with the Tear Lab Osmolarity System (OcuSense). A complete ocular examination was also performed. So the type of ocular allergy was diagnosed.

Results In group a, all the children presented clinical signs of on going ocular allergy with conjunctival redness, follicles and/or papillae. In two cases severe keratitis was present. In group b no ocular signs of conjunctiva anomalies were found. Mean tear osmolarity in group b, was 305mOsm/l and in group a, was 316mOsm/l. Tear osmolarity appeared higher in the ocular allergy group than in the non symptomatic children. Younger children had a higher measure of tear osmolarity.

Conclusion In adults 305mOsm/l is a cut-off value for dry eye. In our study this measure appears similar to adults but could be higher in youngest children. In children with ocular allergy, higher measure of tear osmolarity indicates an ocular surface damage that is underestimated. Tear osmolarity can be useful to manage ocular surface disease in children.

• 4172

The correlation between ocular surface inflammation and corneal fluorescein staining (CFS) in patients with moderate to severe dry eye disease (DED) participating in a randomized clinical trial

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Purpose The relationship between ocular surface inflammation, signs and symptoms in DED remains poorly understood. A correlation between ocular surface inflammation and CFS in DED patients is reported.

Methods DED patients with tear break up time ≤8 seconds and CFS grades 2-4 modified Oxford scale and Schirmer test without anesthesia ≥2 and <10 mm/5min and lissamine green staining, Van Bijsterveld >4 and at least 1 dry eye symptom were randomized to CYCLOKAT® (unpreserved 0.1% cyclosporine cationic emulsion) or vehicle QD. Impression cytology for conjunctival HLA-DR expression (an ocular surface inflammatory biomarker) was performed in a subset of patients.

Results Cytology samples were collected in 89 of 492 patients. At baseline the mean HLA-DR expression was higher in the CYCLOKAT® (84,345 AUF vs 46,888 AUF) arm. Notably, the mean HLA-DR expression increased with baseline CFS grade (grade 2: 48,343; grade 3: 56,749; grade 4: 127,623). At month 6, CYCLOKAT® significantly reduced the HLA-DR expression (-50896 AUF vs -1192 AUF, p=0.022). The efficacy of CYCLOKAT® on improving CFS [as measured by mean change (delta of CYCLOKAT® over vehicle) and % achieving ≥ 2 grade improvement] increased with the CFS grade at baseline (grade 2-4: 0.22 and 33.6% vs 21.8%, grades 3-4: 0.32 and 40.4% vs 27.7%, grade 4: 0.77 and 48.8% vs 19.5%, p<0.05 for all comparisons).

Conclusion The demonstrated correlation between HLA-DR expression and CFS support the role of inflammation in DED and justifies the need for anti-inflammatory therapy. The benefit of CYCLOKAT® appears to be greatest in patients with severe DED.

Commercial interest

• 4173

Response of the lipid and aqueous layers of the precorneal tear film to horizontal saccades. Novel findings and a new paradigm

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Purpose To consider the effect of horizontal saccades on the lipid and aqueous layers of the tear film.

Methods i. The interference pattern of the tear film lipid layer (TFLL) was studied in the left eye of 6 normal subjects, using the DR-1TM video-interferometer. Images were recorded continuously within a single interblink, with the eye in the primary position to capture the TFLL pattern: a. at least 1 second after the blink, when the pattern had stabilised and b. immediately after return to the primary position following a nasal saccade. ii. In a separate study, the movements of the aqueous layer, stained with fluorescein, were recorded during horizontal saccades, using standard slit-lamp video equipment.

Results i. In all subjects, the TFLL pattern after the first return saccade strongly resembled the initial pattern, but showed some degradation with multiple saccades. ii. The stained, precorneal aqueous layer moved with the cornea during saccades, with minimal displacement which was rectified on return to the primary position.

Conclusion Two alternative explanations are offered for these findings: i. The precorneal TFLL is 'glued' to the aqueous subphase so that these fluid layers move together with the cornea, during horizontal rotations of the eye. ii.Cooling of the tear film during the interblink, causes an increase in stiffness of the viscoelastic TFLL, so that it behaves like a stable carapace, uninfluenced by movements of the aqueous layer. Further experiments are planned to resolve these alternative hypotheses.

• 4174

Efficacy of wet chamber warming goggles (Blephasteam®) in patients with posterior blepharitis

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Purpose Posterior blepharitis is a main cause of dry eye. Lid hygiene is an important treatment, but compliance is often poor because of its complexity and lack of specific devices. The aim of this study is to assess the efficacy of wet chamber warming goggles (Blephasteam®) in patients with posterior blepharitis.

Methods In this interventional multicenter prospective uncontrolled study, patients with meibomian gland dysfunction were enrolled. Blephasteam® (Laboratoires Thea, Clermont-Ferrand, France) was used once or twice a day during 10 minutes, with a following lid massage. Main outcome measures were assessed at baseline and after 3 weeks, including symptoms (ocular discomfort on a visual analogic scale-primary endpoint, and separate symptoms), signs of blepharitis, Schirmer test, Break up time, corneal fluorescein vital staining, and tear osmolarity (measured with the Tearlab® system).

Results Thirty patients (16 women, 14 men), mean age 48 ± 22 years (4 to 82 years) were included. After 3 weeks of treatment, mean global visual analogic scale symptom score decreased by 15.2 ± 22 mm (range, +32 to -57 mm on a 100 mm scale)(p=0.004). Mean composite blepharitis score decreased by -3.5 points on the worst eye (range, +1 to -10 on a 20 points scale)(p<0,001). No change was observed for the other parameters among which BUT, IOP and tear osmolarity. Improvement rated by the patient was important in 48 % of cases, moderate in 36% and fair in 16%.

Conclusion Blephasteam® wet chamber warming goggles are a promising alternative to classical lid hygiene techniques. A multicenter extended study is ongoing.

Commercial interest

• 4175 / 402

High resolution images of the tear film lipid layer: effect of the blink cycle

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Purpose Deficiency of the lipid layer causes evaporative dry eye. We have therefore developed a high-resolution microscope to investigate lipid layer structure and how it may relate to evaporation and the blink cycle.

Methods The microscope images a 200 um diameter spot at the center of the cornea, with a resolution of about 1 um. Time after a blink is also recorded. Over 10,000 images of at least "fair" quality were recorded from 375 subjects including dry eyes and normals.

Results 1. Within about 0.1 seconds after a blink, lipid layer reflectance was less than at later times, implying that lipid thickness was lower. In this early interval, cloud-like patches of lipid were more often seen than at later times; they were surrounded by darker (thin) lipid. 2. Some structures in the lipid layer were very fluid, showing pronounced shape changes in a fraction of a second, whereas other structures were stable, with no evident change over several seconds.

Conclusion 1. Immediately after a blink, the lipid layer tends to be thin and often has an unusual appearance. 2. At later times, some structures vary rapidly in shape, indicating that the lipid layer is fluid with a low viscosity. Other structures are stable, suggesting that the lipid layer can have a gel-like structure.

• 4176 / 403

Altered corneal nerve morphology and epithelial wound healing in experimental lacrimodeficient dry eye

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Purpose To analyze the morphological changes of corneal nerves and its influence on corneal epithelial wound healing in a lacrimodeficient dry eye model in the guinea-pig.

Methods Corneal nerve architecture and the rate of corneal epithelial wound healing were studied in guinea-pigs to whom the main lacrimal gland was removed 4 weeks before (dry eye) and in control animals. Eyes were fixed, cryoprotected and incubated with neuronal class III Beta-tubulin antibody. Epithelial migration rate (EMR) and estimated time of healing (ETH) were calculated for 2mm-diameter epithelial corneal debridations stained with fluorescein, photographed regularly until complete closure and analyzed with image processing software.

Results Density (16±6 vs 27±11 nerves/mm2) and length (115±45 vs 186±74 µm) of subbasal nerves decreased significantly in dry eye. Subbasal nerves were less branched and tortuous. Epithelial nerve terminals were also reduced. EMR decreased significantly (63±4 vs 110±1 µm/h) and ETH increased significantly (38.6±1.8 vs 20.1±0.1 h) in dry eye.

Conclusion The morphological appearance and the decreased density, length and branches of corneal subbasal nerves are suggestive of corneal nerve degeneration at 4 weeks after lacrimal gland removal. Lacrimodeficient eyes presented also a slowing-down in corneal epithelial wound healing suggesting an early trophic defect consecutive to nerve damage.(Supported by: SAF2008-00529, CSD2007-00023, BFU2008-04425, BFU2009-07793 and RETICS RD07/0062/0012 from Ministerio de Ciencia e Innovación, Spain, and the Leonardo da Vinci Lifelong Learning Program.)

• 4211

Pneumatic retinopexy for uncomplicated rhegmatogenous retinal detachment

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Purpose Since its introduction in 1985, pneumatic retinopexy (PR) has become an important office based procedure for treating an ever-expanding group of rhegmatogenous retinal detachments (RRD). As an alternative to scleral buckling (SB) or pars plana vitrectomy (PPV), estimates suggest that over 40% of primary RRDs may be managed by PR.

Methods The efficacy of PR is dependant on 4 cardinal steps: (1) Identification and localization of all retinal breaks; (2) Induction of retinopexy around all breaks with cryopexy or laser; (3) Intraocular gas injection; and (4) Consistent post-operative head positioning for appropriate gas tamponade to achieve closure of the retinal breaks.

Results Numerous prospective and retrospective reports have confirmed that the single operation success rate for PR ranges from 65-75%, with a final anatomical success rate of over 95%. New retinal breaks typically occur in 10% of PR cases, and proliferative vitreoretinopathy is noted in approximately 5% of eyes. For repair of primary RRD, final post-operative visual acuity does not appear to differ among eyes initially treated with PR when compared to those treated with SB or PPV.

Conclusion PR has become a valuable technique in the modern era of RRD management. Despite its limitations and shortcomings, multiple clinical studies have clearly established its essential role in the armamentarium of surgical techniques utilized for the primary repair of RRD.

• 4212

Prognostic factors for anatomical and functional results after retinal detachment surgery. The SPR study

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Purpose In the "Scleral buckling vs. primary vitrectomy in rhegmatogenous retinal detachment study (SPR study)" two different surgical methods for the treatment of retinal detachment (RD) were compared in a randomised prospective multicentre clinical trial. This secondary analysis was conducted to investigate possible associations between pre- and intraoperative factors with the functional and anatomical outcomes.

Methods Univariate and multivariate analysis of 48 pre- and intraoperative factors and their association with anatomical outcome, functional outcome and the number of secondary surgical interventions.

Results In phakic patients, a significant correlation of successful outcome could be associated with number of retinal breaks, large breaks, cryotherapy, duration of symptoms, baseline visual acuity, central RD, total RD, drainage during buckling surgery and chain formation of breaks. In pseudophakic patients, factors identified were number of breaks, capsular fibrosis, Yag-laser capsulotomy, retinal laser photocoagulation, and inferior RD.

Conclusion The most important risk factor for functional and anatomical failure was a higher number of retinal breaks. Other risk factors varied between the phakic and pseudophakic patients as well as between functional and anatomical outcomes. These findings are of clinical importance for identification of patients with a higher risk for failure and for the planning of future trials on RD surgery.

• 4213

Subretinal fluid lavage: a novel concept in retinal detachment surgery

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Purpose To review possible causes and therapeutic options for persistent submacular fluid after retinal detachment surgery.Optical coherence tomography identifies persistent subretinal fluid (PSF) after apparently successful retinal detachment repair surgery in up to 94% of patients. PSF is associated with delayed recovery of visual function.

Methods Based on the literature and the results of subretinal fluid analyses, we hypothesised that highly viscous PSF, which interferes with the normal function of the retinal pigment epithelium, can lead to these persistent blebs. We reviewed all reported interventions for PSF. We devised a novel surgical manoeuvre of subretinal lavage to dilute the subretinal fluid (SRF) during surgery. We expected that this would reduce the incidence of PSF. We report our experience with a modified surgical drainage technique in patients with long standing retinal detachments.

Results No postoperative medical or surgical intervention has been proven to be effective in a series of patients. On the contrary, none of the patients undergoing modified drainage and lavage developed PSF.

Conclusion In the absence of an effective cure, prevention appears to be a promising option.

• 4214

Rhegmatogenous retinal detachment associated to vitreous hemorrhage. Role of primary vitrectomy?

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Purpose The incidence of retinal break formation following acute posterior vitreous detachment is variously reported as occurring in between 8% to 15% of patients, associated up to 39% of the eyes with rhegmatogenous retinal detachment.

Methods Retrospective review of noncomparative interventional case series and cases treated in our department

Results The management of patients with fundus-obscuring dense vitreous haemorrhage due to presumptive retinal tears advocates waiting for spontaneous resolution. Surgery is indicated only when a definite retinal tear or retinal detachment is identified. However, the degree of agreement between ultrasound and clinical findings, indicate retinal diagnosed and localized accurately in only 44% of eyes. Early vitrectomy for spontaneous dense fundus-obscuring vitreous haemorrhage and posterior vitreous detachment seems safe. Rhegmatogenous retinal detachment with severe VH is associated with longer duration of preoperative haemorrhage, a higher incidence of severe PVR and worse visual outcome. An 75% incidence of retinal detachment was reported in eyes with a history of retinal detachment in the contralateral eye. Close follow-up and aggressive surgical interventions are suggested in these patients.

Conclusion Acute, spontaneous, nontraumatic posterior vitreous separation with dense fundus-obscuring vitreous hemorrhage is associated with a high incidence of retinal tears and detachment. Close follow-up with clinical examination and ultrasonography is necessary, because many of these eyes may eventually require surgical intervention. Aggressive management with early vitrectomy should be considered when there is a history of retinal detachment in the contralateral eye.

• 4215

Primary vitrectomy alone for pseudophakic retinal detachment

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Purpose To report the anatomic and functional results of primary vitrectomy without scleral buckling for the treatment of pseudophakic rhegmatogenous retinal detachment(PsRD)

Methods One hundred eyes of 98 patients with PsRD were operated by vitrectomy alone. Internal subretinal fluid drainage, cryocoagulation and/or endolaser and fluid-air exchange with sulfur hexafluoride 20% was applied in all cases. The preoperative and postoperative characteristics were analyzed. Main outcome measures were anatomic success rates after initial surgical intervention and after reoperation for primary failures, visual outcome at the last follow-up visit,and complications.

Results Mean follow-up +/- standard deviation (SD) was 12 +/- 6.3 months (range, seven to 36 months). Mean final visual acuity +/- SD was 0.42 +/- 0.45 logarithm of the minimum angle of resolution (logMAR) compared with 0.95 +/- 0.73 logMAR before surgery (P < .01). Mean number +/- SD of retinal breaks found before surgery was 1.36 +/- 1.12 (range, zero to five), and an additional 1.58 +/- 2.26 (range, zero to 15) retinal breaks were found during surgery. The retina was reattached successfully after a single surgery in 92 eyes (92%). Recurrence of retinal detachment occurred in eight eyes (8%), caused by proliferative vitreoretinopathy in six eyes (75%) and by new breaks in two eyes (25%). Final anatomic reattachment was obtained in these cases after a mean of 1.75 subsequent operations. Three eyes required permanent silicone oil tamponade so that final anatomic success was achieved in 97 eyes (97%). The most common postoperative complication was ocular hypertonia of more than 21 mm Hg, observed in 36 (36%) eyes, which was managed successfully.

Conclusion Primary vitrectomy provides high anatomic success rate in PsRD eyes

• 4216

20-gauge pars plana vitrectomy vs 23G, 25G in the management of primary and recurrent retinal detachment: pros and cons

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ABSTRACT NOT PROVIDED

• 4221
The first consultation

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Purpose Patients with complaints of seeing badly in the dark need a full ophthalmological workup.

Methods Acquired versus congenital nightblindness has to be questioned in a full anamnesis. Visual acuity, biomicroscopy and fundus examination are essential followed by visual field testing and possibly visual electrophysiology (flash ERG)

Results Several causes of congenital and acquired nightblindness can be found. Not all patients complaining of seeing badly in the dark are "nightblind"

Conclusion A full clinical ophthalmological work up can identify adequately several causes of night blindness

• 4222
Causes of night blindness

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Purpose To describe the causes of both genetically determined and acquired night blindness.

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

Results Phenotypes and genotypes of genetically determined diseases leading to night blindness are very different. An important distinction to be made is the one between stationary and progressive diseases. Indeed, other than night blindness the visual outcome differs considerably between different conditions.

Conclusion The causes of night blindness are diverse. Taking a thorough history in combination with an extensive clinical examination and psychophysical and electrophysiological tests most often allows a to make a specific diagnosis. Acquired conditions are generally treatable, and should be differentiated from those that are inherited. For genetic disease, it is important to distinguish between progressive and stationary conditions.

• 4223
Electrophysiology of patients with nyctalopia

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The lecture will use a case-based approach to demonstrate the value of electrophysiological testing in the diagnosis and management of patients with nyctalopia. The diagnostic features of various inherited and acquired diseases will be described, including photoreceptor dystrophies, congenital stationary night blindness, fundus albipunctatus, melanoma associated retinopathy, vitamin A deficiency and others.

• 4224
What limits normal visual performance in the dark?

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Purpose Visual performance is affected by changes in the spatial and temporal properties of the retina and/or changes in the quality of the retinal image as a result of increased aberrations and scattered light. The aim of the study was to establish the extent to which retinal and/or optical factors set the limits of visual performance at low light levels.

Methods Pupil size, ocular aberrations, scattered light, chromatic sensitivity and contrast acuity were measured as a function of retinal illuminance. Pupil size was measured continuously and display luminance adjusted for constant retinal illuminance.

Results Mesopic vision describes the range of light levels over which signals from both rods and cones contribute to the visual response. Visual performance changes with light level: Both the amount of scattered light and the rms wavefront aberration were found to increase rapidly with decreasing light level in the mesopic range. This was paralleled by a massive increase in contrast acuity thresholds and a rapid loss of both red-green and blue-yellow chromatic sensitivity.

Conclusion The gradual increase in rod signal as the light levels decreases causes changes in the overall spectral sensitivity of the eye with consequences for visual effectiveness. Cone dominated vision is affected most by optical factors; in rod dominated vision the limiting factor becomes the resolving power of the retina. Key aspects of visual performance, such as spatial and temporal contrast sensitivity and acuity, visual delay and colour sensitivity change with light level. Linking such changes allows us to predict visual performance at low light levels where characteristics of the rod and cone system are so different.

• 4231

Fluorescein angiography in uveitis

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Purpose Fluorescein angiography (FA) is an important test in the evaluation and management of patients with uveitis. FA in uveitis is giving information principally on the superficial structures of the fundus (retina, retinal vessels and optic nerve head / disc), on the retinal pigment epithelium, on the choriocapillaris in the first 60 seconds of angiography as well as immediatelly subclinical pathology such as subretinal neovascular membranes.

Methods FA is indicated when a posterior segment involvement is present or suspected. It should examine the posterior pole, optic disc, and periphery, with angiograms at early, intermediate, and late phases.FA results should be interpreted in relation to the results of clinical examination and other tests

Results There are many roles for FA in the evaluation of patients with uveitis1. Evaluation of the activity and extent of chorioretinitis: 2. Diagnosis of uveitic entities with typical features. 3. Evaluation of retinal vascular involvement : focal, multifocal, or diffuse retinal vascular leakage, occlusive complications, optic disc or retinal neovascularization, 4.Identication of macular complications5. Evaluation of optic disc involvement. 6. Monitoring of response to treatment

Conclusion FA can be helpful in the diagnosis, treatment, and monitoring of patients with posterior segment inflammation.

• 4232

Indocyanine green angiography in uveitis

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ABSTRACT NOT PROVIDED

• 4233

OCT in uveitis

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Purpose To describe the role of optical coherence tomography (OCT) in uveitis.

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

Results The involvement of the posterior pole during an active eye inflammatory disease can entail a reduction of visual acuity, which is sometimes difficult to treat. Albeit fluorescein angiography (FA) is still the gold standard for the detection of blood-retinal barrier (BRB) disruption and has been the best option for the diagnosis of cystoid macular oedema (CMO), OCT represents an essential tool that can ameliorate the interpretation of FA findings. Epiretinal membrane (ERM) and tractional maculopathy may represent a sight-threatening sequela of uveitis. OCT is extremely useful in documenting pathologies at the vitreo-retinal interface, such as the formation of ERM, as well as it is also helpful in proving early infiltrates at the posterior vitreous interface. Although FA still remains the gold standard for the choroidal neovascularization (CNV) assessment, OCT is very helpful in documenting CNV nearby a chorioretinal scar. OCT has been used to study the type of CNV and to find its correlation to RPE.

Conclusion OCT may demonstrate a variety of morphological changes, that may point towards a specific uveitic disease: different forms of macular oedema may be described in uveitis as well as OCT features which can be peculiarly found in several diseases. In addition, OCT can be very useful in documenting both ERM and CNV.

• 4234

Fundus autofluorescence (FAF) in uveitis

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ABSTRACT NOT PROVIDED

• 4235

Cxc chemokine expression profiles in aqueous humor of patients with different

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(2) Laboratory of Histochemistry and Cytochemistry, University of Leuven, Leuven
(3) Rega Institute for Medical Research, Leuven

Purpose To investigate the CXC chemokine expression profiles in the aqueous humor from patients with active uveitis associated with Behçet's disease, VKH disease, and HLA-B27-related intraocular inflammation and to correlate.

Methods Aqueous humor (AH) samples from patients with Behçet's disease (BD) (n=29), Vogt-Koyanagi-Harada (VKH) disease (n=21), and HLA-B27-associated uveitis (n=8), and 42 control patients were assayed for the neutrophil chemoattractants CXCL1/GRO-α and CXCL8/IL-8 and the lymphocyte chemoattractants CXCL9/MIG, CXCL10/IP-10 and CXCL12/SDF-1 with the use of a multiplex chemokine assay.

Results Chemokine levels except CXCL12/SDF-1 were significantly higher in the 3 disease groups than in normal controls. Considering all patients, mean CXCL1/GRO-α levels were 15-fold higher than CXCL8/IL-8 levels and mean CXCL10/IP-10 levels were 22-fold higher than CXCL9/MIG levels. In patients with the same disease activity, AH levels of CXCL1/GRO-α and CXCL10/IP-10 were significantly higher in patients with BD than in patients with VKH disease and HLA-B27-associated uveitis ($p=0.0474$; $p<0.001$, respectively).

Conclusion These data suggest that CXCL1/GRO-α and CXCL10/IP-10 are the predominant CXC chemokines involved in neutrophil and activated T lymphocyte chemoattraction in endogenous uveitis, particularly in BD.

• 4236

Practical & quiz cases II

MARKOMICHELAKIS N
Ocular Immunology and Inflammation Service, Department of Ophthalmology, Athens

ABSTRACT NOT PROVIDED

• 4237

Practical & quiz cases III

BODAGHI B
Ophthalmology, Pitié-Salpêtrière Hospital, Paris

Imaging techniques have definitely changed our diagnostic approach to posterior and panuveitis. Based on their interpretation, it is also possible to revisit the diagnostic work-up in order to propose a more simplified strategy. During this presentation, different situations will be discussed in order to emphasize targeted diagnostic tools and therapeutic options.

• 4238

Practical & quiz cases IV

PAPADIA M
Universita' degli Studi di Genova

ABSTRACT NOT PROVIDED

• 4239

Practical & quiz cases V

HERBORT C (1), KHAIRALLAH M (2), NERI P (3)
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(3) Polytechnic University of Marche, Torrette-Ancona

ABSTRACT NOT PROVIDED

• 4241
What do we (authors, reader, publisher) need ?

DUA H
Queens Medical Centre, Nottingham

ABSTRACT NOT PROVIDED

• 4242
Characteristics of a good paper

WEGENER A
University Clinics, Bonn

ABSTRACT NOT PROVIDED

• 4243
How can we improve the review process (view of the Editor and beyond)

STEFANSSON E
University of Iceland, Reykjavik

ABSTRACT NOT PROVIDED

• 4244
The reviewer: friend or foe?

PLEYER U
Charite, Campus Virchow, Berlin

ABSTRACT NOT PROVIDED

• 4251

Cataract and glaucoma surgery, combined or consecutive, where do we stand?

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Switzerland

The surgical management of concomitant cataract and glaucoma, uncontrolled despite maximum tolerated medical therapy, may be consecutive or combined during the same surgical session. Combined procedures are more demanding techniques with potentially more complication but decrease durably the IOP and allow longer preservation of the visual field. However results in various studies using different surgical techniques give contradictory results and recommendations. During the course an analysis of the actual state of knowledge from the literature will be discussed in details covering the aspect of surgical techniques, efficacy in IOP lowering, visual function, quality of life as well as cost of these two different surgical approaches.

• 4252

Combined approach, the yield of microincisions for cataract surgery

BRON A M
Dijon

Cataract extraction combined with glaucoma surgery remains controversial. Some authors advocate consecutive surgeries arguing that the expected lower inflammation will allow a better outcome of the filtering surgery. However it is well known that cataract extraction after a filter may impair the long term efficacy of glaucoma surgery. Conversely the combined approach is more convenient for the patient with one operation and generally a better visual result. However it is generally considered that the IOP-lowering effect is less effective in combined procedures. Rather than opposing these two approaches, it is probable than according to the characteristics of the patient and the type and the stage of glaucoma, a consecutive or a combined surgery is more appropriate. Therefore the surgeon must be prepared to perform the two types of surgery. Micro incisions for cataract surgery (MICS) offer some substantial advantages vs conventional corneal incisions; a better tightness of the surgical wound allows a better control of IOP during the surgery. Therefore glaucoma surgeries (penetrating or not) are much easier to perform without changing your technique. In this presentation some surgical tips will be given in order to facilitate your combined procedures.

• 4253

Staging: glaucoma first or cataract first?

ZEYEN T
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A combined Phaco-Trabeculectomy will often not have the same result as both procedures separately. The IOP lowering effect of a combined procedure is usually less than that of Trabeculectomy alone. Likewise, post-operative fluctuations of the anterior chamber depth after a combined procedure will influence the post-operative refraction, especially in the early post-operative period and/or if additional procedures (e.g. needling) are necessary to rescue a failing bleb.Therefore, most surgeons will prefer to stage both procedures. Since cataract surgery might compromise an existing filtering bleb, it is recommended to perform Phaco first if the IOP is not too elevated. If the glaucoma is at risk to deteriorate in the short term, filtering surgery should be performed first. It is advisable to wait 6 months between the cataract and glaucoma surgery.

• 4261
TRPM1 and MITF expression in conjunctival melanocytic proliferations

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(2) Ophthalmology, Lausanne

Purpose Downregulation of TRPM1, a transient receptor potential cation channel, has been correlated with a higher metastatic risk in skin melanoma. The promoter of TRPM1 contains MITF binding sites and MITF regulates in vitro the transcription of TRPM1. We have showed a partial loss of TRPM1 mRNA expression in a limited number of conjunctival melanoma. The aim of this study was to further investigate TRPM1 and MITF expression in a broader panel of conjunctival melanocytic proliferations

Methods Expression of MITF and TRPM1 was assessed by immunohistochemistry in 17 conjunctival naevi, 8 PAM (6 PAM with atypia) and 16 conjunctival melanoma. Statistical analysis was performed with JUMP 8,0 software.

Results A complete preservation of both MITF and TRPM1 expression was identified in all the naevi and the PAM. A partial loss of TRPM1 expression was found in 44% of the conjunctival melanoma (2 cases with a scattered loss of expression and 5 cases with a regional loss of expression). There was a significant partial loss of TRPM1 expression in the melanoma group compared with the naevi group (p=0,0027) or with the PAM group (p=0,0331). A partial loss of MITF was identified in 50% of the melanoma with significant reduction compared with the naevi group (p=0,0005) or with the PAM group (p=0,0262). There was a significant correlation between partial loss of TRPM1 expression and partial loss of MITF expression (p<0,001).

Conclusion We demonstrate a reduction of both MITF and TRPM1 expression in conjunctival melanoma compared with benign melanocytic lesions, suggesting that the loss of these proteins might be correlated with tumor progression. The concomitant partial reduction of expression of both genes is in concordance with the regulatory role of MITF on TRPM1 transcription.

• 4262
Strontium brachytherapy in conjunctival melanoma

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(3) Ophthalmology, Antwerp University, University
(4) Ophthalmology, Leiden University, Leiden
(5) Radiotherapy, Amsterdam Medical Center, Amsterdam

Purpose To describe the experience, the indications, the outcome, complications and prognosis of strontium brachytherapy in bulbar conjunctival melanoma.

Methods 46 with conjunctival melanoma, treated with strontium brachytherapy in Leuven, Leiden or Amsterdam, were revised. Clinical indications, visual outcome, prognosis and complications were registered.

Results In 38 patients 6x10 Gy was used, with 2 recurrences and 1 scleral melting. In 7 cases 6x5,9 Gy was used with 4 recurrences. In 3 cases a second strontium brachytherapy application was needed. Although there were in almost all cases transient dry eye symptoms, no major anterior segment problems were seen. With the exception of 1 scleral melting,in a patient where also a previous extended surgery was done with excision of sclera.

Conclusion Strontium brachytherapy is a safe treatment for conjunctival melanomas, when a dosis of 60 Gy is used. It gives rarely complications.

• 4263
Chromosomal alterations in iris melanoma

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Molecular and Clinical Cancer Medicine, Univ. of Liverpool, Liverpool

Purpose Melanomas arising in the iris (IM) are rare comprising about 5% of all uveal melanomas (UM). They are seldom lethal with only 2-4% of IM associated with metastatic spread. The genetic pathogenesis of IM and its favourable outcome, compared with choroidal and ciliary body UMs, is still not well understood. The aim of this study was to investigate whether genetic changes associated with prognosis in choroidal/ciliary body UMs (i.e. monosomy 3 and polysomy 6p or 8q) are also indicative of prognosis in IM.

Methods Changes in chromosome 1p, 3, 6 and 8 copy number were detected in seven IMs by Multiplex Ligation-dependent Probe Amplification. Full clinical, histomorphological and survival information was available for each patient.

Results There were five male and two female patients, whose age ranged from 32-68 years (median 51 yrs). Three patients had received previous proton beam therapy. Two patients died due to metastatic melanoma; both tumours showed polysomy 8q, with one tumour also showing monosomy 3 and the other showing polysomy 6p. Time from diagnosis to metastatic death was longer for the patient with a polysomy 6p tumour (6 yrs) than for the monosomy 3 tumour (3 yrs). The remaining five patients demonstrated no consistent genetic alterations and were alive with no evidence of metastases at the time of analysis.

Conclusion This study suggests that genetic changes in chromosomes 3, 6p and 8q, previously observed for choroidal/ciliary body UM, could also be associated with survival in IMs. Further high-resolution studies with a larger cohort of IM are currently being performed to validate these data.

• 4264
Role of 3.0 Tesla MRI in diagnosis and treatment planning of iridociliary and choroidal melanocytic tumours

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(2) Ophthalmology, Edegem Antwerp
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(4) Pathology, Leiden

Purpose To evaluate the role of 3 Tesla MRI in the diagnosis, measurement and treatment planning of choroidal and iridociliary melanoma and comparison of results with Ultrasound and histology to measure the accuracy of MRI.

Methods : Prospective analyses of consecutive 12 patients, four with iridociliary and eight having choroidal melanocytic tumors. All these patients had ultrasound (10MHz) or UBM (50MHz), 3 Tesla MRI and underwent primary enucleation. The enucleated eyes were examined for gross measurements and histopathology was done.

Results Iris/iridociliary melanocytic tumors showed that MRI was positive in two cases and comparable to UBM. In one case tumor was identifiable only on saggital sections while in one case of Leiomyoma MRI gave much details and enhancement patterns. For posterior tumors MRI was positive in all the eight cases and results were comparable to ultrasound and macroscopic pathology in six cases.

Conclusion 3 Tesla MRI showed comparable results to UBM /USG and macroscopic pathology in 80% of patients. MRI should be performed if clinical and USG are in doubt to get additional information for diagnosis of other melanocytic tumors. An important finding was that for iris-iridociliary melanomas MRI saggital images should be used for interpretation.

• 4265

Autophagic activity in uveal melanomas

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(3) Department of Ophthalmology, Charite, Berlin

Purpose Autophagy is a self-degradation mechanism by which cells recycle their own cytoplasmic constituents and organelles. Experimental data suggest that autophagy is up-regulated by hypoxia in human neoplasia.

Methods The autophagic activity was investigated in a series of 73 uveal melanomas after immunohistochemical staining for the autophagy-associated proteins LC3A and Beclin1. This was assessed in parallel with the hypoxia inducible factor 1α (HIF1α) and its downstream protein lactate degydrogenase 5 (LDH5).

Results Two patterns of LC3A expression were readily made out – diffuse cytoplasmic and cytoplasmic/juxta-nuclear. The former was detected in 37/73 (50.7%) melanomas; the latter in 22/73 (30.1%) tumors. Beclin1 expression was invariably diffuse cytoplasmic and occurred in 37/73 (50.7%) uveal melanomas. LC3A and Beclin1, when highly expressed, were associated with intense pigmentation of the lesion, but only Beclin1 was associated with tumor necrosis ($p<0.05$) and a larger tumor size ($p<0.05$). It is of interest that Beclin1 and perinuclear LC3A expression were significantly related ($p<0.02$). In linear regression analysis, the LC3A juxta-nuclear/perinuclear pattern and the Beclin1 expression were connected with the hypoxia-related proteins HIF1α ($p<0.02$) and LDH5 ($p<0.0001$).

Conclusion Autophagy is commonly up-regulated in uveal melanomas, and may be associated with necrosis and large tumor size. There is a connection between Beclin1 and LC3A juxta-nuclear/perinuclear pattern, and a strong link between autophagy and hypoxia as this is inferred by the intimate relationship of LC3A and Beclin1 with HIF1α and LDH5, the major LDH isoenzyme involved in anaerobic metabolism.

• 4266

Percentage of aberrant cells in uveal melanoma correlates with the patient's prognosis

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(2) Clinical genetics, Erasmus University Medical Center, Rotterdam
(3) Ophthalmology, Erasmus University Medical Center, Rotterdam
(4) Pathology, Erasmus University Medical Center, Rotterdam

Purpose Uveal melanoma (UM) is the most common type of intra-ocular malignancy in adults with an annual incidence of 5-7 cases per million. Almost half of all patients with UM eventually die due to often late appearing metastases. Several clinical, pathological, and genetic factors have been identified as prognostic markers in UM. Non-random chromosomal alterations for instance are present in over 80% of cases and complete loss of chromosome 3, (seen in 50% of all UM) relates to a 4-year overall survival rate of only 30%.

Methods Fluorescence in situ hybridisation (FISH) can be used to evaluate aneuploidy in the tumour cells. This FISH technique enables an in situ analysis of exact number/percentage of tumour cells displaying that particular chromosomal aberration.Tumour heterogeneity has been observed in UM and an obvious question is whether lower percentages of abnormal cells are related to a change in patient's outcome or prognosis.

Results In this study, we assessed the percentages of aberrant tumour cells with FISH for each tumour (N=221) using chromosome 3 and 8 probes.

Conclusion For both anomalies we could demonstrate that a high percentage aberrant tumour cells correlate well with a significantly worse prognosis for the patient.

• 4267

Genetic and histological heterogeneity in uveal melanoma: a peculiar case

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Ocular Oncology Research Group, Liverpool

Purpose Intratumour heterogeneity of uveal melanoma (UM) has become a relevant issue in the era of sampling for prognostication purposes. We present the case of a UM consisting of two very distinct components.

Methods A 53-year-old man was referred for an infero-nasal, collar-stud UM with associated retinal detachment in the right eye. On ultrasonography, the tumour measured 14 x 16mm, with a thickness of 11mm. The patient chose enucleation over other treatment options. The eye was examined morphologically, immunohistochemically and using multiplex ligation-dependent probe amplification (MLPA).

Results Histological sections demonstrated two distinct components: a pale basal part consisting of amelanotic epithelioid melanoma cells with extensive diffuse involvement of the ocular structures. In contrast, the apical part was heavily pigmented comprised only of spindle B cells. Interestingly, MLPA demonstrated complete chromosome 3 loss in the apical (spindle) region but only partial chromosome 3 deletion in the basal (epithelioid) part. Both areas showed polysomy 8. Conversely, immunohistochemistry showed more aggressive features in the basal part rather than in the apical part.

Conclusion This case provides further evidence that there is heterogeneity in UM, and that a single intraocular biopsy may not be reliable for prognostication purposes.

• 4268

Are liver function tests relevant for early detection of liver metastasis of uveal melanoma?

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(2) Service d'ophtalmologie, CHU cote de Nacre, Caen
(3) URESP, Centre de recherche FRSQ du CHA, Hôpital du St Sacrement, Québec
(4) IAE Département IUP Management du Social et de la Santé, Caen

Purpose The liver is the main target for screening for uveal melanoma metastasis, which could be achieved by liver function tests (LFTs). The aim of our study is to analyze the relevance of LFTs for detection of metastatic disease in term of prognostic value and cost evaluation

Methods Patients (n=88, who developed metastasis while undergoing semi-annual follow-up with LFTs including aspartate-aminotransferase (AST), alanine-aminotransferase (ALT), gammagutamylransferase (γGT), lactodeshydrogenase (LDH), and phosphatase alkaline (PA) were included. For assessing the level of LFTs for metastasis only the one preceding screening LFTs before the diagnostic by imaging was recorded. Consecutive patients (n=174) with uveal melanoma were chosen as control from patients who did not develop metastasis

Results We were able to detect metastasis after LFTs abnormality in 40 (45%) patients. However, at the time of the one preceding screening LFTs before the metastasis diagnosis, 51(58%) patients had at least one abnormal LFT. The metastasis diagnosis was missed in 11 patients (13%). The overall sensitivity of LFTs ranged from 12.5 to 58.0% and the predictive positive value ranged from 9.4 to 38.6%. Interestingly we observed false positives in 20.3% with the variable "at least one abnormal LFT". Using financial approach, we calculated the semi-annual screening by LFTs.

Conclusion Using the most important retrospective series analyzing semi-annually all LFTs, we demonstrate that LFTs screening (AST, ALT, γGT, LDH and PA) is not relevant for detection of early metastasis even if the over cost induced by imaging requested for false positive is low

• 4271

An update on patient selection for OOKP surgery: psychosocial assessment

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Sussex Eye Hospital/Sussex Partnership NHS Foundation Trust, Brighton

Purpose This presentation will provide an update on the contribution of Psychosocial factors in the assessment and selection of patients for OOKP surgery. Assessment aims to identify Psychiatric, Psychological and Social issues which may positively or negatively affect physical and psychological outcome. Identification of such factors may not be a barrier to selection and successful outcome, as appropriate measures may be put in place to address factors which may impede physical or psychological recovery.

Methods Drawing on the existing psychological literature on patient assessment for complex surgery and studies carried out with OOKP patients in Brighton, Psychological factors associated with positive and negative biological and psychological outcome are described and the assessment protocol detailed.

Results A model which seeks to assess the contribution of psycho-social factors in the prediction of complicated recovery is being developed and will be described. This is currently being incorporated into a prospective study to test the validity and utility of the model.

Conclusion Attention to Psycho-social factors in selection of patients for OOKP surgery facilitates good bio-psychosocial outcome by encouraging active patient participation in informed decision making about the surgery, good psychological preparation for the procedure and patient and family commitment to after-care and follow-up. For those where surgery is not appropriate or a decision needs to be postponed the selection process can also be of value for both patients and staff.

• 4272

An update on glaucoma in OOKP eyes

LAM FC, HEROLD J, LIU C
Brighton

ABSTRACT NOT PROVIDED

• 4273

An update on imaging and strengthening of the OOKP lamina

QASHOU A, FRANCIS I, HEROLD J, LIU C
United Kingdom

ABSTRACT NOT PROVIDED

• 4274

An update on the Boston Type 1 KPro

CORTINA S
University of Illinois at Chicago

ABSTRACT NOT PROVIDED

• 4275

An update on the use of the Boston Type 1 KPro outside the USA

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ABSTRACT NOT PROVIDED

• 4276

Collagen-based bioengineered corneas: a material development update

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Purpose Our overall objective is to develop novel biomimetic materials that support the regeneration of diseased or damaged corneal tissue. This presentation will provide an update on such materials developed in our group.

Methods We have developed a range of collagen-based materials as mimics of the cell-free corneal stromal extracellular matrix. Promising material formulations were tested pre-clinically for their physical properties (e.g. mechanical, optical, water uptake, etc.) and physiological properties (e.g. interactions with corneal cells, biodegradation, in vivo implantation in animals etc.). One of the early formulations was clinically tested in the corneas of 10 patients, results of which will be discussed.

Results More recently, our team of Canadian and Swedish researchers reported the successful implantation of cell-free, bioengineered corneas into patients with keratoconus and central scarring in a Phase 1 clinical trial. These implants acted as stable scaffolds that promoted functional regeneration of corneal cells and nerves. At 24 months post-operative, six of the ten patients could see four times further than before the operation. With the help of rigid contact lenses – the results in all ten patients were similar to what the traditional corneal transplant with human donor tissue would be, with one patient achieving 20/20 vision and two others with 20/25 vision.

Conclusion Despite the promising clinical results, more robust and elastic materials are required to withstand the adverse host conditions faced for high risk transplantation in severely damaged or diseased corneas as well as for full-thickness corneal implants. Examples of next generation biomaterials that have been implanted into animal models as partial and full-thickness grafts that allow regeneration of nerve sub-types and show resistance to neovascularization will be shown.

Bromfenac® – a new standard in NSAID efficacy

FINDL O

NSAIDs are increasingly used in ophthalmology to reduce surgically induced miosis and inflammation, and in the prevention and therapy of cystoid macular edema (CME). For the treatment of postoperative inflammation following cataract surgery, bromfenac, a new NSAID, has been studied in several clinical trials in recent years. During our discourse, we will elaborate on the following:

- Bromfenac's mechanism of action

- Recent clinical data of pivotal/other bromfenac trials

- Bromfenac's safety, tolerability and use in combination with corticosteroids

Innovative thiomer technology - application to dry eye syndrome

SCHMETTERER L
Vienna

Purpose Pre-clinical and clinical studies were performed to study the safety and efficacy of a novel thiolated biopolymer, namely chitosan-N-acetylcysteine,. The mechanism of action is based on the interaction between thiol groups of the topically applied chitosan-N-acetylcysteine and cysteine-rich mucin (MUC5AC). The hypothesis that this increases polymer residence time on the ocular surface and provides tear film stability was tested.

Methods The efficacy of isotonic and buffered chitosan-N-acetylcysteine eye drops was studied in two different mouse models of dry eye disease. The dosage dependent ocular residence time and biodistribution were investigated in a rabbit model using microPET technology. Long-term irritation and delayed-type hypersensitivity tests with chitosan-N-acteylcysteine eye drop formulation were conducted in rabbits. Three phase one studies in healthy volunteers were performed to find an optimal dose and to test the safety of the formulation in humans.

Results In mice treated with chitosan-N-acetylcysteine decreased expression of ocular surface mRNA of IL-β, IL-10, IL-12α, and TNF was observed, indicating that the formulation decreases surface inflammation in models of dry eye. The residence time of chitosan-N-acetylcysteine eye drops on the ocular surface of rabbits was as high as 22h. Results of a long-term ocular irritation study in rabbits demonstrate that chitosan-N-acetylcysteine was well tolerated and non-irritant to the eye. In the phase I studies in healthy humans, safety and tolerability was demonstrated.

Conclusion Safety and efficacy of chitosan-N-acetylcysteine was shown in different animal models. The long residence time of the polymer at the ocular surface makes it an attractive treatment approach for dry eye disease. Since the phase one studies showed a favourable safety profile in healthy subjects a phase two trial is planned in the near future.

Activation of OX40 Augments Th17 Cytokine Expression and Antigen Specific Uveitis

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Uveitis is a major and common cause of visual disability. Recent studies have shown that Th17 cells are implicated in the pathogenesis of this serious intraocular disorder. Activated T cells express an inducible co-stimulatory molecule called OX40, and OX40 in turn promotes the activation and proliferation of these lymphocytes. Nevertheless, it is unclear whether OX40 plays a vital role in enhancing the effector function of Th17 cells and the severity of uveitis. Here, we demonstrated an increase of OX40 transcription in ovalbumin (OVA)-induced uveitis, whereas anti-OX40L antibody substantially inhibited the antigen specific ocular inflammation. Next, flow cytometry showed that activated Th17 cells expressed OX40, and OX40 activating antibody significantly augmented the production of Th17 cytokines in vitro. To validate the impact of OX40 in vivo, we stimulated OVA-specific T cells with the OX40 activating antibody. Compared to the donor cells without the OX40 activation, adoptive transfer of OX40-stimulated lymphocytes elicited more severe ocular inflammation. Furthermore, IL-17 neutralizing antibody attenuated OX40-mediated uveitis. Thus, our findings suggest that activation of OX40 augmented Th17 cell function, thereby contributing to ocular inflammation. This study enhances our knowledge of co-stimulatory molecule-mediated immunopathological mechanisms of uveitis, and suggests a future therapeutic strategy to treat uveitis by targeting OX40.

Inhibition of the alternative pathway of complement activation reduces inflammation in experimental autoimmune uveoretinitis

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We have shown previously that complement factor H (CFH) and complement factor B (CFB) are constitutively expressed by retinal pigment epithelial cells and their production is regulated by inflammatory cytokines, suggesting that the alternative pathway (AP) of complement activation might play a role in retinal inflammation. In this study, we further investigated the role of the AP in retinal inflammation using experimental autoimmune uveoretinitis (EAU) as a model. Mice with EAU show increased levels of C3d deposition and CFB expression in the retina. Retinal inflammation was suppressed clinically and histologically by blocking AP-mediated complement activation with a complement receptor of the Ig superfamily fusion protein (CRIg-Fc). In line with reduced inflammation, C3d deposition and CFB expression were markedly decreased by CRIg-Fc treatment. Treatment with CRIg-Fc also led to reduced T-cell proliferation and IFN-γ, TNF-α, IL-17, and IL-6 cytokine production by T cells, and reduced nitric oxide production in BM-derived macrophages. Our results suggest that AP-mediated complement activation contributes significantly to retinal inflammation in EAU. CRIg-Fc suppressed retinal inflammation in EAU by blocking AP-mediated complement activation with probable direct effects on C3/C5 activation of macrophages, thus leading to reduced nitric oxide production by infiltrating CRIg(-) macrophages.

Aquaporin expression in blood-retinal barrier cells during experimental autoimmune uveitis

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(3) I.R.I.B.H.M, Campus Erasme, Université Libre de Bruxelles, Brussels
(4) Laboratory of Experimental Hormonology, Université Libre de Bruxelles, Brussels
(5) National Eye Institute, Bethesda
(6) CMP Laboratory, Brussels
(7) Centre for Vision and Vascular Science, Queen's University Belfast, Belfast

Purpose Blood-retinal barrier (BRB) breakdown and retinal edema are major complications of autoimmune uveitis and could be related to deregulation of aquaporin (AQP) expression. We have therefore evaluated the expression of AQP1 and AQP4 on BRB cells during experimental autoimmune uveitis (EAU) in mice.

Methods C57Bl6 mice were immunized with interphotoreceptor retinoid-binding protein. The disease was graded clinically, and double immunolabeling using glial fibrillary acidic protein (a marker of disease activity) and AQP1 or AQP4 antibodies was performed at day 28. AQP1 expression was also investigated in mouse retinal pigment epithelium (RPE) cells (B6-RPE07 cell line) by reverse transcriptase PCR and western blot under basal and tumor necrosis factor α - stimulated conditions.

Results In both normal and EAU retina, AQP1 and AQP4 expression were restricted to the photoreceptor layer and to the Müller cells, respectively. Retinal endothelial cells never expressed AQP1. In vasculitis and intraretinal inflammatory infiltrates, decreased AQP1 expression was observed due to the loss of photoreceptors and the characteristic radial labeling of AQP4 was lost. On the other hand, no AQP4 expression was detected in RPE cells. AQP1 was strongly expressed by choroidal endothelial cells, rendering difficult the evaluation of AQP1 expression by RPE cells in vivo. No major differences were found between EAU and controls at this level. Interestingly, B6-RPE07 cells expressed AQP1 in vitro, and TNF-α downregulated AQP1 protein expression in those cells.

Conclusion Changes in retinal expression of AQP1 and AQP4 during EAU were primarily due to inflammatory lesions, contrasting with major modulation of AQP expression in BRB detected in other models of BRB breakdown. However, our data showed that TNF-α treatment strongly modulates AQP1 expression in B6-RPE07 cells in vitro.

Long-term remission after cessation of interferon- α treatment in patients with severe uveitis due to Behçet´s disease

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Purpose To retrospectively assess the development of visual acuity and the frequency and duration of relapse-free periods in patients who were treated with interferon-α (IFNα) for severe uveitis due to Behçet´s disease (BD) and who completed a followup period of ≥2 years.

Methods IFN alfa-2a was administered at an initial dosage of 6 million IU per day, then tapered to a maintenance dosage of 3 million IU twice per week, and finally discontinued, if possible. In case of a relapse, IFN treatment was repeated. Visual acuity at the end of followup was compared with visual acuity when ocular disease was in remission.

Results Of 53 patients (96 eyes), 52 (98.1%) responded to IFN. In 47 patients (88.7%), IFN could be discontinued when the disease was in remission. Twenty of these 47 (42.6%) needed a second treatment course during a median followup of 6.0 years (range 2.0-12.6 years). Visual acuity improved or remained unchanged in 91 eyes (94.8%). Ocular disease was still in remission in 50% of the patients 45.9 months after cessation of the first IFN course. The relapse rate tended to be lower in women than in men. The BD activity score decreased significantly during followup, but long-term remission for nonocular BD manifestations was not achieved. However, since local treatments were sufficient, no systemic treatment was administered.

Conclusion Our findings indicate that IFNα induces long-lasting remission in patients with severe ocular BD, resulting in a notable improvement in visual prognosis.

New scale for photographic grading of vitreous haze in uveitis

DAVIS J
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Purpose Evaluation of clinical research methodology.

Methods Calibrated Bangerter diffusion filters inducing incremental decrements of spatial contrast were placed in front of the camera lens while photographing a normal eye to simulate vitreous haze. The photographs were digitized and an ordinal scale was created from 0 (none) to 8 (highest level of opacification at which fundus details could be seen). The scale steps correspond approximately to decimal Snellen visual acuities of 1.0, 0.8, 0.4, 0.2, 0.1, 0.04, 0.02, 0.01, 0.002, with approximately 0.3 log step between each step. For validation, digitized fundus photographs of uveitis patients were displayed on a computer monitor for comparison with the standard photos. Three observers graded the test set twice under standard conditions. Interobserver and intraobserver variability and kappa values for agreement greater than chance were calculated

Results Variance component analysis determined that 87.7% of the variance in grades was attributable to the test item rather than to grader or session. The intraclass correlation between graders and grading sessions varied from 0.84 to 0.91. Simple agreement within one grade between graders and sessions occurred in 90 ± 5.5 per cent of gradings. Kappa values averaged 0.91, considered near perfect.

Conclusion A nine-step photographic scale was designed to standardize the grading of vitreous haze in uveitis patients using fundus photographs. The new scale is potentially adaptable to clinical trials in uveitis.

• 4311
Blood-ocular barriers and macular edema

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The blood-ocular barrier system is formed by two main barriers: the blood-aqueous barrier (BAB) and the blood-retinal barrier (BRB). Homeostasis in the retina microenvironment is maintained by the function of the BRB which regulates the movement of chemicals and cells between the intravascular compartment and the retina. The BRB consists of two major topographically distinct components: the endothelium of the retinal vessels (inner BRB) and the retinal pigment epithelium (outer BRB).The barrier function of the retinal vascular endothelium depends on its continuous epithelial-like arrangement with the endothelial cells united by tight junctions, whereas the ability of the retinal pigment epithelium to regulate solute transport depends on the apical tight junctions between these cells. The tight junctions are membrane fusion areas between adjacent cells that serve as a diffusion barrier for paracellular transport and as a "molecular fence", restricting the free movement of transmembrane proteins, and thus maintaining cell polarity and the asymmetric distribution of transmembrane proteins. Among the most important proteins that are associated with tight junctions are occludin, zonula occludens and claudins. Pathologic increase in blood retinal permeability can be caused by endothelial damage, tight junction disassembly, or cytokines such as vascular endothelial growth factor. Several methods have been developed to allow detection, quantification and monitoring of BRB breakdown in experimental and clinical settings. In humans, fluorescein angiography, vitreous fluorophotometry and OCT are the most commonly used.Alterations of the BRB play a crucial role in the development of retinal edema. Macular edema is the result of an accumulation of fluid in the retinal layers around the fovea, contributing to vision loss by altering the functional relationship in the retina and promoting an inflammatory reparative response. The accumulation of fluid is directly associated with an alteration of the BRB. In this situation the protective effect of the BRB is lost and Starling's law applies.

• 4312
Macular edema: clinical pattern and imaging

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Macular edema is a common feature in different retinal and chorioretinal disorders. It is often the major cause of vision impairment in these pathologies. Edema can be evaluated in clinic practice with different diagnostic modalities. Optical coherence tomography (OCT) has become the most important tool for the evaluation and quantification of macular edema. Spectral-domain OCT (SD-OCT) represents the latest advancement in OCT technology and provides unprecedented visualization of retinal structure. Therefore, using SD-OCT it is possible to better characterize the pattern of presentation of macular edema, in regards of the retinal layers involved. Moreover, SD-OCT allows the visualization of photoreceptors alteration, which is directly correlated with visual loss. Another fundamental tool for the evaluation of macular edema is fluorescein angiography (FA). However, this diagnostic technique allows studying the leakage from the vessels, rather than the accumulation of fluid within the retina. Therefore FA provides different information compared to SD-OCT, and the two tools should be considered complementary, rather than interchangeable. Fundus autofluorescence (FAF) is a non-invasive tool that provides additional information in pathologies characterized by macular edema. In particular, the displacement of macular pigment induced by cystoid spaces within the retina increases the autofluorescence from the underlying pigment epithelium. In a confocal system, this results in precise visualization of the cysts that can be therefore monitored throughout the time.

• 4313
General pathophysiology

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Macular edema represents a common final pathway of many intraocular and systemic diseases, which usually involve the retinal vessels. It typically occurs with painless impairment of visual acuity in one eye, but can also be bilateral, depending on the etiology. A macular edema is a nonspecific sign of many ocular disorders. Usually the symptoms progress slowly. Nevertheless, patients often may notice this entity suddenly – this is the case when they examine one eye separately. The appearance can differ with several subtypes existing, depending on the etiology. In this presentation the following mechanisms and problems of this non-specific disease entity will be discussed: Unique construction of the blood-retinal-barrier und general possibilities of alteration.Inflammatory mediators with major focus on Angiotensin II, VEGF and Prostaglandins.Other cytokines and Chemokines as well as Matrix metalloproteinases. Sorbitol pathway and oxidation (Diabetes) – relation to inflammation.Mechanical issues (venous diseases). In addition it will be mentioned how this knowledge on pathophysiology translates into clinical praxis when we design treatment strategies for our patients.

• 4314
Retinal vein occlusion

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Macular edema is a major complication of both ischemic and non ischemic Retinal vein occlusions (RVO). Fluorescein angiography (FA) is the most effective method to determine the presence of macular cystoid edema (CME), its extension, persistence, regression, the degree of ischemia (perfused or non-perfused RVO). Spectral domain OCT (SD-OCT) helps to quantify the changes in retinal thickness, the amount of CME, the presence of sub retinal fluid accumulation and precise analysis of the outer retinal layers, useful as a guide for treatment.According to the recent results of the SCORE Trial, Grid Laser photocoagulation remains the reference treatment for macular edema due to branch retinal vein occlusion (BRVO) but not recommended in Central RVO Recent prospective randomized trials strongly suggest an anti-edematous effect of intravitreal steroids (particularly dexamethasone in a slow release device) and intravitreal anti-VEGF drugs, that may at least temporarily reduce foveal edema and improve visual function.Surgical treatment modalities have been reported for RVOs with a positive action of vitrectomy; the combination with intravitreal steroids and/or tissue plasminogen activator could permit a more rapid and lasting action.Taking into consideration the recent advances in diagnostic tools and management options, recent European practical recommendations and Guidelines, prepared by a collaborative group of retina specialists, are presented to provide the ophthalmologists with guidelines for the clinical approach of RVO.

• 4315
Diabetic retinopathy

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Diabetic macular edema (DME), defined as a retinal thickening involving or approaching the centre of the macula, represents the most common cause of vision loss in patients affected by diabetes mellitus. The pathogenesis and the course of the DME requires a complex approach with multidisciplinary intervention both at systemic and local level.In the last few years many diagnostic tools have been proved useful in the detection and the monitoring of the features characterizing DME. At the same time, several therapeutic approaches can now be proposed on the basis of the DME specific characteristics. Aim of the present chapter is to thoroughly outline the clinical and morpho-functional characteristics of DME and its current treatment perspectives. More specifically, each DME subtype can be successfully managed making the most of the current treatment paradigm, including laser treatment, intravitreal steroids and anti-VEGF, and macular surgery.

• 4316
Macular edema of choroidal origin

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Age-related macular degeneration (AMD) is the result of an advanced alteration of the choriocapillaris and/or the retinal pigment epithelium (RPE), and/or the photoreceptor (PR) layers. The neural retina is only partially involved, and additional pathways are required for the development of edema within the retina. The exudative form of AMD is due to choroidal neovascularization (CNV) that causes a serous detachment of the neurosensory retina which development and importance depends on the activity of the new vessels. Edema involving the outer and ultimately the inner retina develops progressively. The presence of cystoid macular edema is more likely if the retinal serous detachment is long-standing and if the choroidal neovascular membrane has involved most of the subfoveal region.The classic clinical definition of macular edema is an accumulation of serous fluid within the neuro sensory retina increasing thickness of the central retina. However in exudative AMD, the leakage of fluid from the choroidal new vessels may be the origin of fluid collection underneath and within the neuro sensory retina. The normal choriocapillaris leaks on the side facing the RPE in order to assure the nutrition of the photoreceptors. CNV being of choroidal origin presents the same structure histologically as the choriocapillaris. In AMD, the associated inflammatory reactions induce the rupture of the external retinal blood barrier and leads to an exudation within the subretinal space. In addition, after prolonged detachment, the retinal capillaries may become damaged and contribute to the leakage of dye into the extracellular compartment of the retina. The consequent damage of the outer retinal layers determines alterations of the overlying (and underlying) tissues. Several inflammatory mediators and inflammatory cells are likely the key signals, that initiate secretion of numerous cytokines one being vascular permeability factor, referred to as vascular endothelial growth factor (VEGF), present at the site of the angiogenic stimulus. All these factors interact in a complex chain reaction, which is not yet completely understood.

• 4317
Postsurgical cystoid macular edema

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Purpose Cystoid macular edema (CME) is a major cause of reduced vision following cataract and vitreoretinal surgery, with a reported incidence of 0.1- 2.35%. Intraretinal accumulation of fluid determines the formation of perifoveal cysts, which may combine and give rise to lamellar holes. The etiology of CME is not completely clarified. Risk factors, among which preexisting ocular (uveitis, retinal vein occlusion, epiretinal membrane) and systemic conditions (diabetes mellitus, systemic hypertension) as well as intraoperative complications can raise the risk of developing CME postoperatively. Modern surgical techniques have reduced the incidence of CME.

Methods Pseudophakic CME is characterized by poor postoperative visual acuity. Onset of clinically significant CME is generally 4-12 weeks after surgery (peak at 4-6 weeks). Fluorescein angiography (FA) is indispensable in the workup of CME, showing the classical perifoveal petaloid staining pattern and late leakage of the optic disk. Optical coherence tomography (OCT) reveals cystic spaces in the outer nuclear layer. Differential diagnosis with FA and biomicroscopy is crucial for postsurgical CME management.

Results Most cases of pseudophakic CME resolve spontaneously. Available therapeutic interventions, for both prophylaxis and treatment of CME, are based on pathogenesis theories. The value of prophylactic treatment is doubtful, especially long-term postoperatively. First-line treatment should include topical nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, with best results for acute postsurgical CME. In cases of resistant CME, periocular or intraocular corticosteroids represent an option. Antiangiogenic agents, though experimental, should be considered for nonresponsive persistent CME. Surgical options such as laser vitreolysis or vitrectomy should be reserved for special cases.

• 4321

Spatio-temporal responses in the visual cortex evoked from first and higher order thalamic nuclei in tree shrews: a voltage sensitive dyes study

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Purpose The primary visual cortex (V1) received its main thalamic drive from the lateral geniculate nucleus (LGN) through layer IV. In contrast, projections from the pulvinar end in layer I, suggesting that pulvinar exerts a diffuse modulatory influence on V1 activity. However, pulvinar projections to extrastriate areas (XC) mostly terminate in layer IV, suggesting that they provide a driver input to XC areas. Thus, one would expect the spatio-temporal responses evoked by pulvinar activation to be different in striate and XC areas, reflecting the different connectivity pattern (driver vs modulator). We thus measured the spatiotemporal dynamics of voltage sensitive dyes activation in the visual cortex following thalamic electrical stimulation.

Methods Tree shrews were anesthetised and bilateral craniotomies were made on the visual cortex. RH1691 was used to stain the cortex. Stimulating electrodes were placed in LGN and pulvinar.

Results Stimulation of LGN induced fast and local responses in V1, which propagated to XC and contralateral cortex. The temporal profile of the responses was transient and monophasic in V1, and generally bimodal or tonic in XC. Stimulation of pulvinar induced fast and local responses in XC, followed by activation in V1 and contralateral cortex. The propagated waves in V1 were weak in amplitude and diffuse. Co-stimulating pulvinar and LGN produced responses that were weaker than the sum of the responses evoked by the independent stimulation of LGN and pulvinar, even when pulvinar stimulation did not produce any responses in V1.

Conclusion The pulvinar can exert a modulator influence in cortical processing of LGN inputs while it mainly provides driver inputs to XC.

• 4322

Quantifying end-stage electrophysiological function in progressive retinal degenerative disorders (PRDD)

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Purpose PRDD, such as Retinitis Pigmentosa, are accompanied with a gradual reduction of ERG signal to non-measurable amplitudes. We compared alternative means of quantifying normal and pathological ERGs.

Methods Photopic ERGs (DTL electrode, background 30 cd.m-2; flash stimuli: -2.62 to 0.64 log cd.sec.m-2 in 17 steps of ~ -0.2 log-unit) were recorded from 85 normal subjects and 55 patients with PRDD. In a subset of 6 normal subjects, focal ERGs (fERGs) were obtained with the use of a eye patch to restrict the stimulus centrally and at 20o or 40o nasally. ERG descriptors, obtained with Direct Wavelet Transform D(WT) of the ERGs, were compared to the traditional amplitude measurements.

Results In normal, the ERG amplitude gradually decreased from 131.42±31.27µV (Vmax) to 0.71±0.12 µV (dimmest flash used) in two distinct pseudo-asymptotical steps of -15.2±2.0µV.s (step 1) and -0.42±0.1µV.s per decrement respectively (9 steps each). Pathological ERGs as well as normal focal ERGs could always be fitted to this model. Furthermore, while the traditional measurements frequently failed to quantify residual ERGs, including the normal fERGs, the DWT was always able to extract quantifiable and comparable information from the residual response, thus permitting a more favourable prognosis.

Conclusion Analysis of the ERG response in the time and frequency domain (such as DWT) allows for a more precise quantification of the ERG signal especially when it reaches residual amplitudes such as that observed in end-stage PRDD. Our results suggest that modeling ERG attenuation with the DWT improves the staging and prognosis of patients affected with severe PRDD. Supported by FFB (USA).

• 4323

Windows-based software for recording clinical electroretinograms

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Purpose To develop user-friendly Windows-based software for recording submicrovolt clinical full-field electroretinograms (ERGs).

Methods LabVIEW (National Instruments) — a parallel, graphical language based on structured dataflow diagramming created for data acquisition and instrument control — was used to write ERG software that runs on Windows XP. Data acquisition and instrument control are enabled with a National Instruments 16-bit PCI Multifunction DAQ card.

Results This software simulates a signal-averaging storage oscilloscope and has been used in our clinic since 2007 to record responses to 1/minute, 0.5 Hz, and 30 Hz flashes. The front panel includes virtual controls for a digital notch filter, a digital low-pass filter, a digital band-pass filter centered at 30 Hz, and an artifact reject buffer. Responses are saved to a sequential file readable by a spreadsheet program. A key feature when averaging cone ERGs to 30 Hz flashes is that ocular noise is removed independent of signal size, so that a low reject threshold can be used for every patient without attenuating the signal. The program can resolve cone ERGs as small as 0.05 µV to quantify retinal function in nearly all patients with retinitis pigmentosa.

Conclusion Programming in LabVIEW allows the creation of Windows-based software that is user-friendly and state-of-the-art for resolving submicrovolt responses to 30 Hz flashes.

• 4324

Clinical significance of red target increment perimetry

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Purpose To elucidate the significance of red target increment perimetry in diagnostic and occupational assessment

Methods Red target increment perimetry does not rely on color discrimination but merely on red target detection on a white background. In a retrospective study, ten exemplary cases of congenital and acquired color vision deficiencies are evaluated by kinetic, static and microperimetric techniques

Results Daltonism: Red brightness loss is common to protan observers. In marked protanomaly and protanopia severe constriction of red target field is a rule; i.e. within the peripheral visual field of protan observers red objects may remain entirely undetected. Female carriers of protan defects: Red target fields may show constriction to variable extent, but less pronounced than in male protan observers. Rod monochromacy: Since rhodopsin is virtually unable to absorb red light, red target fields are entirely lacking. Stargardt's disease and cone dystrophies: Red target fields are affected earlier and more pronounced than standard white fields. Central serous retinopathy: Red desaturation and red brightness loss are common findings on confrontation testing. Scotomas are detected on microperimetry by red targets while white stimuli still fail to pick up pathology. CAR: Cancer associated retinopathy: Compared to RP, in CAR the cone system shows more involvement. CAR scotomas show up more distinctly in red than in white perimetry.

Conclusion In congenital protan defects, red target increment fields have a significant bearing on occupational demands. In various retinal diseases, field defects for red target increments exceed those for white targets and so, may contribute to early diagnosis.

• 4325

Assessing the wavelength dependence of intraocular scattering by a new optical approach

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Purpose The wavelength dependence of the light scattering is related with the characteristics of the inhomogeneities in the ocular media, and therefore, an objective assessment could be used to the early detection of underlying ocular pathologies. We developed a new optical instrument for measuring light scattered in the human eye at different wavelengths.

Methods Using a double-pass configuration, series of disks of uniform radiance with an increasing angular dimension are sequentially projected on to the retina. As a light source, a white light halogen lamp is spectrally filtered by using a liquid crystal tunable filter, selecting three different wavelengths: 550, 600 and 650 nm (FWHM = ± 50 nm). The disk's retinal images are recorded by a cooled electron-multiplied CCD camera. The derivative of intensity at the center of each disk's retinal image with respect to its radius provides the eye's wide-angle double-pass point-spread function (PSF). The method was applied in an artificial eye with different levels of induced scattering, and in a group of normal subjects.

Results In the artificial eye, the increasing scattering induced is successfully discriminated at the more eccentric angular domain of the wide-angle PSFs. In the group of subjects, the estimated wide-angle PSFs differ from the lower to the larger wavelengths. The PSF at 550 nm is characterized by more intense light scatter in the angular range between 5 and 10 degrees, while the PSF at the 650nm showed a relatively increased scattered light between 0 and 2 degrees. This would be related to the deeper interaction of th

Conclusion An optical objective method is sensitive enough to detect consistently differences in light scatter for different wavelengths.

• 4326

The optical integration technique for the measurement of light scatter in the human eye

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Purpose To develop and demonstrate a new optical technique for the measurement of light scatter in the human eye based on extended source imaging in a double pass configuration.

Methods The experimental setup is based on a double-pass (DP) configuration. Series of disks of uniform radiance having angular dimensions ranging from 0 to 9.1 degrees (radius) are projected on to the eye's retina and DP images are recorded by a cooled electron-multiplied CCD camera. Two spatially separated sub-apertures at the pupil are used for stimulus projection and imaging to minimise back-scatter and reflections. The derivative of the intensity of each recorded disk with respect to disk radius (in angular units) was fitted to a mathematical model of the wide-angle double pass point-spread function (PSF) and from that the underlying single-pass PSF was computed. The setup was first validated using artificial eyes with known scattering properties and used in a group of normal human eyes.

Results The derivative of central disk intensity with respect to disk radius was measurable up to the complete range of the angular dimensions of the projected disks (9.1 degrees of visual field). Different features can be obtained from the estimated PSF to characterize not only the amount of scatter but also its angular dependence.

Conclusion A new optical method to measure scatter in the eye was developed and demonstrated. The procedure is sensitive enough to consistently detect differences in the light scatter intensity between normal healthy eyes and can be a significant step towards the complete optical characterization of the eye.

• 4327

Intracorneal lenses using femtosecond laser for the treatment of presbyopia

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Purpose To investigate the visual outcomes and safety of an Intracorneal lens (Presbia, Presbitech, CA, USA) for the treatment of presbyopia using femtosecond laser (Intralase, AMO, Irvine, CA,160 KHz).

Methods An intracorneal tunnel was created in the non-dominant eye of 15 patients using femtosecond laser. Mean age was 51, 32 ± 3,1. Follow-up was 6 months.

Results Mean uncorrected visual acuity for distance preoperatively, one day, 1 week, 1 month, 3 months, and 6 months after surgery was 20/20, 20/40, 20/40, 20/32, 20/32,20/30 respectively, whereas for near was 20/50, 20/32, 20/30, 20/25, 20/25, 20/25. No intra- or post-operative complications were found.

Conclusion Intracorneal lenses for presbyopia seem to be a safe and effective method in patients aged between 45 to 60 years old.

Commercial interest

• 4328 / 461

ElVisWeb: an interactive web-application for the visualization of ERG recordings based on the Electrophysiology of Vision Markup Language

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Purpose Recently, we proposed a standard for the exchange of electrophysiological recordings of vision, called Electrophysiology of Vision Markup Language (ElVisML). Here we present a Web 2.0 application, ElVisWeb, for visualizing data encoded in ElVisML. It intends to facilitate the exchange of recordings on mailing lists like CEVNet in a standardized way and to allow for sharing of data along with published articles.

Methods Main goals of ElVisWeb were easy usage and deployment. It is developed completely in JavaScript and as web application it does not require any installation on the client. It uses the single-page-interface paradigm (SPI): An ElVisML-file can be pasted into a text-field and a graphical representation of it is compiled. ElVisWeb can be deployed on any web-server or executed locally. For convenience, there is an upload functionality, which requires PHP on the server, however. ElVisWeb leverages open source JavaScript libraries for XML-processing (http://dev.abiss.gr/sarissa) and charts generation (http://www.jqplot.com).

Results A Web 2.0 application for visualization of electrophysiological recordings of vision, ElVisWeb, was successfully implemented. It is designed for easy usage and deployment. Recordings encoded in ElVisML can be visualized with no additional software installation.

Conclusion ElVisML is a standardized way for exchanging electrophysiological data. ElVisWeb is a first step towards an open ecosystem around ElVisML. It provides chart generation for recordings and may be used in mailing lists like CEVNet or for sharing data along with published articles. It is also ready to be used on mobile devices.

• 4331
Accommodative IOL' s and pseudo accommodation

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Purpose To analyze the existing lenses designs, properties as well as the new intraocular lens technology in the field of accommodative IOLs.Moreover, to distinguish the difference between accommodation and pseudoaccommodation.

Methods The restoration of near vision in elder individuals that have entered the presbyopic age is considered one of the major challenges in refractive surgery during the last decade.Accommodative IOLs offer to patients satisfactory near vision by restoring to some degree the dynamic component of the ocular ability for near vision. By implementing several designs of the haptic and the optic part of the IOL, the target is to take advantage of the movement of the ciliary muscle and of the vitreous in order to change position and shape. This offers a change of the overall dioptric power of the eye and the facilitation of near vision.

Results Pseudophakic patients' ability for good distance and near visual acuity without correction has been characterized as apparent accommodation, or pseudoaccommodation. It has been attributed to several factors such as the pupil size, total and corneal aberrations, degrees and axis of astigmatism, potential of visual perception and axial movement of the intraocular lens.the i-Trace technology has an important role in the evaluation of accommodation and pseudoaccommodation in pseudophakic eyes not only subjectively but optically.

Conclusion Accommodative IOLs represent the future in the battle for the correction of presbyopia and restoration of near vision.

• 4332
Small aperture keratophakia for correction of presbyopia

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Purpose To assess the safety and efficacy of a small-aperture optic device for the treatment of presbyopia in emmetropic presbyopes.

Methods The Kamra Inlay, formerly known as the AcuFocus ACI corneal inlay (AcuFocus, Irvine, CA), is an ultrathin microperforated, opaque artificial aperture (3.8 mm outer diameter and 1.6 mm inner diameter) made of highly biocompatible polyvinylidene flouride (PVDF). A randomized pattern of minute holes allows nutritional flow through the implant to the anterior stroma. Following creation of a superior-hinged flap in the non-dominant eye, a Kamra inlay was centered on the stroma based on the first Purkinje reflex in 32 emmetropic patients with a mean age of 51.20 ± 2.2 years. Manifest refraction and visual acuity at three years postoperative are reported here. Four year data will be presented at the meeting.

Results In the implanted eye, mean spherical equivalent shifted from 0.19 ± 0.22 D preop to 0.08 ± 0.68D at 3 years. Mean UNVA improved from J7/J8 to J1 at 3 years. Mean UIVA went from 20/40 preop to 20/25 at 3 years. Mean UDVA decreased slightly from 20/16 to 20/20 at 3 years. At 3 years, all eyes achieved UDVA of 20/32 or better. Mean binocular UDVA was 20/16. There were no explants. Two inlays had to be recentered due to initial misplacement. During the follow up period, no irritation, inflammatory reactions, or changes in corneal appearance were observed.

Conclusion The Kamra corneal inlay improves near and intermediate vision without severe loss of distance visual acuity in emmetropic presbyopes by increasing the depth of field, based on the small aperture optics concept.

Commercial interest

• 4333
Lens refilling (Phaco-Ersatz)

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Purpose To demonstrate that the content of the crystalline lens can be replaced in vivo by a polymer designed to mimic the properties of the young lens to restore accommodation while maintaining ametropia, that polymer exchange can be performed anytime during follow-up and that Phaco-Ersatz also allows reversibility to IOL implantation in the bag.

Methods A safe endolenticular surgical technique was developed to remove relatively hard nucleus via a small capsulorhexis (~1.2mm) by US phacoemulsification (0.7mm titanium tip). The rhexis is closed by a mini-capsulorhexis valve (~2mm), the polymer injected and then cured by low intensity light delivered by a custom made handprobe. Three families of polymers were developed allowing independent adjustment of the elastic modulus and index of refraction. These polymers were tested in 2 ex-vivo accommodation simulators (EVASI and II) on human and primate eyes and their biocompatibility assessed in monkeys and rabbits for periods up to 8 months.

Results A safe endolenticular surgical technique was developed to remove relatively hard nucleus via a small capsulorhexis (~1.2mm) by US phacoemulsification (0.7mm titanium tip). The rhexis is closed by a mini-capsulorhexis valve (~2mm), the polymer injected and then cured by low intensity light delivered by a custom made handprobe. Three families of polymers were developed allowing independent adjustment of the elastic modulus and index of refraction. These polymers were tested in 2 ex-vivo accommodation simulators (EVASI and II) on human and primate eyes and their biocompatibility assessed in monkeys and rabbits for periods up to 8 months.

Conclusion Phaco-Ersatz can be performed safely and is an effective method to restore accommodation.

Commercial interest

• 4334
The use of electro-optical materials to restore accommodation

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Purpose We present a review of current developments to restore accommodation by means of electro optical materials embedded in glasses, contact lenses or intraocular lenses.

Methods Considered electro optical effects include electro active polymers, electro refractive polymers and the electrowetting principle. Possible solutions about how to measure the accommodation demand and to supply electrical energy inside the eye are also discussed.

Results Electrowetting uses the ability of a liquid to maintain contact with a surface and having a certain curved shape which can be altered by an electric field. Electro active polymers can change the size and shape under a changing electric field. Electro refractive polymers change the refractive index under an electric field. The electro active and electro refractive polymers can be put into pixelate optics were each pixel can be adjusted independently. Optical properties, energy consumption and dynamic properties of electro optical applications are compared with other accommodation restoration techniques.

Conclusion Commercial application of electro optical materials in glasses already exist, the use in contact lenses and intraocular lenses is under development.

• 4335

Experimental femtosecond laser lens surgery

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Purpose To review the current developments and new experimental applications of femtosecond lasers (FsL) in lens surgery, including cataract and the treatment of presbyopia. FsL lentotomy has been shown effective to soften the lens matter easing cataract extraction. Because the main cause for presbyopia is the stiffening of the lens nucleus with age, FsL lentotomy could be applied to treat it, provided the cuts inside the lens do not induce a significant opacity.

Methods Commercial FsL lasers systems for cataract surgery are already available, using repetition rates of 100 kHz at 1041 nm, similar to those of corneal FsL. We have developed a custom build multimodal non-linear microscopy platform modified to work as a nano-surgery scalpel using a FsL with a repetition rate of 80 MHz at 860 nm. This allows cutting inside the lens matter at a much smaller scale than the current lens surgical FsL systems.

Results Using a single FsL system, we imprinted complex patterns in 2D and 3D configurations inside human donor lenses. These results were analyzed through transmitted infrared light and Two-Photon Excitation Fluorescence (TPEF) microscopy. We observed an increase of the TPEF signal on the targeted regions. In addition, we found that the caused damage is highly confined without any apparent effect on the surrounding tissue.

Conclusion While current FsL lentotomy systems can soften the lens nucleus to ease cataract extraction, optical quality at the optical axis is compromised. Experimental FsL with modified parameters is able to further confine the damage in order to preserve the lens clarity, a requirement for FsL lens presbyopia surgery.

• 4341
Histopathology of Behçet's uveitis

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Purpose To report the histological findings in an eye with severe Behçet's disease.

Methods A 17-year-old male had a longstanding history of chronic intraocular inflammation, which was treated with high dose steroids, immunosuppression and biological agents (anti-TNF therapy). Despite this aggressive treatment, he suffered persistent uveitis, and had also undergone cataract and pars plana vitrectomy with silicone oil tamponade. Eventually the patient underwent enucleation of his left eye, which had become blind and painful. The specimen was sent to the Pathology Dept. RLBUHT, for morphological examination.

Results Histological sections of the enucleated eye demonstrated extensive pathological changes. These included: chronic keratitis with associated neovascularisation; severe chronic granulomatous iridocyclitis with the development of anterior synechiae with angle closure, as well as extensive posterior cyclitic membrane formation with ciliary process destruction. The inflammation, which was characterised by dense lymphocytic and plasma cell infiltrates, extended posteriorly into the choroid, focally involving the retina. Chronic vasculitis resulted in a typical "onion-skinning" appearance of some blood vessels. There was optic disc cupping. Immunohistochemistry was performed to characterise the lymphocytic and plasma cell populations.

Conclusion This case is a rare example of end-stage Behçet's disease in which the histopathological alterations will be demonstrated.

• 4342
Vitreo-retinal interactions and optical coherence tomography study in Fuchs' uveitis

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Purpose To evaluate an describe vitreo-retinal interactions by Optical Coherence Tomography (OCT) in Fuchs' uveitis.

Methods Retrospective study including 29 patients (31 eyes) with Fuchs' uveitis who underwent OCT evaluation. Vitreo-retinal interface was analyzed and morphological changes described and compared to the normal controlateral eye (except 2 bilateral cases).

Results Vitreo-retinal modifications were seen on OCT in 90% of Fuchs' uveitis patients. The main vitreo-retinal interactions that could be described were : retinal surface fibrosis (43.3%), epiretinal membrane (33.3%), vitreo-retinal traction (23.3%), foveal vitreous opacity (23.3%).

Conclusion Vitreous involvement is a characteristic feature of Fuchs' uveitis with cellular infiltration and/or vitreous opacification, moreover, these OCT findings show that there is a high prevalence of vitreoretinal abnormalities in Fuchs' uveitis.

• 4343 / 424
Anti-inflammatory mechanisms of mapracorat, a novel selective glucocorticoid receptor agonist, in human conjunctival fibroblasts

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Purpose Mapracorat (BOL-303242-X; ZK 245186) is a selective glucocorticoid receptor agonist (SEGRA), under clinical evaluation for the treatment of inflammatory eye and skin diseases. It is structurally distinct from glucocorticoids and NSAIDs. Data suggest an improved side effect profile of this compound compared to traditional glucocorticoids. This study was to determine its anti-inflammatory mechanisms.

Methods Primary human conjunctival fibroblasts (HConF)were challenged with IL-1ß and Luminex technology or ELISA was used to determine the effect of mapracorat on IL-1ß-induced cytokine, prostaglandin E2 (PGE2) and matrix metalloproteinase (MMP) release in the presence or absence of mifepristone (RU-486), a glucocorticoid receptor antagonist. The effect of mapracorat on IL-1ß-induced cyclooxygenase-2 (COX-2) expression was assessed by Western blotting. Dexamethasone was used as the control.

Results IL-1ß induced release of multiple cytokines, including IL-6, IL-8 and monocyte chemotactic protein-1 (MCP-1), and of PGE2 and MMPs (MMP-1 and MMP-3), as well as the expression of COX-2. Mapracorat inhibited cytokine, PGE2 and MMP release as well as COX-2 expression in a dose-dependent manner with comparable effectiveness as dexamethasone. The inhibition of cytokine and PGE2 release was fully or partially reversed by mifepristone.

Conclusion Mapracorat acts as a potent anti-inflammatory agent in HConF by inhibiting multiple intracellular mediators. The fact that mapracorat is effective on inhibiting PGE2 pathway suggests that it may reduce post-surgery pain. Clinical significance of these findings needs further investigation.

Commercial interest

• 4344 / 425
Skin tattoos and the development of uveitis

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Purpose To report a case of recurrent non-granulomatous anterior uveitis associated with tattoo inflammation.

Methods A 28-year-old female presented to our ophthalmology department with a sharp shooting pain, photophobia and redness in both eyes but more pronounced in the right eye. A bilateral anterior uveitis was noticed. Simultaneously she experienced a rash at the site of her skin tattoos. The patient had her skin tattooed quite extensively at the chest, the back and around the umbilicus, between 13 years and one year ago.

Results Investigations for causes of anterior uveitis, including general and infectious serologic testing, ACE, HLA-B27 and chest X-ray were normal. Clinical pneumological examination, thoracic CT and abdominal ultrasound showed no arguments for sarcoidosis. A tattoo biopsy showed a granulomatous response of lymphocytes and histiocytes around tattoo pigment, there was no histological evidence for sarcoidosis.

Conclusion Tattoo granulomas can be a manifestation of sarcoidosis but may also be a delayed hypersensitivity reaction to pigment containing metallic tattoo compounds. The association of recurrent anterior uveitis with swelling of skin tattoos is an unusual occurrence. Similar cases of uveitis associated with tattoo inflammation have been reported in the literature.

• 4345 / 426

Acute retinal necrosis. 3 case reports

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Purpose To present three case reports of acute retinal necrosis (ARN) syndrome and discuss the aspects of diagnosis, treatment and prognosis.

Methods Retrospective analysis of clinical, laboratory, photographic and angiographic records of three immunocompetent patients with acute retinal necrosis syndrome.

Results Two male 22 and 36 years old and one female 25 years old patients had typical clinical symptoms of ARN syndrome: sudden decrease of vision acuity, eye pain, multiple areas of peripheral retinal necrosis, occlusive vasculitis, opticopathia, anterior uveitis and vitritis. Serum Ig G antiviral (VZV, HSV, CMV) titers were the basis for the etiological diagnosis. After applying systemic antiviral and steroid therapy, a rapid improvement of symptoms with the development of pigmentation in the areas of retinal whitening was observed in all patients. Retinal detachment occurred in 2 male patients and was successfully treated.

Conclusion Acute retinal necrosis syndrome is one of the vision threatening diseases for immunocompetent patients with poor prognosis. Early diagnosis and urgent antiviral therapy is therefore of vital importance for visual outcomes. Long term follow-up is necessary due to high risk of retinal detachment.

• 4346 / 427

Slowly progressive corneal opacification in a patient with known mucocutaneous leishmaniasis and HIV

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Purpose To present a case of corneal opacification and anterior uveitis in a patient with systemic Leishmaniasis

Methods Case report

Results A 40-year old HIV-positive patient was already followed for conjunctival involvement in systemic Leishmaniasis. Treatment with Glucantime was effective, but had to be stopped because of acute pancreatitis. A switch to Ambisome was made, but did not result in complete resolution.Slow appearance of corneal stromal opacities was also noted at this time. In January 2011 the patient consulted in emergency and was diagnosed with bilateral acute anterior uveitis as well as manifest progression of the stromal opacification. Regarding the inflammation, a good initial response was obtained with topical prednisolone acetate. However, a slumbering reaction remained present in the anterior chamber and an increase of the keratic precipitates was noted. On tapering of the steroids, several relapses occurred.The intrastromal opacities were still increasing, resulting in worsening visual acuity. An in-vivo confocal microscopy of the cornea was performed and showed presence of cystic structures in the stroma, possibly related to intracorneal presence of the parasite. Because of insufficient response of the anterior chamber reaction to topical steroids, anterior chamber tap was performed and PCR showed positive for Leishmania.A tentative treatment with intrastromal and intracameral injection of Amphotericin B was initiated.

Conclusion We report an atypical ocular presentation of Leishmaniasis, with proven presence of the organism in the aqueous humor, and presence of the cystic structures on in-vivo confocal microscopy. A tentative treatment with intrastromal and intracameral injection of Amphotericin B was initiated.

• 4351

Anterior segment optical coherence tomography study of the surgical outcome of the filtrating surgery in glaucoma

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Purpose To study the outcome of various filtrating surgery techniques in patients with glaucoma witthe Visante Anterior Segment Optical Coherence Tomograph (AS-OCT)

Methods Fourty seven patients (47 eyes) (age 55 to 87) were enrolled after they had undergone filtrating surgery for glaucoma (Sclerectomy, Trabeculectomy, and combined surgery associating phacoemulsification and Sclerectomy or Trabeculectomy). Antimetabolites were used in all patients (mitomycin C or 5-Fluoro Uracile). Intraocular pressure was recorded 6 months, 3 months and 1 month before surgery as well as 3 months, 6 months, 1 year and 2 years postoperatively.Each time the patients underwent full ophtalmological examination with subjective slit lamp evaluation of the bleb.Morphological evaluation of the bleb was performed with the Visante AS-OCT in all patients after a minimum period of one year after surgery. The trabeculectomy / sclerectomy site as well as the morphology of the scleral flap, the conjunctival flap, the iris, and the relationship between these structures were analyzed

Results In most cases, a good correlation was observed between the AS-OCT evaluation of the bleb and the measured IOP. AS-OCT was helpful in determining the functional properties of filtration blebs in cases in which the target IOP was no reached.

Conclusion AS- OCT is a valuable tool for an accurate functional evaluation of the outcome of filtrating surgery in patients with glaucoma.

• 4352

The effect of cataract surgery on imaging optic nerve head topography with the Heidelberg Retina Tomograph®

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Purpose The purpose of this study was to determine whether phacoemulsification cataract surgery with intraocular lens (IOL) implantation has an effect on measuring optic nerve head (ONH) topography using the Heidelberg Retina Tomograph (HRT).

Methods The study population inculuded 31 women and 12 men aged 59-81 years with no previous history of eye diseases, surgery, laser procedures or medication. The patients underwent first-eye cataract surgery for senile cataract. HRT II with software version 1.6 was used to obtain three-dimensional images of the ONH as a part of a meticulous eye examination. The quality of the HRT image was assessed using topography standard deviation (TSD). The topography measurements are considered unreliable if TSD is more than 50 µm. Re-examination took place one month after surgery.

Results Before surgery the topography measurements were unreliable in 33% (14/43) of the eyes; in 4 of these cases ONH topography could not be calculated at all. One month after cataract surgery the ONH topography could be calculated in all eyes and only one had unreliable topography measurements. The mean TSD was 39 µm before and 22 µm after surgery when calculated for all eyes with measurable topographies. The change in the TSD was statistically significant ($p<0.0005$). The image alignment between the HRT examinations before and after surgery was excellent in 67% (26/39). Magnification changes occurred in 13% (5/39) of the eyes.

Conclusion Phacoemulsification cataract surgery with IOL implantation improves the image quality of the HRT. Because of magnification changes and image misalignment, HRT follow-up over cataract surgery was unreliable in more than one third of eyes.

• 4353

Is choroidal thickness different between glaucoma patients and healthy subjects?

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Purpose The aim of our study was to evaluate and compare choroidal thickness (CT) of healthy subjects and primary open-angle glaucoma patients with spectral domain optical coherence tomography (SD-OCT) and to seek a correlation between CT and glaucoma severity.

Methods Sixty-five healthy eyes, 27 eyes with early glaucoma , 21 eyes with moderate glaucoma and 30 eyes with advanced glaucoma were included in this cross-sectional study (one eye per patient). Retro-foveolar CT, foveolar retinal thickness and average retinal nerve fiber layer thickness (RNFL) were measured by SD-OCT. Humphrey 24-2 visual field was also performed and mean defect (MD)recorded. Spherical equivalent (SE) was measured with automatic refractometer.

Results Average retro-foveolar CT was statistically lower in glaucoma patients than in healthy subjects p=0.0023. The CT was not different according to glaucoma stage (p=0.078). We found a statistically significant correlation between CT and MD (p = 0.040), but not with CT and age (p=0.053), CT and retinal foveolar thickness (p=0,789), CT and RNFL thickness (p=0.732) and CT and SE (p=0.202).

Conclusion This preliminary study showed that retro-foveolar CT measured by SD-OCT was significantly thinner in glaucomatous patients than in healthy subjects.

• 4354

Evaluation of the corneal pachymetry and biomechanical parameter changes in patients treated by prostaglandin topical medication

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Purpose To assess the possible corneal changes after topical prostoglandins treatment.

Methods Prospective study including 15 patients newly diagnosed with OHT or POAG needed to be treated.The patients had complete basic ophthalmological examination before treatment (D0). IOP was measured with Goldmann aplanation tonometer, Pascal contour tonometry and ocular response analysis (ORA). The corneal biomechanical parameters, CRF and CH were measured as well with ORA. Axiale length and the anterior chamber depth were measured using IOL master. The pachymetry was performed using an ultrasound pachymeter. These examinations were repeated on D42 and D90. Anova test for repeated measurements was used for statistical analysis

Results The mean CCT was 552.6 ± 30 µ on D0, 548.8 ± 32 µ on D42 and 542.6 ± 31µ on D90. There was a significant difference between the CCT measurements on D0 and D90 (p= 0.006). The mean CRF on D0, D42 and D90 was: 11.8 ± 2.3 mmHg, 10.6 ± 1.7 mmHg and 10.7 ± 1.8 mmHg respectively. There were no significant differences between these values.The mean CH on D0, D42 and D90 was: 8.8 ± 2.1 mmHg, 9.6 ± 1.6 mmHg and 10 ± 2 mmHg respectively. There were no significant differences between these values.

Conclusion In this study we found a significant decrease of CCT after topical prostaglandins treatment. We didn't find any significant change in corneal biomechanic parameters after treatment.

• 4355 / 218
Optic disc assessment using confocal scanning laser ophthalmoscope in normal tension glaucoma with disc hemorrhage

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Purpose To evaluate which optic disc parameters have a relationship with the presence and the location of disc hemorrhages in normal tension glaucoma (NTG)

Methods This retrospective study included patients with early NTG with mean deviation with – 10 dB or better in 24-2 Humphrey visual field analyzer. Eyes in the whole study group were divided into those with and without disc hemorrhage. Optic disc stereometric parameters measured using the Heidelberg Retina Tomograph (HRT) III were compared between each group with and without disc hemorrhage. Within the group with disc hemorrhage, the location of disc hemorrhage was analyzed. Sectoral disc parameters were compared between two common locations where disc hemorrhage developed.

Results Forty-three patients with disc hemorrhage and 46 patients without disc hemorrhage were included in this study. Mean deviation and pattern standard deviation showed no significant difference between two groups. There was no significant difference in global optic disc parameters of HRT between two groups. Disc hemorrhage was displayed mainly in inferotemporal (23 eyes, 53.5%) and in superotemporal (12 eyes, 27.9 %). Regarding to sectoral disc analysis of inferotemporal quadrant, the value of cup shape measure and cup disc area ratio was higher in the disc hemorrhage group compared to the group without disc hemorrhage (P=0.0013, P=0.013, repectively). The subset analysis of disc parameters within the disc hemorrhage group, showed that superotemporal maximum cup depth in eyes with superotemporal disc hemorrhage was greater compared to inferotemporal maximum cup depth in eyes with inferotemporal disc hemorrhage (P=0.017).

Conclusion The change of optic disc parameters in early NTG patients with disc hemorrha

Commercial interest

• 4356 / 219
GDx-VCC vs GDx-ECC in glaucoma diagnosis

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Purpose To compare results provided by scanning laser polarimetry variable corneal compensation (VCC) vs enhanced corneal compensation (ECC) and evaluate correlation to visual field results in glaucoma patients.

Methods Study included 339 eyes of 182 patients screened by the glaucoma unit of the University Eye Clinic of Pavia (Italy). Patients were submitted to complete ophthalmic examination, standard automated perimetry (SAP), scanning laser polarimetry with GDx-VCC and GDx-ECC. Quality image (Q), typical scan score (TSS), nerve fibers index (NFI), nerve fibers layer average thickness in a band around the optic nerve head (TSNIT average) and in the upper (TSNIT sup) and lower sector (TSNIT inf) were evaluated for each exam. Q, TSS and morphometric parameters provided by VCC and ECC were compared using Wilcoxon signed-rank test and Lin correlation coefficient. Correlation between GDx and perimetric global indexes and was evaluated with Pearson correlation index "r."

Results 204 images out of 339 (60%) were of good quality (Q>7) with VCC and 325 out of 339 (96%) with ECC. 140 images out of 339 (41%) were atypical (TSS<80) with VCC but only 20 out of 339 with ECC (6%). ECC vs VCC constantly displays lower TSNIT thickness and higher NFI. All comparisons between ECC and VCC parameters showed statistically significant differences confirmed by a moderate to poor concordance between the two instruments.Structure/function correlation was better for ECC parameters and first of all for NFI.

Conclusion ECC provides better quality images than VCC. High quality exam is the first condition to reproduce a more reliable RNFL structure. ECC points out lower RNFL thickness and higher NFI and reveal a better correlation to perimetric indexes MD and PSD as compared to VCC. GDx-ECC could improve early glaucoma diagnosis.

• 4357 / 220
Anterior segment optical coherence tomography changes post laser peripheral iridotomy in primary angle closure suspects in an Asian population

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Purpose Multiple modalities have been used to image the anterior chamber angle. We quantified changes in novel parameters associated with angle closure, namely anterior chamber area (ACA) and volume (ACV); anterior chamber width (ACW); lens vault (LV) and iris thickness, area and curvature using ASOCT, in a cohort of primary angle closure suspects (PACS) after laser peripheral iridotomy (LPI).

Methods A prospective study of primary angle closure suspects > 50 years of age after LPI. ASOCT images (Visante, Carl Zeiss Meditec, Dublin, CA) from 176 subjects were analyzed quantitatively using customized software, before and 1 week after LPI.

Results The mean age of the 176 participants was 63.0 ± 7.3 year and majority of the subjects were Chinese (95.5%) and women (76.7%). After LPI, the angle width opened significantly with increase in mean angle opening distance [AOD 500, 0.11 vs. 0.18 mm, p< 0.001), trabecular iris surface area (TISA500, 0.06 vs. 0.08 mm^2, p< 0.001) and angle recess area (ARA, 0.12 vs. 0.17 mm^2, p< 0.001). Mean ACA (14.9 vs. 16.0 mm^2, p< 0.001) and ACV (91.6 vs. 103.0 mm^3, p< 0.001) increased significantly after LPI, but there was no change in ACW (11.21 vs. 11.24 mm, p = 0.3), anterior chamber depth (2.16 vs. 2.17 mm, p = 0.16) or LV (783.6 vs. 788.6µm, p = 0.72). Mean iris curvature was reduced (0.375 vs. 0.180 mm, p< 0.001) after LPI, but there was no significant change in iris thickness or area.

Conclusion LPI results in a significant increase in the angle width in subjects with narrow angles. ACA and ACV increased after LPI but there was no change in ACD, ACW, LV or iris thickness and area. The increase in ACA/ACV is attributed to be due to decreased iris curvature after LPI.

• 4361

PCR-based circulating melanoma cells detection in uveal melanoma

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Purpose To investigate the presence of circulating melanoma cells (CMCs) in patients affected by posterior uveal melanoma in different stages of the disease and to determine their prognostic relevance.

Methods Blood samples from 14 healthy donors and 23 patients affected by posterior uveal melanoma were collected. Fourteen patients were included at the time of initial treatment without any evidence of metastatic disease using liver ultrasonography and Pet-CT (non-metastatic group). Nine patients were included at time of initial treatment of liver metastasis (metastatic group). mRNA expression of tyrosinase, MelanA/MART1 and GP100 as a surrogate marker for the presence of CMCs was analyzed by real-time RT-PCR and compared with patient characteristics.

Results There was no significant difference on tyrosinase, MelanA/MART1 and GP100 levels between healthy donors and uveal melanoma patients ($p>0.05$). There was also no significant difference between non-metastatic vs metastatic group ($p>0.05$). High levels of tyrosinase, MelanA/MART1 and GP100 in non-metastatic patients were not related to the development of metastasis in a median follow-up time of 24 months ($p>0.05$).

Conclusion PCR-based detection of tyrosinase, MelanA/MART1 and GP100 in uveal melanoma patients appear unrelated with presence/absence of the disease and with the disease stage.

• 4362

Adjuvant intravenous therapy by fotemustine in uveal melanoma: a randomised study

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Purpose To describe the protocol of adjuvant therapy by intravenous fotemustine in uveal melanoma

Methods Patient with uveal melanoma are included in a randomised protocol if their tumor has the inclusion criteria of high metastatic risk- Clinical : largest tumor diameter ≥ 15 mm with extrascleral extension or retinal detachment , or largest tumor diametre > 18mmOr Genomic : tumor with at least complete or partial monosomy 3 associated to a gain of 8q , by BACs/CGH-array performed on fine needle aspiration biopsy or on enucleation specimen.The calculation of the number of patients to be included uses the method of Freedman

Results 178 patients were screened.131 patients were not included because of refusal of the biopsy(11), technical problems with the biopsy(32), no genomic high risk (24), refusal of the chemotherapy protocol , general health problem(cardiovascular , age , co morbidity, other cancer) or delay before the patient was by the oncologist.

Conclusion Inclusion of patients in adjuvant therapy trials is difficult. More multicentric studies are necessary.

• 4363

Quality of life after treatment of uveal melanoma

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Purpose Uveal melanoma threatens the patient with metastatic death, visual handicap, loss of independence, financial hardship, and facial disfigurement. Ocular treatment is aimed not only at preventing metastatic death but also enhancing the patient's quality of life by conserving the eye and useful vision. The aim of this study was to measure quality of life after treatment of uveal melanoma and to correlate psychological well-being with age, sex, prognosis, ocular outcomes, family support and other factors.

Methods We measured functional well-being, anxiety and depression in 511 patients treated for uveal melanoma in the previous five years and, using hierarchical linear regression analysis, we correlated the results with sociodemographic characteristics, baseline ocular features, tumour stage, ocular treatment, and post-treatment ocular symptoms.

Results Levels of function, depression and anxiety were similar to normative values. All outcomes were unrelated to visual acuity, tumour characteristics, whether or not the eye was preserved and the time since being treated.Women were more anxious than men, and older patients were more depressed than younger ones. Patients with good social support had consistently better outcomes than those with poor support.Patients with local recurrence at the time of completing questionnaires tended to be more anxious than others, but were not more impaired in depression or function. All PROMS were associated with ophthalmological symptoms. Patients with worse symptoms had poorer function and worse depression and anxiety.

Conclusion Patients can be reassured that good psychological outcomes are normal, especially if there is good social support.

• 4364

Verteporfin photodynamic therapy of retinal optic disc haemangioma

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Purpose Retinal optic disc haemangioma are difficult to manage. Observation as well as therapeutical interventions may result in irreversible visual loss. We investigated verteporfin photodynamic therapy (PDT) as the initial treatment method for these tumours.

Methods Retrospective review of patients with optic disc haemangioma not associated with v. Hippel-Lindau disease and a minimum follow-up of 1 year.

Results Between January 2009 and June 2010, we treated three patients with PDT and standard parameters as the initial intervention. All patients presented with symptomatic visual loss caused by macular oedema. In a 67-year-old female patient, complete regression could be achieved with a single PDT after 14m follow-up. Best corrected visual acuity (BCVA) improved from 6/60 to 6/18. In a 55-year-old male patient, no regression of the angioma could be induced despite 5 consecutive PDT sessions. After a 24m follow-up, BCVA decreased from 6/9 to counting fingers. In a 24-year-old female patient, a single PDT induced complete regression and BCVA improved from 6/12 to 6/9 over 12m. The treatment was initially complicated by a shutdown of the choroidal perfusion with temporary visual loss immediately following the PDT.

Conclusion In this small series, treatment response of optic disc haemangioma to PDT varied significantly between cases. A complete regression of two angiomas as well as no visible reaction to PDT in a third case could be observed. Alternative treatment modalities should be employed if the haemangioma does not respond to the initial treatment cycles and is complicated by progression of the disease.

• 4365

Development of new models of orthotopic primary human retinoblastoma xenografts

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Purpose To develop preclinical orthotopic models of primary human retinoblastoma

Methods Orthotopic models of human retinoblastoma have been developed from three subcutaneous xenografted models that have previously been established and characterized in our laboratory, i.e. RB102-FER, RB111-MIL, and RB200-GS that have been maintained in nude mice. Mice bearing xenografts were sacrificed and tumors were dissected to obtain a suspension of fresh tumor cells at a concentration of 8000 cells/ l in DMEM serum-free medium. Under intraperitoneal anesthesia, 2 l of cell suspension was injected into the subretinal space of the right eye for 3 groups of mice using a 32G needle via a Hamilton syringe. Each group was constituted by 2 female SQUID mice and 3 male nude mice. After subretinal injection, ophthalmic examination of the mice was done every 15 days with binocular microscope. When tumor cells invaded vitreal cavity and anterior chamber, the mice were sacrificed for ophthalomological pathological analyses.

Results Tumor cells developed in all injected eyes, whatever the mouse categories used, 4 weeks after orthotopic transplantation for RB102-FER and 6 weeks after for RB200-GS. In contrast, no tumor growth was observed in injected eyes of the RB111-MIL model. In the 2 first xenografts, the proliferation started with a white hemorrhagic retinal mass; three weeks later, the vitreous was invaded by tumor cells that extended to the anterior chamber. Pathological examination of the injected eyes confirmed the presence of a massive infiltration of the retina, vitreous and anterior chamber by retinoblastoma cells.

Conclusion We have then developed two new models of orthotopic primary human retinoblastoma that well reproduce the patient's tumors.

• 4366

CNS abnormalities in retinoblastoma patients

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Purpose The presence of CNS abnormalities on MR images in a large group of consecutive patients with retinoblastoma (RTB) is evaluated. Mental retardation and congenital brain anomalies are reported in patients with RTB, mostly in combination with 13q deletion syndrome. Pineoblastoma (PNB) is the most important and "life threatening" condition associated with hereditary RTB, but recent studies suggest an association with pineal cysts. This association is important because some PNB mimic pineal cysts

Methods CNS MR images of 320 consecutive patients with RTB from 2000 to 2010 were evaluated by neuroradiologists for tumors, structural anomalies, myelinization, and coincidental findings. Clinical records were reviewed for laterality, heredity, and the presence of the 13q deletion syndrome.

Results The hereditary group (patients with bilateral and unilateral proved RB1-germline mutation) included 42 (48.2%) of 87 patients. Nine patients had 13q deletion syndrome. Normal findings on brain MR images were seen in 305 (95.3%) patients. One PNB was detected in a patient with hereditary RTB and 2 arachnoid cysts in 2 sporadic unilateral RTB patients; one cerebral and corpus callosum atrophy and 3 pineal cysts were also detected (2 non hereditary, 1 in 13q deletion syndrome). Corpus callosum agenesis was found in 3 patients (two in 13q deletion syndrome, 1 in hereditary RTB) and corpus callosum hypoplasia in 6 patients (2 twins, 4 sporadic RTB, 1 familial RTB). Chiari I syndrome was found in two cases

Conclusion PNB is associated with hereditary RTB, and structural brain abnormalities are associated not only with 13q deletion syndrome. Pineal cysts can be detected in patients with sporadic RTB and/or with 13q deletion syndrome.

• 4367

Propranolol in the management of orbital and periocular pediatric hemangioma

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Purpose To discuss the use of propranolol (and other β-blockers) in the treatment of pediatric orbital and periocular capillary hemangiomas, and perform literature review.

Methods Two babies (3 and 5 months) affected by orbital capillary haemangioma with cutaneous periocular involvement were treated by oral propranolol (2 mg/kg/day) as a sole treatment. Complete baseline local and systemic examination revealed no contraindication to treatment. A strict follow-up protocol was performed to monitor tumor changes and any side effect. Follow-up was longer than 12 months.

Results Both patients had significant improvement with resolution of the orbital component and slower resolution of the cutaneous side. No local or general (mainly hypotension, hypoglycaemia and asthma) side effects of propranolol were observed.

Conclusion Propranolol appears to be a safe and effective option in the management of infantile capillary haemangioma. The role of other β-blockers, even topically applied, should be considered.

• 4368

Puzzling case of choroidal tumour: paraganglioma or neuroendocrine carcinoma, diagnosis and treatment options

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Purpose A monophthalmic patient was referred with different choroidal tumors in his only left eye, for advise about the diagnosis and different treatment options.

Methods In 2006 the right eye was enucleated for melanoma. In 2009 a skin melanoma on the head was resected, and in 2010 a neuroendocrine adenocarcinoma (NEAC) of the prostate was diagnosed with a liver metastasis of NEAC. Multiple metastatic lesions were detected by ct on liver, spine and abdomen without any complains. The different treatment options and correlations between these 4 tumors were investigated

Results After review of the 4 biopsies the final diagnosis was: 2 different tumors: a paraganglioma in the left eye with skin metastasis and NEAD in the prostate with hepatic metastasis. The tumors in the left eye are presumed to be metastases of one of the originals or a new location of one. Both type of tumors have common clinical and pathologic characteristics and a genetic predisposition is suggested. In most cases there is a favorable prognosis. The vision of the left eye was 7/10 with diffuse metamorphopsia, because of subretinal fluid around the tumors. The treatment options were discussed and external beam radiation to the left eye was performed to stabilize the tumors. He was in general good health, although multiple detected metastases on imaging

Conclusion This case shows a very rare paraganglioma in one eye in a patient with multiple NEAD and metastates in the other eye; this demonstrates the possible genetic link between both rare entities

• 4371

S100 expression in normal and pathological sclerocorneal limbus

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Purpose Several molecules have been proposed as corneal epithelial stem cell (SC) markers but none of them is able to identify SC in normal or pathological conditions. S100 proteins make up the largest subfamily of the EFhand Ca+binding protein family. The function of S100 is unknown but its expression was already known in pterigium and corneal epithelium in keratoconus.The aim of this study was to evaluate expression of S100 proteins as an early marker of SC deficiency.

Methods The expression of S100 proteins was evaluated in four healthy sclerocorneal limbus and in five cases of pathological limbus due to severe inflammation: a case of corneal melting and perforation in advanced herpes simplex (HSV) disease, three cases of endophthalmitis and a case of fungal infection were analyzed. All samples were fixed in formalin,embedded in paraffin and stained by immunohistochemistry

Results In normal limbus, S100 proteins were positive and in particular we observed no difference between different dimension crypts. No expression of S100 was detected in almost all pathological cases.

Conclusion This result suggest that S100 proteins can be useful as marker of early pathological changes in SC niches.

• 4372

CREB is involved in growth of pterygia

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Purpose Pterygium represent a fibrovascular lesion of ocular surface with tumor-like characteristics, such as proliferation and infiltration. Although the exact pathogenesis of pterygium is unknown, and controversy exists about cells origin and nature of initial tigger required for its development. In this study we investigated the role of the transcription factor cAMP response-element binding protein (CREB) in pterygial and normal conjunctival tissues of humans.

Methods Samples of primary (n=14) and recurrent (n=4) pterygia and normal bulbar conjunctivas (n=3), surgical removed, were analyzed in this study. Formalin-fixed, paraffin embedded tissues were used for immunohistochemical staining with CREB, vimentin, ki67, survivin, MMP7, p63, cycin D1 or p53 antibody.

Results Immunoreactivity for CREB was detected in primary and recurrent pterygia. CREB positivity was localized in the epithelial compartment of pterygia and it was absent in the stroma and normal conjunctiva. We observed a good correlation between CREB and other markers commonly overexpressed in pterygia (in particular vimentin, survivin and MMP7). An interesting aspect is the localization of CREB and ki67 positive cells, suggesting that the noxa pathogena have an effect on epithelial cells that express CREB and induce epithelial proliferation factors, followed by stromal growth.

Conclusion These preliminary results point to the epithelial origin of pterygia. They also throw fresh light on CREB function and may be of assistance in the elaboration of new approaches to the treatment of pterygium.

• 4373

Meganuclease targeting herpes simplex virus protects against viral endothelitis: an organ culture model

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Purpose Despite advances in antiviral therapies, past history of HSV keratitis is associated with poor prognosis of subsequent penetrating keratoplasty.The aim of this study is to assess the antiviral property of a meganuclease targeting HSV in the prevention of HSV endothelitis.

Methods Normal rabbit corneas were placed in organ culture using an immersion method and transduced by a recombinant adeno-associated virus (rAAV) allowing constitutive expression of meganucleases targeting HSV-1 genome or containing the same expression cassette with a non-coding sequence. These organs were then submitted to infection by recombinant HSV-1 F(1) virus equipped with a LacZ expressing cassette at M.O.I. 0.001 to 0.1% in liquid or semi-solid medium. Infection rates for plaques or cells in endothelium were established by immunostaining of envelope protein gD or X-gal staining after the end of first or second lytic cycle.

Results Meganuclease targeting the ICP0 gene which encodes an E3 ubiquitin ligase involved in viral reactivation and replication did not change infection rates in the present organ culture model, but reduced the average size of plaques in endothelium with a decrease of 27-46%. Conversely, the meganuclease directed against the major capsid protein UL19 lowered the number and size of plaques, both being reduced by half at M.O.I. 0.001%. Consequently, the expression of a meganuclease in endothelium, evidenced by RT-PCR, could either reduce infectious particle production or induce cell resistance to HSV-1.

Conclusion These meganucleases are currently checked for their anti-infective properties in an in vivo model of endothelitis.

• 4374

Cultivated oral mucosa epithelium transplantation (COMET) in bilateral limbal stem cell deficiency

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Purpose To present results of COMET technique in corneal surface reconstruction in bilateral limbal stem cell deficiency.

Methods Study group: 13 patients (17 eyes) suffering from limbal stem cell deficiency (LSCD) afterchemical burns (7 eyes) or from aniridia related LSCD (10 eyes). Preoperative vision was ranged from hand movements to 0,05. Oral mucosa epithelium was collected and tripsinized. Single cells were seeded on denuded amniotic membrane. Cultures were carried in standard conditions in supplemented DMEM HAM/F12 mixture medium in presence of inactivated 3T3 fibroblasts for 8 days. Histologic examination and immunostaining for epithelial cytokeratins confirmed epithelial origin before transplantation. After superficial keratectomy carries with stratified epithelium were transplanted on the denuded corneas. Corneal surface stability was evaluated as well as visual outcomes.

Results Postoperative follow-up ranged from 6 to 12 months. 6 months after surgery 76,4 % of eyes showed stabile epithelium. In 23,5 % of eyes corneas reminded cloudy due to recurrent conjuctival neovascularization or stromal haze. All failed grafts were from ocular burns patients group. Visual acuity ranged from hand movement to 0.4.

Conclusion COMET is a new method for bilateral corneal epithelial disorders offering the patient satisfactory stabilization of the corneal surface.

• 4375

Documentation of distribution of normal conjunctival vessels and their changes by mild irritation of photography using automated algorithm

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Purpose To quantify distribution of conjunctival vessels in normal eyes and the changes induced by the irritation of photography.

Methods Digital slit lamp photography of the upper and lower conjunctiva of 728 healthy eyes was done in 4 groups with different orders of succession of the photography in each person. A radon transform based algorithm was used to segment vessels and compute area occupied by vessels (AOV) of different sizes in each image. AOV of small, medium and large vessels were compared in the first photos of cases, and in the successive photos of each person using ANOVA (post hoc: Tukey) and paired sample T tests.

Results AOV of the 3 sizes of vessels had normal distribution in all images. In the first images of photography (un-irritated eyes); AOV of medium sized vessels was the largest and was less in both fields of the left eye than the upper field of the right eye. Irritation of photography, caused an increase in AOV of the large vessels first, followed by increase in AOV of medium sized vessels accompanied by a decrease in AOV of small vessels, and finally a small increase in AOV of small vessels.

Conclusion Medium sized vessels are the most abundant in un-irritated eye. During mild irritation, changes in large conjunctival vessels are documented first. Medium and small sized vessels seem to respond later.

• 4376 / 406

Topical application of autologous adipose-derived mesenchymal stem cells (AdMSCs) for persistent sterile corneal epithelial defect

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Purpose To report a patient with post-traumatic persistent sterile corneal epithelial defect treated with topical application of autologous AdMSCs.

Methods A 35-yr-old man was referred to our clinic for treatment of post-traumatic persistent corneal epithelial defect previously treated as infection. 1 yr before CxL was performed for keratoconus stabilization. Examination showed a central corneal epithelial defect with stromal opacification and thinning. Corneal sensitivity was decreased, while corneal scraping cultures were negative for bacterial or fungal infection. Despite conventional treatment (patching, artificial tears, soft contact lens & autologous serum) no corneal epithelial healing progress occurred 50 days after injury. A PKP was scheduled due to risk of corneal perforation. While waiting for graft, we proposed to the patient the alternative treatment of autologous AdMSCs. IRB was obtained and approved from the Hospital.

Results Corneal epithelial healing process was started 10 days after topical application of MSCs, isolated through liposuction. 1 month later, complete corneal epithelial healing was observed. 1 yr later, corneal epithelium remained intact with mild anterior stromal opacification. The patient's current UCVA lies between 6-7/10.

Conclusion Topical application of autologous adipose-derived MSCs seems to promote corneal epithelial healing in a patient with persistent sterile corneal epithelial defect refractory to other treatments. Differentiation or trans-differentiation of MSCs into corneal epithelial/stromal cells and/or production of trophic factors could be possible mechanisms behind the corneal healing process.

• 4411
Optical coherence tomography in retinal detachment cases

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Purpose To report the contribution of optical coherence tomography (OCT) in the assessment of macular pathology following retinal detachment surgery.

Methods OCT imaging was employed to assess macular pathology following pars plana vitrectomy or scleral buckling for the management of retinal detachment cases.

Results The presence of persistent subretinal fluid, cystoid macular oedema and the formation of epiretinal membranes or macular holes were demonstrated during optical coherence tomography imaging postoperatively. In the era of spectral domain OCT greater attention has also been directed in the evaluation of any alteration, and/or disruption of the junction line between photoreceptor inner and outer segments and in the external limiting membrane. An attempt has also be made to correlate the anatomical results following surgery with visual recovery.

Conclusion OCT imaging enhances the visualization of macular anatomy following retinal detachment surgery. A correlation between anatomical and functional results can be established in some cases.

• 4412
Epiretinal membranes following retinal detachment surgery

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Purpose To study the factors that influence the development of secondary epiretinal membrane (ERM)formation after retinal detachment repair and to report anatomic and functional results.

Methods The patients had received either pars plana vitrectomy or scleral buckling for their retinal detachment repair. The patients underwent pars plana vitrectomy with ERM removal in the second surgical procedure.

Results Foveal morphological changes influence best corrected visual acuity outcome in patients with secondary ERM after retinal detachment repair.

Conclusion ERM development is a known complication of retinal detachment repair. The anatomic and functional results can be improved in these patients by removal of the ERM.

• 4413
Macular holes after retinal detachment surgery

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Purpose To study the incidence, characteristics and management of Macular Holes (M.H.) developing after retinal detachment repair.

Methods The records of 4 patients with M.H. following retinal detachment were reviwed. All patients underwent three-port pars plana vitrectomy, internal limiting membrane removal, 14% C3F8 gas tamponade with post-operative face down positioning for two days.

Results Macular holes were diagnosed from 1 to 9 months post-operatively. Macular hole closure was achieved in all patients. Functional improvement was compromised by pre-existing macular pathology.

Conclusion Macular holes may develop after retinal detachment repair and they can be managed with conventional M.H. surgery.

• 4414
Glaucoma and retinal detachment

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ABSTRACT NOT PROVIDED

• 4415

Pneumatic retinopexy complications

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Purpose To review the incidence of new and missed retinal breaks, the risk for PVR formation and the danger of other intraoperative or postoperative complications after pneumatic retinopexy (PR) for retinal detachment comparing with those after scleral buckling procedure and vitrectomy.

Methods All cases having undergone PR in our clinic during the last 8 years for primary retinal detachment or redetachment were reviewed for intraoperative or / and postoperative adverse events. The findings were compared with those from the literature which studied in any prospective or retrospective way the complications after PR, scleral buckling and vitrectomy for retinal detachments without PVR.

Results Improper gas entrapment (anteriorly, subretinal or subconjuctival) and high intraocular pressure were observed intraoperatively or soon after the procedure. New retinal breaks and PVR development were the most common findings in the late postoperative period.

Conclusion The relatively high incidence of new breaks suggests that proper case selection and close follow-up are probably required. PR seems to be the method of choice after retinal redetachment due to missed retinal breaks after vitrectomy.

• 4416

Silicone oil complications

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ABSTRACT NOT PROVIDED

• 4421

ElVisML: A little less conversation. Experiences with the Electrophysiology of Vision Markup Language in clinical routine and in a multi-center trial

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Purpose The International Society for Electrophysiology of Vision (ISCEV) started a process of standardization in electrophysiology of vision to increase comparability of recordings. Standardization is important, especially in clinical trials. However, there is no standard for encoding electrophysiological data of vision. Recently, we proposed such a standard, called Electrophysiology of Vision Markup Language (ElVisML). Here we give an overview of our experiences in the application of ElVisML in clinical routine and in a multi-center clinical trial.

Methods The University Eye Hospital Tuebingen runs three Espion (Diagnosys Ltd) systems, all connected to a central database, which is integrated into a hospital information system (HIS). ERG recordings are added to patients electronic health records (EHR) as ElVisML file. The software system of the STZ eyetrial ERG reading center uses ElVisML as a native format for the electronic exchange of ERG recordings between stakeholders of the reading process.

Results Integrated into a HIS, ElVisML allows for a network-wide access to ERG recordings and long-term archiving. Compliance to regulatory requirements of the reading center are successfully implemented in a multi-center study (2 sites, 20 patients, 4 examinations) using ElVisML: An audit trail is realized by revisions of ElVisML files, conformance checks are automatically enforced during each step of the workflow using data included in ElVisML.

Conclusion Open standards like ElVisML help to ensure quality, validity, and integrity of ERG recordings, provide manufacturer independent access, and long-term archiving in a future-proof format in clinical routing as well as in reading centers.

Commercial interest

• 4422

Progression of electroretinogram responses in Stargardt-fundus flavimaculatus: a longitudinal study

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Purpose To investigate the progression in Stargardt-fundus flavimaculatus (S-FFM) by repeated clinical and electrophysiological examination.

Methods A longitudinal study of 59 patients with S-FFM was undertaken. The mean age at the initial examination was 31.6 years; mean follow-up interval was 10.5 years. Electrophysiological tests included pattern and full-field electroretinogram (ffERG); clinical ophthalmic examinations were performed. Patients were classified into 3 groups as previously published (Lois et al, 1999); Group 1 had dysfunction confined to the macula; Group 2 had macular and generalized cone dysfunction; Group 3 had macular, generalized cone and generalized rod dysfunction. Initially, there were 27 patients in Group 1, 16 patients in Group 2, and 16 patients in Group 3. The data obtained at follow-up were compared with those originally obtained. An amplitude reduction of > 50% or a peak time shift of >3 ms for the 30Hz flicker ERG or bright flash a-wave were considered clinically significant. Molecular analysis of the ABCA4 gene showed likely disease causing variants in 30/40 patients.

Results During follow-up, 3/27 patients from Group 1 progressed to Group 2, and 2/27 patients to Group 3. Eight of 16 patients of Group 2 progressed to Group 3. Significant deterioration in ERG was observed 13/59 patients. Electrophysiological progression occurred in 22% of Group 1, 50% of Group 2, and 100% of Group 3.

Conclusion All patients with initial rod involvement demonstrated clinically significant electrophysiological deterioration; only 20% of the patients initially having normal ffERGs showed significant deterioration. These data confirm and elucidate the role of ffERG in the prognosis of patients with S-FFM.

• 4423

The importance of dark adapted cone function in ERG interpretation

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Purpose The ISCEV Standard for ERG does not include a measure of dark-adapted cone function. Prior to the introduction of the Standard, use of a red flash under dark-adapted conditions was a well-recognised part of ERG but its use appears subsequently to have declined. The purpose of the presentation is to demonstrate the importance of the dark-adapted red flash ERG in clinical ERG interpretation.

Methods Retrospective case based presentation. Use of a red flash under dark adaptation can evoke an ERG in which there the early part of the waveform arises from the dark-adapted cone system and the latter part of the waveform from the rod system. The intensity of the red stimulus can be adjusted so that the rod-system derived part of the waveform has an amplitude similar to that of the rod specific ERG b-wave (DA 0.01).

Results Cases will be shown where use of the dark-adapted red flash ERG enabled an improved interpretation of the bright flash ERG (DA 11.0). Disorders addressed will include fundus albipunctatus; vitamin A deficiency; RGS9 mutation ("bradyopsia") and retinitis pigmentosa. An electronegative ERG waveform can occur arising in dark adapted cones, consistent with the so-called "photopic hill" phenomenon occurring in dark adapted cones exposed by an absence of rod function. The DA 11.0 ERG a-wave can reach in excess of 150μV under such circumstances, giving the potential for misdiagnosis of a form of inner retinal dysfunction such as may occur in CSNB.

Conclusion The ISCEV Standard ERG waveforms are intended as a minimum data set. Use of a red stimulus under dark adaptation is a valuable addition to that data set and may prevent misinterpretation of the ISCEV Standard ERGs. The decline in the use of this ERG appears unjustified in routine clinical practice.

• 4424

Electroretinogram and patterned visual evoked potentials as detectors of retinal dystrophy in children affected by Joubert syndrome: a longitudinal survey

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Purpose Joubert syndrome (JS) is a rare autosomal recessive congenital malformation of the brainstem and cerebellar vermis. The pathology can be associated with retinal dystrophy (RD). In a previous study we presented the data of retinal involvement and their relationship with electrophysiology in 26 JS patients. The longitudinal data are shown in a part of this sample.

Methods All the children had repeated clinical examinations. The electroretinogram (ERG) was performed without sedation. One recording skin electrode was placed on the bridge of the nose. The stimulation included the maximal combined response and a 30 Hz response after a brief adaptation. For the patterned visual evoked potentials (PVEP) a sequence of checks of 15, 30, 60, 120 and 300 minutes of arc was presented. All the JS children had both ERG and PVEP repeated from 2 to 4 times. A total of 13 JS affected children for the ERG and 12 for the PVEP were analyzed. Comparisons between percentage of reliable responses were performed by Fisher exact test.

Results A significant difference between JS children with and without RD in 30 hz ERG ($p=0.050$) and 120, 60, 30, and 15 minutes of arc ($p=0.006, 0.002, <0.001, <0.001$ respectively) was found.

Conclusion ERG and PVEP repeated measures are valuable means for the diagnosis and follow-up of RD in JS (patients).

• 4425

Colour vision in Stargardt disease

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Purpose To investigate the type and severity of colour vision deficiencies (CVDs) in Stargardt disease (STD). And, to establish how the degree of CVD relates to best-corrected visual acuity (BCVA), full field ERG (ffERG) and duration of disease.

Methods A retrospective, cross-sectional study of 97 patients with a clinical diagnosis of STD included a comprehensive medical history and a full clinical work-up, with extensive colour vision testing. Eight patients underwent anomaloscopy. ABCA4 was screened in 92 patients.

Results Patients were allocated to 5 BCVA groups and to 3 ffERG groups.Normal colour vision was found in almost 30% of patients. R/G CVDs increased as BCVA declined. More than 50% had a deutan type R/G CVD, although protan R/G CVDs became progressively apparent as BCVA decreased. A predominance of pseudoprotanomaly was evident only on anomaloscopy. Additional Blue/Yellow (B/Y) CVDs were noted in 25% of patients. B/Y CVDs and BCVA higher than 0.75 were seen in adult-onset STD. CVDs evolve to scotopization in patients with low BCVA and/or longstanding disease. Duration of disease did not correlate well with CVDs. Also, no statistically significant differences in ERG results were found between groups with or without a CVD.

Conclusion Since colour vision function is better correlated to BCVA than either disease duration or ffERG, it is a rather reliable indicator of disease severity. The presence of CVDs may help to establish an early diagnosis of STD.

• 4426

AZOOR defined (Acute Zonal Occult Outer Retinopathy)

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Purpose To identify common diagnostic findings in 25 patients with AZOOR, first described by Gass in 1993 as a syndrome with rapid loss of one or more large zones of outer retinal function. We were interested in better defining recog-nizable diagnostic features and the natural history.

Methods Patients were identified by sudden onset of zonal functional loss (scotomata) on kinetic visual fields, and abnormal electroretinograhy. All patients had full clinical examinations, family histories for autoiommune disease and retinal degeneration, kinetic visual fields, autofluoresence imaging, electroretinography, Western blots for anti-retinal antibodies (ARAs).

Results There were unifying patterns among patients; all but 4 patients were women, over half had family members with other autoimmune disorders, the disease had asymmetric presentation in 35% of patients. The ERG was always abnormal in eyes with the scotomata, and in most the photopic b-wave amplitudes were markedly decreased in eyes with large scotomata. Enlarged blind spots extending into equatorial regions were a strong and common feature of the scotomata, which could be seen on autofluorescence. Pigment deposits were very uncommon. Western blots were very positive with an average of 6.5 immunoreactive anti-retinal antibody bands (normal <1.2). Negative waveforms, occurred in 3/25 patients, and 30Hz flicker amplitudes abnormal in 19/25 with only 12/25 with delayed ITs. Patients with recent onset had a better response to immuno-suppressant therapy.

Conclusion AZOOR is another atypical retinopathy that has anti-retinal antibodies as a common feature. The ERG suggests that pathologic anti-cone antibodies play a key role, and given the pattern of scotomata, the ARAs access the retina via the optic canal or peripapillary region.

• 4441
Herpes simplex virus

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Purpose Herpetic simplex anterior uveitis (HSAU) is a major infectious entity. Prompt diagnosis of HSAU is essential, usually based on typical clinical features. Treatment is based on antivirals and corticosteroids.

Methods Review of clinical features, outcomes, and management of HSAU.

Results HSAU is typically acute and unilateral disease, with patients suffering from blurred vision, photophobia, pain, and redness. Inactive or active corneal involvement is often associated. The corneal sensation can be decreased relative to the controlateral cornea. However corneal involvement can be absent.Inflammation is more often granulomatous, and the typical herpetic keratic precipitates (KPs) are large, flat and usually do not respect the Arlt's triangle, but tend to accumulate on the central corneal endothelium. Anterior chamber cells and flare of varying degrees of severity, with or without posterior synechiae, are noted. Iris atrophy and pupillary distortion are common. Increased intraocular pressure (IOP) is also frequently observed and is very suggestive. The IOP rise is related to acute trabeculitis. The course tends to be recurrent. Laboratory tests are necessary especially in patients with atypical clinical presentation. Detection of viral DNA in ocular fluids by PCR is the gold standard for the laboratory diagnosis of HSAU. The key to successful treatment of HSAU is the use of topical corticosteroids combined with systemic antivirals for the treatment of recurrences followed by prophylactic antiviral therapy combined with low-dose corticosteroid drops. Visual prognosis might be good, especially in patients who have only anterior uveitis without corneal desease

Conclusion An increased awareness of the characteristic clinical features and the role of PCR for early diagnosis and appropriate treatment are important.

• 4442
Varicella zoster virus

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Purpose Patients with herpes zoster ophthalmicus (HZO) are referred to ophthalmologists for prevention or treatment of its potential complications. Without prompt detection and treatment, HZO can lead to substantial visual disability. The purpose of this presentation is to summarize the typical signs and symptoms of anterior uveitis associated with varicella zoster virus (VZV).

Methods Presentation of typical signs and symptoms of anterior uveitis associated with varicella zoster virus (VZV).

Results Varicella zoster virus is often associated with corneal complications such as epithelial, stromal, and disciform keratitis; anterior uveitis; necrotizing retinitis; and cranial nerve palsies in relation to the eye. Postherpetic complications, especially postherpetic neuralgia (PHN), are frequently observed. Cranial nerve palsies are common and most often involve the facial nerve, although palsy of the oculomotor, trochlear, and abducens nerves may occur in isolation or (rarely) simultaneously. Complete ophthalmoplegia can also been seen. Vasculitis within the orbital apex (orbital apex syndrome) or brainstem dysfunction is postulated to be the cause of cranial nerve palsies.

Conclusion The management of VZV ophthalmic involvement, includes a multidisciplinary approach aiming to reduce complications and morbidity

• 4443
Cytomegalovirus

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Cytomegalovirus-associated anterior uveitis is a recently described entity. Based on the PCR-analysis of the aqueous humor, the diagnosis may be confirmed in patients with unilateral hypertensive anterior uveitis with mild iris atrophy but without posterior synechiae. Two different subtypes of the disease have been reported so far. It has been shown that more than 50% of cases of Posner-Schlossman syndrome are CMV-induced. The type and distribution of keratic precipitates are major clinical elements for the diagnosis of the infection. Interestingly, retinitis has never been described in this group of patients and none of them is immunosuppressed. In Europe, the association of FUuchs heterochromic cyclitis and CMV has not been confirmed. Rarely, PCR tools are insufficient and local antibody production may help diagnostic confirmation.The most important issue remains the therapeutic management of these patients. Specific anti-CMV drugs have been proposed but the route of administration, the dosages and the duration of therapy remain controversial. Topical anti-CMV drugs are promising but rarely efficient as an induction regimen. Systemic valganciclovir is highly efficient and proposed for at least 2 months with a close follow-up to detect any further relapse.

• 4444
Anterior uveitis with intraocular fluid analysis positive for rubella virus

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Purpose To compare the clinical characteristics and visual prognosis of patients with anterior uveitis (AU) with intraocular fluid analysis positive for Rubella virus (RV), Herpes Simplex virus (HSV) or Varicella Zoster virus (VZV) in order to discriminate rubella virus AU from herpes virus AU.

Methods Retrospective, observational study.Clinical records of 106 patients with anterior uveitis and positive Polymerase chain reaction and/ or Goldmann-Witmer coefficients for RV (n=57), HSV (n=39) and VZV (n=10) were analyzed. Demographic constitution, ophthalmological characteristics and visual prognosis were compared.

Results All three types of viral AU were characterized by unilateral involvement (80-97%). RV-AU was characterized by younger age at onset and chronic course, and was typically associated with cataract at presentation. Heterochromia was present in 23% of RV-AU patients. AU associated with HSV or VZV infection occurred characteristically in older patients and frequently followed an acute course. Associated clinical features included conjunctival redness, corneal edema, history of keratitis and development of posterior synechiae. HSV-AU had more often severe AU whereas the presence of vitritis was more common in RV-AU and VZV-AU. The prevalence of documented IOP above 30mm Hg (25-50%, P=0.06) and development of glaucoma (18-30%, P=0.687) were similar in all three groups. Retinal scarring was seen in 22% of RV-AU eyes, 0% HSV-AU eyes and in 11% of VZV-AU eyes Visual prognosis was favorable for all three groups.

Conclusion Our results point out clinical differences between RV-AU, HSV-AU and VZV-AU and might be especially of value to ophthalmologists who lack the possibility of intraocular fluids analysis to discriminate rubella virus AU from herpes virus AU.

• 4445

Diagnostics of virus-induced anterior uveitis

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Purpose Virally induced anterior uveitis, accounting for more than 10 % of cases, is the most common form of infectious anterior uveitis. A distinction between the various possible infectious agents is important for therapy and prognosis, but frequently not possible basing only on history and clinical grounds only. In these cases, a laboratory confirmation of the clinically presumed diagnosis is of interest.

Methods A Medline search was conducted using the search terms "anterior uveitis", "virus" and "diagnostic". After exclusion of reviews and studies including less than ten samples, the remaining were assessed for their diagnostic yield with focus on the viruses of the herpes family (HSV-1, HSV-2, VZV, CMV, EBV, HHV6-8), Rubella and Parechovirus including ELISA, PCR and immunoblot testing from paired samples of aqueous humour and serum.

Results Based on intraocular antibody synthesis and PCR, herpes vriuses represent the majority of viral anterior uveitis instances. Cytomagalovirus- and Rubella-associated anterior uveitis have obviously been underestimated in their role, whereas the clinical relevance of Parechovirus and other forms of more recently described viral anterior uveitis cases has as yet to be determined.

Conclusion Basing on published evidence, a systematic diagnosis of infectious agents in presumed viral anterior uveitis has to be postulated for all cases without a clear clinical diagnosis or a poor response to therapy. If access to a qualified laboratory is lacking, a parallel sample of serum and aqueous humour should be collected and be referred to one of the international referrence laboratories if the clinical situation is developing unfavourably.

• 4446

The project of "virus-induced anterior uveitis"

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Purpose To summarize the clinical signs of virus-induced anterior uveitis and to compare our understanding with the results of a Symposium recently hold in Berlin, comparing proven to unproven cases of herpes simplex virus (HSV), varicella-zoster virus (VZV), cytomegalovirus (clinically like Posner-Schlosman Syndrome), and rubella virus (clinically the picture of Fuchs heterochromic uveitis).

Methods Presentation of typical signs and symptoms of anterior uveitis which may be viral induced. This will include secondary glaucoma, keratitis, iris color changes, synechiae, complications like cataract and macular edema.

Results Typically viral induced anterior uveitis only sometimes leads to posterior synechiae (HSV, VZV), mostly to a mild anterior chamber inflammation, and very rarely to macular edema

Conclusion We plan a worldwide prospective trial for reaching more information about the role of virus in anterior uveitis, with tap of the anterior chamber and evaluation of the antigen and the antibody response.

• 4451

The Sanger Mouse Genetics Programme: high throughput characterisation of knockout mice

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Purpose The Sanger Mouse Genetics Project (MGP) is committed to making a significant contribution to the functional annotation of the mammalian genome by generating, characterising and archiving in the order of 200 lines of knockout mice per year, including 125 lines which have been processed as part of the EUMODIC consortium. Phenotypic data on a spectrum of disease conditions are obtained for each mouse line without the need for any prior assumptions about function by performing a standardised battery of phenotyping screens. The data generated will help to further the understanding of the interplay of genes and disease and provide an insight into the various underlying biological pathways. All phenotyping data and biological resources generated by the project are openly available to the scientific community.

Methods Eye morphology is routinely assessed using a standard parameter assessment list in conjunction with the Slit Lamp and Ophthalmoscope and images are collected when abnormalities are identified. Expression profiling via the lacZ reporter gene is performed for each mutant line in adults and at E14.5. We collaborate with University of Iowa who are performing a pathology review of H&E stained paraffin sections and also sectioning of lacZ positive eyes.

Results To date, the eye screen has been completed on over 310 mutant lines. Here we report examples of novel eye-related abnormalities identified by the eye morphology, embryonic lethality and/or expression screens performed by the Sanger MGP. We will present how to identify a potentially interesting mouse mutant on our database and discuss the impact our knockout mouse models might have on your research.

• 4452

Scheimpflug analysis and OCT as new and rapid screening tools in the mouse

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Purpose The purpose of this study was the establishment of Scheimpflug imaging and Optical coherence tomography (OCT) in the Vision Screen of the German Mouse Clinic (GMC).

Methods Mouse eyes were analyzed by Scheimpflug imaging, OCT, Slit lamp biomicroscopy, Funduscopy, and Histology.

Results The GMC is a large scale phenotyping center where mouse models for human diseases are analyzed in a standardized way. More than 550 parameters are investigated by mouse researches and clinicians from various fields. The screens in the GMC are designated to 14 different areas including behaviour, neurology, energy metabolism as well as vision and eye development. In our attempt to optimize the Vision Screen, we tested the suitability of Scheimpflug imaging and OCT for high-throughput investigations of the mouse eye by evaluating data of the inbred lines C57BL/6J (B6) and C3HeB/FeJ (C3H). Both methods confirmed previous findings with well established Slit lamp biomicroscopy, Funduscopy, and Histology. Scheimpflug measurements with non-anaesthetized 13-week-old mice indicated transparent lenses with comparable background densities for both B6 and C3H. Pupil dilating with atropine was necessary to optimize lens imaging. Concerning OCT results, B-scan images of the C3H fundus proved pigment patches and vessel attenuations that are typical for this inbred line. Moreover, the underlying degeneration of retinal outer plexiform and nuclear layers was successfully visualized. Mouse handling was more time-consuming compared to Scheimpflug imaging. In particular, mice had to be anaesthetized and mouse eyes required a contact lens.

Conclusion Our data demonstrate that Scheimpflug imaging and OCT represent suitable tools for rapid screening of lens density and fundus morphology in the mouse.

• 4453

Visual phenotyping at the "Institut Clinique de la Souris"

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Purpose Visual diseases come in many flavors, with a large variety of affected tissues (eye anterior segment, retina, optic nerve, cortex ...), ages of onset, rate of progression and causal factors. In Western countries, if the majority of these diseases are now curable, millions of people are still affected by blindness or low vision, as many retinal diseases (age-related macular degeneration, retinitis pigmentosa, diabetic retinopathy, glaucoma...) still lack efficient treatments. In a facility devoted to mouse phenotyping as the Mouse Clinic Institute (MCI), it is thus of major importance to propose an efficient visual phenotyping platform, to pick up visual defects in screened mutants, to assess the beneficial effects of potential treatments or the eventual adverse effects of drugs targeting the CNS.

Methods Mouse mutant lines from the Eumodic European project, as well as lines from specific academic projects, go through clinical observation (slit lamp, fundus imaging) in the context of a behavioral phenotyping pipeline, or are assessed in more details with angiography, optomotor response, electroretinography, retinal histology and/or immunohistochemistry.

Results To illustrate the possibilities offered by the MCI visual phenotyping platform, we will present results obtained from recent projects, including comparison between C57BL/6J and 6N control mice.

Conclusion In an environment allowing for an in-depth phenotyping, from behavior to biochemistry, metabolism and cardiology, the MCI visual phenotyping platform provides a comprehensive set of tests to get the most out of genetically modified mice.

• 4454

Rete mirabile in mouse retina?

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Purpose One possible definition for rete mirabile, the "wonderful net", is a capillary network interrupting one arteriole, as happens in kidney. In a glomerulus, the afferent and efferent arterioles are communicated by a capillary tuft. It is generally accepted that in mouse retina, capillaries communicate directly arterioles with venules. However, this must be difficult in a tissue where normally there is not concordance between the number of arterioles and veins. In the current study, we explored the presence of retia mirabilia in mouse retina which could explain the mismatch between retinal arterioles and venules.

Methods Retinas from C57BL6 and CD1 mice were used. After partially clamping of the common carotid arteries, hypoxia was detected using the Hypoxiprobe-1 Kit (Chemicon). Mice were intravenously injected with 60 mg pimonidazole/kg body weight in phosphate-buffered saline. Pimonidazole specifically binds to proteins in hypoxic cells at an oxygen pressure equal to or lower than 10 mmHg. Thirty minutes after injection animals were euthanized and pimonidazole binding proteins were detected in the retina by immunohistochemistry.

Results Direct capillary connections between retinal arterioles were found in C57BL6 and CD1 mice, indicating the presence of retia mirabilia. No venules were found between arterioles in the rete mirabile areas. In order to know if these retia mirabilia have some function in retinal oxygenation, partially clamping of common carotid arteries was performed and hypoxia was detected in the retina using the Hyposiprobe-1 Kit. Interestingly, rete mirabile areas were less hypoxic than conventional capillary areas.

Conclusion There are retia mirabilia in mouse retina and these vascular structures could be important in retinal oxygenation.

• 4455

Optic disc coloboma in the mouse

JACKSON I

ABSTRACT NOT PROVIDED

• 4471

Tear film topography

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Purpose Patient complaints such as blurry vision are a very common symptom of dry eye syndrome. We will summarize technologies to measure the optical effects of tear film instability.

Methods There are several noninvasive techniques for assessing the kinetics of tear film : high-speed videokeratoscopy, dynamic wavefront sensing and lateral shearing interferometry. Interferometry or break up time are sensitive techniques for recording tear film surface irregularities in a noninvasive manner.

Results However, in order to understand the visual complaints associated with tear film instability, we need some dynamic visualization of the corneal tear film quality. Shack-Hartmann wavefront sensor and wavefront aberration could realize an objective evaluation of optical quality of the eye between blinks. We will discuss the use of higher-order aberrations fluctuations during 10 seconds. At last, we will try to quantify the visual impact of dry eye using objective scattering index.

Conclusion Dynamic aberration maps may be used for diagnosis of dry eye and for monitoring drops efficiency.

• 4472

Measurements of the dynamic aberrations induced by the tear film

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The static higher-order aberrations of the eye are easily measured with most commercially available wavefront aberrometers.However it has been only recently that the dynamic wavefront aberrations induced by the tear film (which plays a crucial role in the quality of vision)have been measured.In this presentation we will focus on the use of double pass wavefront aberrometry OQAS™ (Optical Quality Analysis System) for measuring vision quality disturbances caused by anabnormal tear film, in various clinical situations.

• 4473

Straylight as measure for quality of vision and the tear film

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Purpose In this presentation an overview will be given on the basic optical effects connected with the tear film. A prominent role of the tear film is to create a smooth surface for the most powerful refractive interface of the eye, i.e. the air-cornea interface. On the other hand, the tear film itself can disturb proper imaging if light is scattered in it, or if its surface is not perfectly smooth.

Methods Surface effects on optical image formation can be described with aberrometry. Only, in the case of the epithelial surface, present aberrometers do not have sufficient resolution to describe the fine irregularities. The group of Thibos designed a way to address this problem using the shape of the spot images of the Shack-Hartmann aberrometer. Effects of light scattering can be assessed using straylight measurement (implemented in the C-Quant from Oculus).

Results Both aberrometric and straylight outcomes combine to form the ocular point-spread-function defining the functional problem originating from optical defects in the tear film. The aberrometric errors dominate the central part of the PSF, and thus visual acuity. Straylight corresponds to the peripheral part of the PSF, and dominates in complaints like glare and hazy vision. Literature models for both aspects of the optical problems in the eye media were used to delineate their effects on the PSF.

Conclusion Two domains must be differentiated: the aberration domain and the small particle scatter domain, with corresponding parts (small angle vs large angle) to the PSF. Straylight typically originates ffrom small particles, as opposed to aberrations originating from refractile humps and bumps extending over large distances (tear film surface) or small small distances (epithelial surface).

Commercial interest

• 4474

The implications of the Meibomian glands dysfunction in the quality of vision

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ABSTRACT NOT PROVIDED

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Posters

• 201

Optic vesicle-like neurospheres derived from the H9 and H1 human ES cell lines

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Purpose To compare cell fate and differentiation potential of retinal cultures derived from two commonly used human embryonic stem cell (hESC) lines over time.

Methods H1 and H9 hESC lines of similar passage were differentiated toward a retinal lineage using a previously published protocol. Highly enriched populations of optic vesicle (OV) stage retinal progenitors from each line were manually separated and allowed to differentiate for up to an additional 120 days. The sequence and timing of expression of markers indicative of retinal development were determined via RT-PCR and immunocytochemistry.

Results A greater number of OV-like neurospheres were obtained from H1 hESCs than H9 hESCs at day 20 of differentiation. By contrast, the appearance of pigmented RPE within OV-like neurospheres occurred earlier and more frequently in H9 cultures. However, beginning at approximately day 50 of differentiation and throughout the remainder of the study, a similar pattern of neuroretinal marker expression was observed between both hESC lines. More specifically, markers of ganglion cell differentiation were observed initially, followed by the appearance of photoreceptor and retinal interneuron markers.

Conclusion RPE and neuroretinal cell types can be obtained from differentiating H1 and H9 hESCs in a sequence reminiscent of normal human retinal development. However, differences were seen in the proclivity of these lines to produce multipotent retinal progenitors and RPE, as well as the timing of differentiation of certain retinal cell types. Therefore, caution should be used when directly comparing results obtained from different hESC lines.

• 202

Transduction of mesenchymal stem cells with an ecdysone inductible lentiviral vector expressing luciferase gene

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Purpose Several studies, using limbal stem cells or mesenchymal stem cells (MCSs), have confirmed the usefulness of these cells to repair epithelial and stromalcorneal tissue. However the reparation process might be hampered by a strong inflammatory reaction inducing non-physiologic remodelling of healing tissue. The use of genetically modified cells with inducible gene to control the stromal reaction might offer an opportunity to improve new treatments in ophthalmology.

Methods We aimed at transducing MSCs with an Ecdysone inducible lentivirus. To the end, we generated a conditional expression vector, expressing the luciferase under an ecdysone expression system. We have transduced MSCs and evaluated their ability to synthetize on « demand » the luciferase. Following validation of the process in cultured cells, the genetically modified cells will be evaluated in vivo, in rat.

Results Using an in vitro recombination system, we generated a lentiviral vector containing the luciferase as transgene, placed under an Ecdysone promoter (« E/Luc »). To obtain an effective control of the luciferase, we generated a second vector containing the RXR gene and VgEcR gene under a constitutive promoter (« V/R »). Viral recombinant vectors were produced through 293T cells. MSCs were first transduced by the « V/R » vectors followed by the "E/Luc" lentiviruses. Finally, we have tested the responsiveness of the Ecdysone system in MSCs by adding Ponasterone and enzymatic activity of the Luc gene.

Conclusion We predict that it could be applied to follow in vivo MSCs after their corneal engraftment. Upon validation of the system, the use of inducible gene expression could be applied to pathological wound-healing.

• 203

Viral vectors for gene transfer into corneal endothelial cells

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Purpose Corneal endothelium is an ideal target fot gene therapy approached thanks to its anatomical location at the posterior surface of the cornea and its monolayer character. Lentiviral vectors have been shown by our group to be suitable vectors for the transfer of DNA into corneal endothelial cells (EC). Searching for an alternative to these HIV-based vectors, aim of this study was to determine the suitability of non-pathogenic adeno-associated viral vectors (AAV) for gene transfer to EC.

Methods Flowcytometric comparison of protein expression after transduction of EC using a lentiviral vector or AAV 2/2 with GFP in murine EC (Balb/C) and in human EC (cell line and primary cells). Proof of principle experiment to demonstrate the functionality of lentiviral gene transfer of the anti-apoptotic proteins Bcl-xL.

Results Kinetics of the protein expression after transduction of EC using lentiviral vector are considerably different compared to gene transfer using AAV. Contrary to AAV overexpression of the reporter protein after lentiviral gene transfer occurs very rapid. Moreover, we detected significant differences in transduction rates between human and murine EC lines as well as betweeen human EC lines and human corneas.

Conclusion AAV vectors seem to be an alternative to lentiviral vectors for gene tranfer to EC. Considering the storage of human donor corneas in eye banks in organ culture over four weeks, translation of AAV from bech to bedside, e.g. to reduce apoptosis in corneas, seems to be feasible.

• 204

Evaluation of human retinal pigment epithelial cells growth on elastin-like recombinamer substrates

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Purpose In our previous published data (J Biomed Mater Res A. 2011) it was shown that ARPE19 cells were growing well and maintaining certain characteristics of RPE cells on the Elastin-like recombinamers (ELR-IK, ELR-RGD). The purpose of this study is to evaluate the growth pattern of primary human RPE (hRPE) cells over these ELRs for possibility to start in-vivo study as a possible treatment for AMD.

Methods hRPE cells were seeded on sterilized control surfaces (polystyrene, glass) as well as on ELR films that were obtained by solvent casting onto glass and subsequent cross-linking containing a bioactive sequence, RGD (ELR-RGD) and, without any specific sequence, as control (ELR-IK). Cells were analyzed to study cell adhesion, proliferation, morphology and specific RPE antigen (RPE65) expression by staining with DAPI, Rhodamin-phalloidin and antiRPE65 antibody at 12, 24, 72, 120, 168 and 360 hours.

Results hRPE cells seeded on ELR-films as well as controls were proliferating; maintaining their similar morphology and expression of RPE65 antigen at different time points studied. Cells on ELR-RGD were growing better than that on ELR-IK and glass but lesser than that on polystyrene. The growth rate of hRPE cells over polystyrene and ELR-RGD surfaces was increasing with time intervals than glass and ELR-IK surfaces. There was a very clear difference of hRPE cells growth rate on different surfaces at 360 hours.

Conclusion ELR-RGD was good substrate for hRPE cells growth and that maintained the similar morphology and RPE65 antigen expression as seen on control surfaces. These results require further in vitro and in vivo studies with hRPE cells to determine if ELR-RGD could be useful as a vehicle for transplantation of hRPE cells in patients with AMD.

• 205

Trypan blue staining method for quenching the autofluorescence of RPE cells for improving protein expression analysis

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Purpose The purpose of this study is to develop and validate Flow Cytometry (FC) and Immunohistochemistry (IHC) methods for rapid and accurate measurements of cell proteins corresponding specific fluorescence signals above background noise using Trypan blue (TB) for quenching the autofluorescence (AF) emitted by Retinal pigment epithelial (RPE) and Ciliary body stem (CBSC)cells.

Methods RPE and CBSC cells were isolated, cultured and trypsinized using already published methods. AntiRPE65 immunolabelled cells were post treated with 10, 20 and 40 µg/ml TB at 4C for 10 min for FC analysis. 3-5 mm small pieces of retinal tissue were pre treated with 20, 200 and 2000 µg/ml of TB at room temperature for 15 min, followed by embedding in paraffin wax, cutting into 3 µm thick retinal tissue sections (RTSs), dewaxing, anti RPE65 immunolabelling and observing under a microscope. Immunolabelling with isotype-matched unspecific Abs, primary and secondary antibody were used as controls. Cytomicx RXP and Adope photoshop were used for FC and IHC results analysis.

Results FC and IHC results showed that post-treatment of immunolabelled RPE cells and pre-treatment of retinal tissue pieces with 20 µg/ml of TB reduce the AF and facilitate to detect the fluorescence signals corresponding to specific cell proteins with higher mean fluorescence intensity (MFI).

Conclusion We concluded: 1.-Incubation of cells and tissues with 20 µg/ml of TB reduces AF. 2.-For FC analysis, the cells should be post-treated with TB and for IHC analysis, the tissues should be pre-treated with TB. 3.-The methods significantly increase the quality and value of cell protein analysis performed by FC and IHC techniques.

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AICAR induces autophagy in ARPE-19 cells

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Purpose The pathogenesis of age-related macular degeneration involves impaired protein degradation in retinal pigment epithelial (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 the present study, the effects of AICAR (AICA ribonucleotide, 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside) and MG-132 (proteasome inhibitor) on autophagy regulation in ARPE-19 cells were evaluated.

Methods The AMP activated protein kinase (AMPK), p62 and ubiquitin protein levels were analyzed by western blotting. pDendra2-hLC3 construct was used to detect macroautophagy in confocal microscopy analysis. Transmission electron microscopy was used to detect protein aggregates and autophagosomes. Cellular permeability was measured by analyzing lactate dehydrogenase levels in culture medium.

Results MG-132 (5 microM) triggered the accumulation of perinuclear aggregates that strongly colocalized with p62 and ubiquitin. AICAR (2mM) induced autophagy clearance of p62 and ubiquitin positive protein aggregates without increasing cellular permeability. Cellular energy status regulator AMPK or p-AMPK levels were not significantly changed in response to AICAR treatment.

Conclusion Our findings open new avenues for understanding the mechanisms of proteolytic processes and indicate that AICAR could be useful in the acceleration of protein clearance in RPE cells.

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Aging and BDNF-deficiency upregulates heat shock protein expression in mouse retina

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Purpose To examine heat shock protein (HSP) expression in retinas of mice that lack brain derived neurotrophic factor (BDNF+/-) and their wild type littermates (WT) at young and old age.

Methods Eyes from 2- and 22-months old WT and BDNF+/- mice (The Jackson Laboratory, Bar Harbor, ME, USA) were used. HSP 27 kDa (HSP27), 60 kDa (HSP60) and 70 kDa (HSP70) protein levels in retina were determined by Western blotting. Paraffin-embedded retinal sections were immunostained for HSPs to determine their localisation and abundance in various retinal layers.

Results Western blot analysis of the whole retina showed a 2-fold increase in HSP27 and HSP60, and a 1.5-fold increase in HSP70 in aged WT mice as compared to young mice. The lack of BDNF significantly upregulated HSPs expression in retina. Thus, young BDNF+/- mice had similar expression levels of HSPs in retina as in old WT mice, whereas a further increase in HSPs expression was observed in aged BDNF+/- mice as compared to young BDNF+/- mice.

Conclusion Aging is associated with an increased expression of HSPs in the mouse retina. The lack of BDNF induces similar expression of stress-related proteins in retina already at young age as it is seen at old age under normal BDNF levels.

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BDNF-deficiency upregulates SIRT2 expression but does not affect cellular metabolism in mouse retina

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Purpose Brain derived neurotrophic factor (BDNF) is essential for cell development, function and survival. Mammalian sirtuins (SIRT) are deacetylase enzymes that are known to play an important role in longevity. In the present study we aimed to compare SIRT1 and SIRT2 expression in retinas of mice that lack brain derived neurotrophic factor (BDNF+/-) and their wild type littermates (WT) at young age in relation to cellular metabolism.

Methods Eyes from 2-months old WT and BDNF+/- mice (The Jackson Laboratory, Bar Harbor, ME, USA) were used. SIRT1 and SIRT2 protein levels in retina were determined by Western blotting. Paraffin-embedded retinal sections were immunostained for SIRT1 and SIRT2 to determine their localisation and abundance in various retinal layers. Metabolic state of mouse retinal cells was assessed by measuring NAD+, NADH and total NAD levels using resazurin-based assay.

Results Western blot analysis of the whole retina showed that SIRT1 expression is similar in WT and BDNF+/- mice. However, there was a significant upregulation of SIRT2 protein level in BDNF+/- mice compared to WT littermates. Assessment of NAD+, NADH and total NAD levels showed similar cellular metabolic state in retinas of WT and BDNF+/- mice.

Conclusion Our results indicate increased tubulin deacetylation in retinas of BDNF+/- mice, which is independent from cellular energy metabolism.

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Interleukin-10 promotes macrophage infiltration in mouse retina

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Purpose Inflammation, specifically macrophage infiltration, is known to promote a number of pathologic processes including eye neovascularization. In the current study, we explored the macrophage retinal infiltration in a mouse model that over-expressed interleukin-10 (IL-10) in the retina.

Methods A transgenic mouse model in C57BL6 background that overexpress IL-10 under the control of the glial fibrillar acidic protein (GFAP) promoter was analysed. Retinas from transgenic and their wild type (wt) littermates were studied by immunohistochemistry.

Results The IL-10 transgenic mice (tg-IL10) expressed higher levels of IL-10 in the retina compared to wild type mice. Histologically, when compared to wt, the cytoarchitecture of the transgenic retinas did not show any differences. The only morphological alteration observed was a CD11b+ macrophage infiltration in the retina and the irido-corneal angle of tg-IL10. These macrophages were fully loaded with melanin. Our observations show that the number of macrophages in tg-IL10 retinas was approximately ten fold superior than in wt. Interestingly, the 80% of macrophages in tg-IL10 retinas were localized along blood vessels. This finding supports previous work in other paradigmas reporting infiltrated macrophages located along blood vessels, which may be involved in the modulation of blood vessel growth and regression.

Conclusion A significant increase in the number of macrophages aligning along blood vessels has been observed in the retina of a transgenic model that produces IL-10 under the control of GFAP promoter. This preliminary result suggests that IL-10 promotes macrophage perivascular infiltration in mouse retina.

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Effect of autocrine vascular endothelial growth factor on the survival of retinal Müller cells under oxidative stress

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Purpose Autocrine vascular endothelial growth factor (VEGF-A) is a known survival factor for the developing and mature retina, stimulating both endothelial and neural cells. We examined whether survival of Müller cells under oxidative stress was related to stress-induced VEGF-A synthesis.

Methods Rat Müller cells were treated with hydrogen peroxide, and cell survivals were analyzed with a flow cytometry with annexin V-fluorescein isothiocynate and LDH assay. The expression of VEGF-A, VEGF-R1, and VEGF-R2 was determined by semiquantitative RT-PCR or Western blot analysis.

Results Hydrogen peroxide–induced cell death was increased with dose dependent manners. Treatment of hydrogen peroxide on rat Müller cells induced the expression of VEGF-A, VEGF-R1, and VEGF-R2 with dose dependent manners.

Conclusion In the present study, survival of Müller cells under oxidative stress was related to stress-induced VEGF-A synthesis. Further study is needed to reveal the protective role of VEGF-A on retinal Müller cells.

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Role of toll-like receptor 2 and 4 of keratocytes on corneal innate immunity

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Purpose To investigate the role of keratocytes in corneal innate immune system and cross-talk of keratocytes with resident antigen presenting cells (APCs), especially through toll-like receptor (TLR)2 and TLR4.

Methods Firstly, primary cultivated C57BL/6 (B6) mouse keratocytes were stimulated by Pam3CSK4 (TLR2 agonist) or lipopolysaccharide (LPS; TLR4 agonist) and then were evaluated for their cytokine secretion. To demonstrate the cross-talk between B6 keratocytes and APCs, cytokine changes under Pam3CSK4 or LPS challenge were assessed in co-culture condition of B6 keratocytes with mouse dendritic cell line (DC 2.4) or mouse macrophage cell line (Raw 264.7). The reversal effect was checked out using keratocytes from TLR2 knockout (KO) or TLR4KO mice.

Results Primary cultivated keratocytes from B6 mice per se actively secreted pro-inflammatory cytokines, especially interleukin (IL)-6, with a dose-dependent manner in response to Pam3CSK4 or LPS challenge. With co-culture of keratocytes with APCs, secretion of IL-6 and tumor necrosis factor (TNF)-α was markedly increased and it was counterbalanced by concurrent increase in IL-10 and tumor growth factor (TGF)-β1. After Pam3CSK4 or LPS stimulation, this cytokine balance was completely broken down by overwhelming amplification of IL-6 and TNF-α secretion, especially in co-culture of keratocytes with macrophages, rather than with dendritic cells. Using keratocytes from TLR2KO or TLR4KO mice, we could find the reversal of Pam3CSK4 or LPS-responsive dose-dependent increment pattern in IL-6 and TNF-α.

Conclusion These results implied that keratocytes and their TLRs could be key components for the ocular homeostasis and pathogen-associated ocular innate immunity.

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The effects of thermal sources emitted infrared radiation (IR) on rabbit corneal and crystalline lens extracellular molecules and the influence of cyclooxygenase (COX) inhibition

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Purpose To investigate the effect of acute and chronic exposure to IR on rabbit corneal and lens metalloproteinase-2 (MMP-2), MMP-9 and glycosaminoglycans (GAGs) and the influence of COX inhibition.

Methods Fourteen (14) New Zealand rabbits were used totally. Chronic exposure to IR included 4 month irradiation of 3 rabbits, whereas 3 animals were the control group. Regarding acute exposure, 8 rabbits were used, diclofenac sodium eye drops 0.1% were instilled in their right eyes and 4 of them were irradiated for 12 hours. By comparing the left irradiated with the left non-irradiated eyes, the effect of IR exposure was investigated. COX inhibition role with and without IR exposure was determined, by comparing the left with the right eyes of the irradiated and the non-irradiated rabbits separately.The cornea and lens were extracted, followed by gelatin zymography to determine MMP-2 and MMP-9 activity, GAGs isolation, measurement of uronic acids and electrophoresis on cellulose acetate membranes for GAGs analysis.

Results Chronic IR exposure induced the activity of corneal and lens pro-MMP-2 activity but did not affect GAGs. Acute exposure increased corneal and lens pro-MMP-2 activity and lens heparan sulfate amount, whereas the use of diclofenac sodium was unable to influence these effects.

Conclusion Corneal and lens acute and chronic IR exposure induced the activity of pro-MMP-2. Acute exposure, also, increased lens heparan sulfate amount.

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Differential effects of irradiation with X-rays and carbon ions on normal and tumoral uveal melanocytes

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Purpose The local treatment of uveal melanoma (UM) proposed is in the majority of the cases the protontherapy or the radiotherapy of contact by patches. However, these treatment ends in blindness in 60 % of the cases. Indeed, the hadrons which are proton and carbon ion possess a Transfer of Linear Energy (LET) higher than the conventional radiotherapy (X-rays and γ). Our previous findings highlight the key role of the WTB-Raf/MEK/ERK pathway in the control of proliferation of UM cells. Our project investigate the positive and negative effects of the irradiation on the UM and healthy uveal melanocytes. It thus seems interesting to analyze the effects of the irradiation on ERK1/2 activation and the link between these pathways with the cell cycle.

Methods We characterize the radiosensibilities, after irradiation by X-rays and carbon ion, of six UM cell llines (92.1, Mel 270, SP6.5, MKT-Br, µ2 and TP17) and two types of healthy cells: the human uveal melanocytes (NUM) and the epithelial cells of the human retina (ARPE19).

Results We showed that carbon ion present with regard to the X-rays a relative biological effectiveness (RBE) of 1.86 to 2.46 at 10% survival. We showed that the irradiations X and carbon had the same effects by provoking a stop of the cellular cycle in phase G2 / M until 120 hours. According to the type of irradiation, two mechanisms are observed on the ERK1/2 signaling pathway. X-ray induced a transitory suractivation of ERK1/2. Whereas, ERK1/2 activation was constantly inhibited by carbon beam

Conclusion These preliminary results show that the carbon beam present a better biological efficiency than X-rays in uveal melanoma cells leading a sustain inhibition of ERK1/2 pathway.

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Effect of fixation and embedding methods on collagen fibril diameter and spacing

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Purpose The corneal tissue are usually fixed in fixatives and embedded in resin for ultrastructural studies. Here we study the effect of these fixatives and resins on the collagen fibril (CF) diameter and the spacing between the fibrils.

Methods Four normal human post-mortem corneal buttons of 24, 25, 54 and 75 year old individuals were used. A part of each cornea was fixed in paraformaldehyde (4%) and embedded in LR White at 4°C under UV light for 24hrs. A second part of each cornea was fixed in glutaraldehyde (2.5%) + osmium tetroxide. The third part of each cornea was fixed in 2.5% glutaraldehyde containing cuprolinic blue in sodium acetate buffer for ultrastructural studies. The tissues were embedded in spurr resin at 70°C for 12 hrs. Ultra-thin sections were stained with uranyle acetate and lead citrate.

Results In the tissue, fixed paraformaldehyde (4%) and embedded in LR White at 4°C under UV light for 24hrs, the CF diameter was 24± 2.3nm and spacing between CF was 40.0±4.2nm.In the tissue fixed in glutaraldehyde (2.5%) + osmium tetroxide, and embedded in spurr resin, the diameter was 28.37 ± 5.84nm and spacing between CF was 45 ±4.57nm.In the tissue, fixed in 2.5% glutaraldehyde containing cuprolinic blue in sodium acetate buffer and embedded in spurr resin, the diameter was 38.6 ± 4.0nm and spacing between CF was 52.5 ±5.3nm.

Conclusion Our study shows that there is a variation in the collagen fibril diameter and spacing depending on the method of fixation and embedding resins. This needs to be considered when comparative studies employing different methods.

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Ultrastructural organisation of stingray and shark corneal stroma

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Purpose Collagen fibrils and proteoglycans are the main components of the corneal stroma. We report here ultrastructural organisation of collagen fibrils and proteoglycans of corneal stroma in stingray and shark.

Methods Four corneas of stingray and shark were fixed in 2.5% glutaraldehyde containing cuprolinic blue in sodium acetate buffer and processed for electron microscopy. Tissues were embedded in TAAB 031 resin. Measurements were carried out by using the 'AnalySIS LS Professional program'

Results The corneal stroma of shark is thicker (336µm) compared to stingray stroma (143µm). The corneal stroma in both fish consists of parallel running lamellae containing collagen fibrils and proteoglycans. The lamellae in sharks are thicker in the anterior stroma (12.14µm), middle stroma (18.3µm) and posterior stroma (13.0µm) compared to stingray lamellae in anterior stroma (7.6µm), middle stroma (8.9µm) and posterior stroma (5.2µm). In both fish lamellae of middle stroma was thicker compared to anterior and posterior stroma. In both fish, lamellae were obliquely crossed by bundles of collagen fibrils, which are known as sutures. Proteoglycans are larger in stingray compared to shark.

Conclusion The presence of sutures is the unique feature of these fish. It has been reported that these sutures inhibit the swelling of the cornea in sharks.

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Use of imaging techniques to reveal connectivity within the human fovea and to predict consequences of lesions

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Purpose A knowledge of connectivity from the central photoreceptors and their axons, via the bipolar cells to the retinal ganglion cells (RGC), is required to understand the consequences of lesions in different locations of the human fovea. The purpose was to create a model of the connectivity within the fovea based on information available in recent non-invasive studies of the normal fovea with optical coherence tomography (OCT) and adaptive optics (AO).

Methods OCT data from the study by Lujan et al. (2011) of the thickness of the Henle fiber layer (HFL) at various eccentricities was used in combination with data of cone density and visual resolution obtained from AO studies. An angle of 6 degrees was assumed between the cone axons and the external limiting membrane, at eccentricities between 0.2 and 1 mm, to calculate the lateral displacement from the cone photoreceptor cell body to the cone pedicle. Cone density and visual resolution was obtained from published AO studies (Wolfing et al., 2006; Rossi & Roorda, 2010).

Results The thickness (HFLt) versus eccentricity along the horizontal meridian was derived from Lujan et al. (2011) and used to calculate the lateral displacement of cone pedicles. Zones in the cone pedicle layer and RGC layer connected to corresponding regions of the cone mosaic (0-0.2 mm, 0.2-0.4 mm, 0.4-0.6 mm) were calculated and related to AO estimates of visual resolution.

Conclusion Our model may be useful to visualize functional connectivity and to predict the effect of lesions within the fovea. A maximal effect of lesions in the bipolar and RGC layers, due to the displacement caused by the cone axons, may be anticipated at an eccentricity of about 0.5 mm or 2 degrees.

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Outcome of trabeculectomy in uveitis patients with secondary glaucoma

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Purpose To review the clinical outcome of our series of patients with uveitis and secondary glaucoma in which a trabeculectomy has been performed.

Methods Each patient was classified according to clinical presentation, pre and postoperative IOP, visual acuity and number of antiglaucoma drops needed. The outcome of trabeculectomy was classified in 3 categories: absolute success defined as IOP controlled (< 21 mmHg) without other treatment, relative success defined as IOP controlled with hypotensive drops and failed when IOP was not controlled or required hypotensive drops and oral acetazolamide. Success ratio with and without perioperative mitomycin were compared.

Results Mean visual acuity, IOP and number of drop used decreased at 3 month and at last follow-up. The mean follow-up was 19.3 months (2.9 – 67.1 months). At 3 month, we found 80% of overall success (53,33% of relative success and 26,67% of absolute success) and 20% of failure. At final follow-up, we also found 80% of overall success(56,67% of relative success and 23,33% of absolute success) and 20% of failure. Patients in whom perioperative mitomycin were used where more likely to have a favorable outcome (last follow-up: 83.33% vs 75%) but this difference between the two groups was not statistically significant.

Conclusion Our data are in accordance with the rest of the literature which shows that trabeculectomy with antimetabolite agents allows IOP control in the majority of patients. However, many of them will still need topical hypotensive drugs.

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Optic disc assessment using confocal scanning laser ophthalmoscope in normal tension glaucoma with disc hemorrhage

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Purpose To evaluate which optic disc parameters have a relationship with the presence and the location of disc hemorrhages in normal tension glaucoma (NTG)

Methods This retrospective study included patients with early NTG with mean deviation with – 10 dB or better in 24-2 Humphrey visual field analyzer. Eyes in the whole study group were divided into those with and without disc hemorrhage. Optic disc stereometric parameters measured using the Heidelberg Retina Tomograph (HRT) III were compared between each group with and without disc hemorrhage. Within the group with disc hemorrhage, the location of disc hemorrhage was analyzed. Sectoral disc parameters were compared between two common locations where disc hemorrhage developed.

Results Forty-three patients with disc hemorrhage and 46 patients without disc hemorrhage were included in this study. Mean deviation and pattern standard deviation showed no significant difference between two groups. There was no significant difference in global optic disc parameters of HRT between two groups. Disc hemorrhage was displayed mainly in inferotemporal (23 eyes, 53.5%) and in superotemporal (12 eyes, 27.9 %). Regarding to sectoral disc analysis of inferotemporal quadrant, the value of cup shape measure and cup disc area ratio was higher in the disc hemorrhage group compared to the group without disc hemorrhage (P=0.0013, P=0.013, repectively). The subset analysis of disc parameters within the disc hemorrhage group, showed that superotemporal maximum cup depth in eyes with superotemporal disc hemorrhage was greater compared to inferotemporal maximum cup depth in eyes with inferotemporal disc hemorrhage (P=0.017).

Conclusion The change of optic disc parameters in early NTG patients with disc hemorrha

Commercial interest

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GDx-VCC vs GDx-ECC in glaucoma diagnosis

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Purpose To compare results provided by scanning laser polarimetry variable corneal compensation (VCC) vs enhanced corneal compensation (ECC) and evaluate correlation to visual field results in glaucoma patients.

Methods Study included 339 eyes of 182 patients screened by the glaucoma unit of the University Eye Clinic of Pavia (Italy). Patients were submitted to complete ophthalmic examination, standard automated perimetry (SAP), scanning laser polarimetry with GDx-VCC and GDx-ECC. Quality image (Q), typical scan score (TSS), nerve fibers index (NFI), nerve fibers layer average thickness in a band around the optic nerve head (TSNIT average) and in the upper (TSNIT sup) and lower sector (TSNIT inf) were evaluated for each exam. Q, TSS and morphometric parameters provided by VCC and ECC were compared using Wilcoxon signed-rank test and Lin correlation coefficient. Correlation between GDx and perimetric global indexes and was evaluated with Pearson correlation index "r".

Results 204 images out of 339 (60%) were of good quality (Q>7) with VCC and 325 out of 339 (96%) with ECC. 140 images out of 339 (41%) were atypical (TSS<80) with VCC but only 20 out of 339 with ECC (6%). ECC vs VCC constantly displays lower TSNIT thickness and higher NFI. All comparisons between ECC and VCC parameters showed statistically significant differences confirmed by a moderate to poor concordance between the two instruments.Structure/function correlation was better for ECC parameters and first of all for NFI.

Conclusion ECC provides better quality images than VCC. High quality exam is the first condition to reproduce a more reliable RNFL structure. ECC points out lower RNFL thickness and higher NFI and reveal a better correlation to perimetric indexes MD and PSD as compared to VCC. GDx-ECC could improve early glaucoma diagnosis.

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Anterior segment optical coherence tomography changes post laser peripheral iridotomy in primary angle closure suspects in an Asian population

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Purpose Multiple modalities have been used to image the anterior chamber angle. We quantified changes in novel parameters associated with angle closure, namely anterior chamber area (ACA) and volume (ACV); anterior chamber width (ACW); lens vault (LV) and iris thickness, area and curvature using ASOCT, in a cohort of primary angle closure suspects (PACS) after laser peripheral iridotomy (LPI).

Methods A prospective study of primary angle closure suspects > 50 years of age after LPI. ASOCT images (Visante, Carl Zeiss Meditec, Dublin, CA) from 176 subjects were analyzed quantitatively using customized software, before and 1 week after LPI.

Results The mean age of the 176 participants was 63.0 ± 7.3 year and majority of the subjects were Chinese (95.5%) and women (76.7%). After LPI, the angle width opened significantly with increase in mean angle opening distance [AOD 500, 0.11 vs. 0.18 mm, p< 0.001), trabecular iris surface area (TISA500, 0.06 vs. 0.08 mm^2, p< 0.001) and angle recess area (ARA, 0.12 vs. 0.17 mm^2, p< 0.001). Mean ACA (14.9 vs. 16.0 mm^2, p< 0.001) and ACV (91.6 vs. 103.0 mm^3, p< 0.001) increased significantly after LPI, but there was no change in ACW (11.21 vs. 11.24 mm, p = 0.3), anterior chamber depth (2.16 vs. 2.17 mm, p = 0.16) or LV (783.6 vs. 788.6µm, p = 0.72). Mean iris curvature was reduced (0.375 vs. 0.180 mm, p< 0.001) after LPI, but there was no significant change in iris thickness or area.

Conclusion LPI results in a significant increase in the angle width in subjects with narrow angles. ACA and ACV increased after LPI but there was no change in ACD, ACW, LV or iris thickness and area. The increase in ACA/ACV is attributed to be due to decreased iris curvature after LPI.

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Evaluation of the efficacy of patterned laser trabeculoplasty: pilot study

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Purpose To evaluate the efficacy of Pascal Laser Trabeculoplasty (PLT) employing reduced energy levels in patients with OHT or POAG.

Methods Prospective, pilot study including 12 patients with OHT or POAG. Pascal laser trabeculoplasty was performed on the inferior 180° of the treated eye after titrating the energy for each patient. The IOP was measured with Goldmann applanation tonometer (GAT) on laser treatment day (D0), 1 week post laser (D7) and 1 month post laser (D30). Anova for repeated measurements was used for the statistical analysis.

Results The mean IOP on D0 was 25.2 ± 1.4 mmHg (range: 22 to 28.4 mmHg), mean IOP on D7 was 23.1 ± 1.5 mmHg (range: 19.8 to 26.4 mmHg) and mean IOP on D30 was 20.6 ± 1.1 mmHg (range: 18 to 23.1 mmHg). There was no significant difference between the D0 IOP and D7 IOP (p= 0.43) but between D0 IOP and D30 IOP (p= 0.001)

Conclusion Patterned laser trabeculoplasty causes significant IOP decrease after 1 month. In this pilot study The IOP drops by 20% after 1 month.

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Nurse-led glaucoma clinics - the pros and cons

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Purpose Addressing the need for increased capacity in glaucoma follow-up clinics by delegating resposibility to a trained nurse practitioner.A specialist hospital-based study.

Methods A senior nurse practitioner (NP) was trained by a glaucoma specialist in the management of glaucoma follow-ups. Once training was completed, glaucoma cases were transferred to NP-led clinic for follow-up alongside consultant clinic. Certain criteria had to be met for inclusion in NP clinic:1.Good compliance and control on topical treatment+/-laser 2.Stability of visual fields over previous 3 years 3.No post-surgical cases4.No complex cases or co-morbidities

Results 200 follow-up cases were accomodated in NP clinic over a period of 3 years, thus adding capacity to an increasingly overburdened service.There were no cases lost to follow-up, a non-attendance rate of 2% and no cases had a progression of visual fields MD>0.75dB/year. The most frequent reasons for seeking advise of the specialist were the need to change treatment regime due to increasing IOP (10%),or poor comliance/tolerability to treatment (10%).

Conclusion 1.NP-led clinics add capacity without compromising on standard of care 2.NP skills and confidence improved with regular practice 3.Patients' experience was excellent 4.Capacity was freed up in consultant clinic to see more complex cases in a timely manner 5.Training does take a long time 6.In order to run smoothly and safely the NP-led clinic had to be alongside the consultant clinic 7.There is a limit to the number of cases that can be seen in NP clinic without compromising on quality of care.

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Usefulness of dynamic gonioscopy during systematic survey of glaucoma patient in a university hospital

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Purpose A narrow iridocorneal angle (ICA) is a risk factor for glaucoma progression. However, many patients treated for primary open angle glaucoma (POAG) have never been assessed with dynamic gonioscopy. In this study, we performed dynamic gonioscopy in patients referred for progressing POAG and suspicion of glaucoma (GS) to evaluate the rate of misdiagnosed narrow ICA.

Methods We retrospectively analysed the clinical data of consecutive glaucoma or GS patients referred for evaluation from November 2009 to October 2010. All patients had been previously diagnosed with open ICA. Patients were examined by a single ophthalmologist. The evaluation included detailed medical history, comprehensive ophthalmologic examination, diurnal hourly monitoring of the intraocular pressure, static automated perimetry, retinal nerve fiber layer thickness analysis, central pachymetry and dynamic gonioscopy (Possner® lens).

Results 135 patients were included. The mean age was 53.6 years (+/- 6.2 years). Prior to our evaluation, glaucoma and GS patients had been followed 5.2 years (+/- 3.4 years) with an average of 4.2 visits and 2.2 visual fields. 58 patients (43%) had never undergone gonioscopy. A narrow angle was diagnosed in 18 patients (13.3%), including 5 patients with plateau-iris configuration confirmed by ultrasonic biomicroscopy (27.7% of narrow angles).

Conclusion A narrow ICA is not a rare finding among patients diagnosed with POAG or GS patients. Dynamic gonioscopy should be performed systematically for all glaucoma and glaucoma suspect patients, especially in cases of glaucoma progression despite an efficient and well conducted treatment. Lens size evolution with time requires repeated evaluations.

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The role of Mas receptors in an experimental rat glaucoma model

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Purpose To evaluate the neuroprotective and/or oculohypotensive effects of potent angiotensin system agents known to reduce intraocular pressure in the normotensive rabbits by using an experimental laser-induced glaucoma model in rat eye.

Methods Experimental glaucoma was induced unilaterally using laser photocoagulation of the episcleral and limbal veins of male Wistar rats twice in one week intervals. The fellow eye was untreated, thus serving as a normotensive control. Mas receptor agonist angiotensin (1-7) and antagonist A-779 as well as their combination were injected intravitreally. IOP was measured by rebound tonometer during the follow-up time of two weeks. At the end of the study the animals were sacrified. The eyes and the optic nerves were collected. The neurodegenerative changes were evaluated from the optic nerves using a modified Gallyas silver-staining method.

Results Mean IOP in laser treated and untreated eyes were 27.4 mmHg and 10.5 mmHg during two weeks follow up time. A significant axonal destruction was detected in glaucomatous eyes vs fellow eye with normal IOP. Intravitreal administration of test compounds did not reduce IOP. However the group of rats that were treated with A-779 had significantly lower area of neurodegenerative axons in the optic nerves as compared to the other groups.

Conclusion In laser induced glaucoma model IOP elevates rapidly leading to severe destruction of ganglion cell axons like occurs in normally slowly developing neuropathy. In this model Mas receptor antagonist A-779 had an IOP-independent neuroprotective effect on retinal ganglion cells whereas Mas receptor stimulation did not reduce IOP and had no influence on axonal damage.

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Congenital glaucoma: from the diagnosis up to the surgery. About a case

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Purpose The surgical treatment is, at present, universally accepted as treatment of choice in the congenital primary glaucoma. However, sometimes at the time of diagnosis, the conditions of the eye disable to carry out the surgery in safety conditions.

Methods We present the case of a baby of 8 months, who was referred to our department for pain and corneous opaqueness of 48 hours of evolution. Exploration shows the presence of edematous cornea, with increase of the horizontal diameter (12 mm, opposite to 10 mm of the contralateral eye). With the possible diagnostic of congenital glaucoma, ultrasound scan was performed to confirm the increase in the axial length, and determination of the intraocular pressure(Perkins tonometry and Tono-Pen, under topical anesthesia), which confirmed numbers abnormally high (38 and 42 mmHg respectively).

Results Confirmed the diagnosis, and given the inability to carry out the goniotomy due to the corneal edema, began treatment with fixed combination dorzolamida/timolol 2 times a day for 5 days. The improvement of the corneous condition after the guideline of medical treatment, allowed the angular exploration and the surgery in safety conditions 7 days later.

Conclusion In the managing of the congenital glaucoma, given the special characteristics of the patient, in many cases is necessary to delay the surgery in time. It is important to perform a thorough ophthalmological and systemic exploration in newborn patients to optimize the conditions of the eye before the surgery, allowing that this one should carry out, and making it less difficult, as far as possible.

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Closed angle glaucoma and myopia as an adverse effect of topiramate

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Purpose To present a case report of a patient under topiramate treatment for a depression syndrome, with bilateral acute and closed angle glaucoma as drug adverse effects

Methods Thirty-seven-year-old male developed bilateral severe blurred vision. Exploration showed bilateral acute myopia and closed anterior chambers. Intraocular pressures were 48 mmHg in both eyes, with shallow anterior chambers, and closed angles. His refraction was -6.25 diopters in right eye, and -8,50 in left eye. During ophthalmic exploration he developed eye pain and corneal edema.

Results All symptoms and clinical findings, including myopia and pain, resolved completely upon discontinuation of topiramate and administration of antiglaucoma drugs.

Conclusion Topiramate may cause acute bilateral angle-closure glaucoma , so blurry vision, eye pain or altered image perception in treated subjects should be carefully explored by an ophthalmologist.Acute angle closure may result in important intraocular pressure elevation and irreversible optic nerve damage, causing permanent visual loss; so treatment must be withdrawn immediately when alarm symptoms appear.

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A phase 2, randomized study evaluating the safety and efficacy of Catioprost® (unpreserved latanoprost 0.005% emulsion) compared to Travatan Z® in subjects with glaucoma and ocular surface disease

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Purpose Ocular Surface Disease (OSD), recognized in 50% of glaucoma patients, can decrease anti-glaucoma therapy compliance. Benzalkonium chloride (BAK) has been shown to induce OSD. Catioprost® is an unpreserved latanoprost 0.005% cationic emulsion. The design of a study comparing the efficacy and safety of Catioprost® versus a BAK-free prostaglandin agonist, Travatan Z® (travoprost 0.004%) in patients with glaucoma and OSD is described.

Methods Patients with elevated IOP at baseline requiring treatment with ocular anti-hypertensive therapy were enrolled in this multicenter, phase II, investigator-masked, randomized study. Following a washout period, patients demonstrating OSD symptoms and signs (corneal fluorescein staining, CFS, score≥1 on the modified Oxford scale and a tear film break up time, TFBUT, ≤10) in at least one eye at the baseline visit were randomized to either Catioprost® or Travatan Z® QD with follow-up study evaluations at month 1 and 3.

Results 105 patients were randomized. Change in diurnal IOP, a change in the global symptoms (ocular discomfort, burning, dryness, grittiness, stinging) and objective signs (CFS, TFBUT, conjunctival hyperemia) of OSD at month 1 and 3 will be presented. Safety outcomes will also be reported.

Conclusion Preservative free prostaglandin agonists reduce the risk of ocular toxicity associated with BAK. However, their effect on restoring ocular surface damage is unclear. In this study, the efficacy and safety of an unpreserved latanoprost 0.005% cationic emulsion relative to BAK-free travoprost 0.004% solution on reducing IOP and improving the signs and symptoms of OSD will be revealed.

Commercial interest

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Relationship of intraocular pressure with risk factors of metabolic syndrome

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Purpose To evaluate the relationship of intraocular pressure with risk factors of metabolic syndrome in healthy Korean population

Methods A total of 30893 healthy participants underwent automated multi-phasic test including tonometry, fundus photography, body mass index measurement and metabolic syndrome risk variables such as systolic and diastolic blood pressure, total cholesterol, high density lipoprotein, triglyceride and fasting blood glucose. The subjects were divided into six age groups by decades ranging from 20 29 years to over 70 years. The relationship between IOP and metabolic syndrome risk variables was examined using multiple regression analysis.

Results The mean IOP was 15.5±3.2 mmHg, and was significantly higher in men than in women at 20-69 years aged groups($p<0.05$). IOP was associated with systolic and diastolic blood pressure, total cholesterol, triglyceride, body mass index and fasting blood glucose($p<0.05$). Systolic and diastolic blood pressure, total cholesterol, triglyceride and fasting blood glucose values had significantly positive relation with IOP ($p<0.05$), and high density lipoprotein had significantly negative relation. In analysis, intraocular pressure had significant relation with age, gender, systolic and diastolic blood pressure, total cholesterol, triglyceride and fasting blood glucose, but there was no significant relation with body mass index and high density lipoprotein($p>0.05$).

Conclusion As increased IOP was associated with metabolic syndrome risk variables, it is necessary to control increased total cholesterol, triglyceride, and blood glucose levels in the normal population to prevent or control the IOP elevation.

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Low pressure glaucoma: patients threatened of vision worsening and blindness

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Purpose To study the presence of systemic diseases in low pressure glaucoma (LPG) and primary open-angle glaucoma (OAG) patients, and the specific characteristics of functional and structural damages in those two types of glaucoma.

Methods all consecutive glaucoma patients diagnosed and treated for a period of 6 months (October 2010 – March 2011). They were evaluated by routine methods and stereoscopic examination of the optic nerve, computer perimetry (Humphrey) and Stratus OCT. The existence of systemic diseases has been studied in details in all patients, with emphasis on vascular risk factors. Additional specialized consultations and examinations were conducted.

Results IOP was lower than the statistically defined normal IOP values in 44 (55%) out of 80 studied patients. Within this group of LPG patients we established the presence of specific topographic changes in the optic nerve and typical changes in the layer of ganglion cells and nerve fibers. In compliant patients with disease progress and IOP values between 19-20 mm, we established significantly higher prevalence of systemic diseases leading to general and local ischemia: uncontrolled blood pressure, diabetes mellitus, etc. We followed also the subsequent functional differences in the development of damage in optic nerve and visual field in the two groups.

Conclusion Until recently, IOP has been considered the only factor for control and prevention of glaucomatous damage. Literature data and our observations explicitly demonstrate the existence of additional risk factors in the pathogenesis of glaucoma, indicating for the necessity of lower level of IOP. Preserving vision and quality of life of patients depends both on the timely decision for lower IOP target in patients with LPG and inju

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Ocular response analyzer in pre-perimetric glaucoma

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Purpose To compare corneal biomechanical parameters measured by Ocular Response Analyzer (ORA) in pre-perimetric glaucoma eyes (PPG), versus intra-ocular hypertension (OHT), open angle glaucoma (OAG) and normal subjects (NS).

Methods Comparative study including 317 eyes: 165 normal (NS), 64 OHT, 46 OAG and 42 PPG. PPG criteria: intra-ocular pressure (IOP) > 21 mm Hg, glaucomatous alterations of the optic disc and no visual field defect. Measured parameters: corneal hysteresis (CH), corneal resistance factor (CRF), Goldmann correlated IOP (IOPg), corneal compensated IOP (IOPcc), IOP by Goldmann aplanation tonometry (GAT) and central corneal thickness (CCT). Statistical analysis used non parametric tests and significant p value < 0,05.

Results Whatever the parameter, there is no significant difference between PPG and OAG groups. GPP mean CH value (9,5 ± 1,5) was statistically different compared with NS (10,2 ±1,5), but no difference was found with OHT (9,6 ± 2) or with OAG (9,2 ± 1,8). No significant difference was found between PPG mean CRF value (10,2 ± 1,6) and those measured in NS (10,1 ±1,6), OHT (10,9 ± 2,1), and OAG (9,9 ± 1,5). PPG mean CCT (533 ± 39 µm) value was different only from OHT (552 ± 46 µm). For IOP parameters (IOPg, IOPcc, TAG), PPG eyes presented no difference with OAG eyes, but there was difference with OHT and with NS. Whatever the parameter, there was a great overlap of values between groups.Previous reports have demonstrated that CH is lower in OAG, and CRF higher in OHT. This study found that PPG eyes have the same corneal biomechanical parameters as OAG, and that PPG presents difference with OHT (CCT) and with normal eyes (CH).

Conclusion ORA seems to be useful for early diagnosis of pre-perimetric glaucoma.

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The relationship between corneal biomechanical properties and intraocular pressure

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Purpose To determine the relationship between the biomechanical properties and the intraocular pressure (IOP) measured with the Goldmann applanation Tonometer (GAT) and a noncontact tonometer (NCT). Repeatability of corneal biomechanical properties was also assessed.

Methods One randomly selected eye of 106 healthy subjects was assessed using the Ocular Response Analyzer (ORA), a noncontact tonometer, an ultrasound pachymeter and the Goldmann tonometer, on two separate days. The order of measurement was randomized between the ORA and the NCT, followed by measurements of central corneal thickness (CCT) and IOP with the GAT. The main outcome measures were corneal hysteresis (CH), corneal resistance factor (CRF), central corneal thickness (CCT) & IOP.

Results The Pearson correlation coefficients between the GAT IOP on one hand and CH, CRF & CCT on the other, respectively, were: 0.323(P < 0.0001), 0.579 (p < 0.0001), & 0.421 (P < 0.0001) in session 1. The corresponding values for the NCT were: 0.565 (P < 0.0001), 0.772 (P < 0.0001) & 0.681 (P < 0.0001) respectively. The highest correlation coefficients obtained (with both tonometers) when IOP was plot against 'CCT + CRF', were: 0.562 (P<0.001) and 0.788 (P<0.0001), for the GAT and the NCT, respectively in session 1. Repeatability indices in the first session were ±2.91mmHg, ±2.51mmHg, and ±0.01µm, respectively, for CH, CRF, & CCT. Reproducibility indices were ±3.11mmHg, ±2.78mmHg and ±0.03µm for CH, CRF and CCT, respectively.

Conclusion CH, CRF, and CCT are all significantly correlated with IOP, more so when the IOP is measured with a NCT. When plot together, CCT &CRF were best able to explain the variation of IOP. All three corneal biomechanical properties showed good repeatability and reproducibility indices.

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Intraocular pressure after cataract surgery measured with Pascal dynamic contour tonometer, Goldmann applanation tonometer and pneumotonometer

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Purpose The aim of this study was to compared the effect of cataract extraction by phacoemulsification and posterior chamber lens implantation on measured intraocular pressure (IOP) using the Goldmann applanation tonometer, the Pascal dynamic contour tonometer (DCT), the Goldmann applanation tonometer (GT) and pneumotonometer (PT)

Methods 97 eyes were measured in the operated eye one day before and one day, one week and one month after cataract surgery with the three tonometers, the IOP, ocular pulse amplitude (OPA),and central corneal thickness (CCT)

Results Corneal edema induced by phacoemulsification cataract surgery resulted in statistically significant increases in CCT (87,8 µm SD 56,8 ;p< 0,001), Pascal DCT IOP (4,8 mmHg, SD 8,0; p< 0,001),Goldmann IOP (1,4 mmHg, SD 5,1;p<0,015) and OPA (0,9 mmHg, SD 3,5; p< 0,025) but not in pneumotonometry IOP (1,1mmHg, SD 5,3; p=0,065). Changes in IOP measured by GT and PT were less than those measured by the Pascal DCT. The variation between the Pascal DCT (Rho 0,247; p=0,038), and Pneumotonometer (Rho 0,358; p=0,002) was strongly correlated to the change in CCT

Conclusion Corneal edema after phacoemulsification cataract surgery increased IOP readings in the three tonometer compared, this increment is bigger in Pascal DCT readings. Changes in CCT are statistically significant associated with increased Pascal DCT IOP readings. Change in corneal biomechanics may in part be responsible for increased in the measured of IOP with Pascal DCT and GT

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Comparison of Ex-Press® miniature implant with standard trabeculectomy after combined glaucoma surgery

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Purpose To evaluate postoperative outcomes after combined phacoemulsification andglaucoma surgery with Ex-PRESS miniatureimplant compared with combined surgery withstandard trabeculectomy.

Methods Prospective series of 24 consecutiveeyes we compared 12 eyes in patients treatedwith combined phacoemulsification and glaucomafiltering surgery with the Ex-PRESS miniatureglaucoma implant under a scleral flap with 12 matchedcontrol eyes in patients who underwentcombined cataract and glaucoma surgery with trabeculectomy.

Results The average follow-up was 10 months(range 3.4 to 14) for the Ex-PRESS group and 12.3months (range 4.0 to 16.5) for the trabeculectomygroup. The mean IOP was significantly higher inthe early postoperative period in the Ex-PRESSgroup compared with the trabeculectomy group.Complications rate in the early postoperative periodwas significantily higher in the trabeculectomygroup. No significant differences were objectifiedin success between both groups after the first week.

Conclusion The Ex-PRESS implant is an effectivealternative to standard trabeculectomy inselected cases which makes possible to reduce the classic early postoperative complicationsassociated with trabeculectomy.

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Ahmed glaucoma valve implantation for neovascular glaucoma after vitrectomy for proliferative diabetic retinopathy

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Purpose To evaluate the safety and efficacy of Ahmed Glaucoma Valve implantation (AGVI) for the management of neovascular glaucoma (NVG) associated with proliferative diabetic retinopathy (PDR) in the vitrectomized eyes.

Methods We reviewed the medical records of patients with NVG associated with PDR who underwent AGVI for intraocular pressure (IOP) control and compared the surgical outcome according to vitrectomy history. The main outcome measures were: postoperative IOP control, visual acuity, and complications. Success was defined as an IOP of ≤21 mm Hg and ≥6 mm Hg, without further glaucoma surgery or loss of light perception and devastating complications.

Results A total of 38 patients (38 eyes) were included.The cumulative probabilities of success after AGVI were 88.2% after 6 months and 85.2% after 1 year., Cox proportional hazards regression showed the intraocular silicone oil tamponade as a risk factor for the surgical failure (odds ratio=4.543, P=0.047). Final visual acuity improved or stabilized in 30 patients (78.9%) Complications were comparable with previous studies.

Conclusion Despite some complications that necessitate surgical intervention, the AGVI is a safe and effective procedure that enables successful IOP control and vision preservation in patients with NVG associated with vitrectomy for the PDR

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Digital analysis of the trabecular pigmentation using positive pixel count algorithm

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Purpose To analyze the trabecular pigmentation after sinustrabeculectomy using semi thin slices with optical microscopy and morphometrically and compare with clinical data.

Methods 10 glaucoma patients (10 eyes), 6 males and 4 females, underwent conventional sinustrabeculectomy. The trabecular specimens were prepared as semi thin slices (stained with Toluidin Blue) and analyzed using optical microscopy. The semi thin virtual slides were made by ScanScope and analyzed with Aperio Positive Pixel Count algorithm. The demographic, clinical and morphometrical data were analyzed using SAS Enterprise Guide 4.2 statistic software.

Results Correlation analysis of quantitative morphometric and clinical variables were not statistically significant: the probability coefficient between number of positive pigment pixels and pachymetry, highest IOP and glaucoma duration was higher than 0.05.

Conclusion 1. There was no statistic significance between morphometric and clinical variables. 2. Further studies of the trabecular tissue, using larger cohort are required.

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Relationship between retinal nerve fiber layer evaluation and visual field results in healthy and glaucoma individuals

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Purpose To determine the relationship between retinal nerve fiber layer (RNFL) thickness measured with spectral-domain optical coherence tomography (OCT) and the retinal sensitivity tested by standard automated perimetry (SAP).

Methods Two hundred and five subjects (100 healthy and 105 with different levels of glaucomatous damage subjects) were prospective and consecutively recruited. Only one eye per participant was randomly chosen. Glaucoma patients had intraocular pressure higher than 21 mmHg and glaucomatous optic disc appearance. All of them underwent imaging with the Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) and at least one reliable perimetry. SAPs were performed with a Humphrey Field Analyzer, using the 24-2 SITA Standard strategy. Left eye data were converted to a right eye format. The Kolmogorov Smirnov test was applied to check that the data were normally distributed. Threshold values of SAP were converted to a linear scale. Pearson correlations were calculated between the 52 threshold values tested by 24-2 algorithm of SAP and OCT parameters

Results Age was not different between both groups (p=0.09). In the whole sample, the strongest correlation was found between point 15 of SAP and RNFL thickness at inferior quadrant (r=0.670; p<0.001). The healthy group showed few and mild correlations. In the glaucoma group, the strongest correlation was also found between point 15 of SAP and inferior RNFL thickness at inferior quadrant (0.664; p<0.001).

Conclusion Normal individuals had mild correlations between few functional and structural parameters, while glaucoma patients showed mild to moderate correlations.

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Effect of cataract in Fourier-domain OCT measurements using two optical coherence tomographers

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Purpose To evaluate the effect of cataract in retinal nerve fiber layer (RNFL) thickness measurements using Fourier-domain (FD) Optical Coherence Tomography (OCT). To test the intra-session reproducibility of RNFL thickness measurements and the quality of images in patients before and after the cataract surgery using Cirrus and Spectralis OCT.

Methods Thirty eyes of 30 subjects (15 men and 15 women; aged from 67 to 86 years) underwent three 360° circular scans centred on the optic disc by the same experienced examiner using the Cirrus and Spectralis OCT instruments one month before and one month after cataract surgery. Differences between the two visits were analyzed. Repeatability was studied by intra-class correlation coefficients and coefficients of variation (COV) for both visits and OCTs. The quality of images was also compared between the visits.

Results RNFL differences were detected between both visits for temporal and nasal quadrant ($p<0.05$). RNFL average thickness was 95.4 µm in pre-surgery visit and 96.1 µm in post-surgery visit with Cirrus OCT; and 99.0 µm vs 102.4 µm using Spectralis OCT. Reproducibility was good in both visits, but it achieved higher values in post-surgery evaluation (mean COV of 5.61% in first visit vs 4.44% in second visit using Cirrus, and 5.76% vs 4.12% using Spectralis). Intra-class correlation coefficients were higher than 0.818. The quality of images was better in post-surgery evaluations.

Conclusion Cataract affects RNFL thickness measurements, reproducibility and the quality of images obtained by Cirrus and Spectralis OCT.

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A formula to predict spectral-domain OCT retinal nerve fiber layer measurements based on time-domain OCT measurements

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Purpose To establish and validate a formula to predict spectral-domain optical coherence tomography (SD-OCT) retinal nerve fiber layer (RNFL) thickness from time-domain (TD)-OCT RNFL measurements and other factors.

Methods From healthy participants and patients with glaucoma, SD-OCT and TD-OCT scans were obtained on the same day. Univariate and multivariate linear regression relationships were analyzed to convert Stratus TD-OCT measurements to Cirrus SD-OCT measurements. Other baseline characteristics included were age, gender, intraocular pressure, central corneal thickness, spherical equivalent, anterior chamber depth, optic disc area, visual field mean deviation, and pattern standard deviation. The formula was generated using a training set of 220 patients and then evaluated on a validation dataset of 105 patients.

Results Univariate analysis determined that TD-OCT RNFL thickness, age, optic disc area, visual field mean deviation, and pattern standard deviation were significantly associated with SD-OCT RNFL thickness. Multivariate stepwise regression analysis using available variables yielded the following equation: SD-OCT RNFL = 0.746 × TD-OCT RNFL + 17.104 ($R2 = 0.879$). In the validation sample, the multiple regression model explained 85.6% of the variance in the SD-OCT RNFL thickness.

Conclusion This formula based on TD-OCT RNFL thickness may be useful in predicting SD-OCT RNFL thickness. Other factors associated with SD-OCT RNFL thickness, such as age, disc area, and mean deviation, did not contribute to the accuracy of the final equation.

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The effect of cataract on spatial and temporal contrast sensitivity tests in glaucoma

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Purpose To investigate the efficacy of spatial and temporal contrast sensitivity (CS) tests for detecting early glaucoma in the presence of cataract

Methods Twenty-seven early glaucoma patients (mean age 60 ±10.2 years) with early cataractous signs were selected together with twenty-seven control subjects matched for age and cataract type. Cataracts were graded using the grading scheme of Casser et al (1997).Measurements of grating spatial and temporal CS at 20 HZ in central vision were performed in each group for spatial frequencies (SF) 0.5, 1.5 and 3 c/d with and without glare. Visual acuity, visual fields sensitivity measurements and structural tests using Heidelberg Retina Tomograph (HRT) were also performed.

Results Overall reduction in both spatial and temporal CS at all SF was found for glaucoma patients compared with cataract patients with a significant mean difference of 0.2 log units ($p < 0.01$). This difference correlated well with measurements of visual fields or and HRT parameters. The effect of the glare on CS was significant ($p < 0.01$) and was similar for both groups. A significant correlation ($p< 0.05$) was found between the glare factor and the glaucomatous damage assessed by HRT.

Conclusion Our results indicate that both spatial and temporal CS tests can distinguish glaucomatous vision loss from vision loss resulting from cataracts, the temporal test providing better separation at higher SF. The CS reduction due to the presence of glare increased with the glaucomatous damage, suggesting that there maybe an increase in intraocular straylight in glaucoma.References:1.Casser L, Fingeret M, and Woodcome T. Atlas of Primary Eyecare Procedures, ed 2, 1997

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Relationship between time- and spectral-domain optical coherence tomography in glaucoma

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Purpose To evaluate the relationship of retinal nerve fiber layer (RNFL) thicknesses obtained with two different optical coherence tomography (OCT) systems, time-domain OCT (Stratus; Carl Zeiss Meditec, Dublin, Ca) and spectral-domain OCT (Cirrus; Carl Zeiss Meditec), in healthy and glaucomatous eyes.

Methods Seventy healthy and 71 glaucoma individuals were prospective and consecutively selected. Only one eye per subject was included in the study. Glaucoma patients had intraocular pressure higher than 21 mmHg and abnormal standard automated perimetry (SAP). All participants underwent a comprehensive ophthalmic examination and at least 2 reliable SAPs. Peripapillary RNFL measurements were acquired with 2 different OCT systems (Stratus and Cirrus OCTs). Kolmogorov-Smirnov test was applied to check normality of variables. Then, Pearson´s correlations were calculated between parameters of both OCTs in the healthy and glaucoma groups.

Results Mean age was 56.1 ± 12.1 and 62.2 ± 9.1 years in the healthy and glaucoma groups, respectively ($p=0.07$). Moderate to strong correlations were observed between equivalent parameters of both devices. The strongest correlations were found for average RNFL thickness ($r=0.928$; $p<0.001$) and RNFL thickness at inferior quadrant ($r=0.925$; $P<0.001$) in the glaucoma group. The RNFL thickness at 3 o'clock position showed the mildest correlation ($r=0.435$; $p<0.001$) in the healthy group.

Conclusion Although RNFL parameters cannot be interchanged between both devices, the RNFL measurements of time- and spectral-domain OCTs had strong correlations in glaucoma patients.

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The relationship between RNFL thickness and rim thickness by Cirrus® HD OCT

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Purpose To study the relationship between RNFL thickness and rim thickness by Cirrus HD OCT

Methods This prospective comparative study was conducted on 50 eyes from 50 glaucoma patients and 30 eyes from healthy 30 subjects. They were imaged by Cirrus HD OCT and the RNFL thickness and rim thickness data were analyzed. The correlations of the angles of the peaks in the RNFL thickness profile or rim thickness profiles with the axial length and spherical equivalent of refractive error (SE) were analyzed by simple linear regression

Results The global average RNFL thickness and rim thickness was significantly thinner in the glaucoma group than in the control group. The angles of the peaks in the RNFL thickness and rim thickness showed good correlation in both glaucoma and control group. Myopia affected the distribution of the peaks in the RNFL thickness and rim thickness. However, the effect were different between RNFL thickness and rim thickness

Conclusion The rim thickness had good correlation with RNFL thickness. And the degree of glaucoma and myopia affected the distribution of RNFL thickness and rim thickness

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Peripapillary retinal nerve fiber layer thickness measurement with 3 spectral domain OCT devices

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Purpose To compare peripapillary retinal nerve fiber layer (pRNFL) thickness measurement using 3 Spectral Domain OCTs (SD-OCT) in normal and glaucomatous patients

Methods Observational case series. 145 eyes of 78 patients underwent a complete examination and a standard automated perimetry followed by pRNFL OCT evaluation with the RTVue OCT (Optovue), the 3D-OCT 2000 (Topcon) and the Spectralis (Heidelberg). Each patient was scanned by the same well-trained examiner. pRNFL measurements were comparated across the 3 devices using repeated measures analysis of variance (ANOVA) and multiple comparaison t-tests with Bonferroni adjustements. Bland-Altman plots were constructed to assess the level of agreement between each pair of OCTs.

Results The study included 66 normal eyes, 24 ocular hypertension, 10 preperimetric, 23 mild, 14 moderate and 8 severe glaucomas. Overall pRNFL thickness mean was greatest on the Topcon (96,2±14,9), intermediate on the RTVue (93,8±16,5) and lowest on the Spectralis (84,5±18,5). The ANOVA test demonstrated a mean thickness difference (overall, superior, inferior, nasal and temporal) between the 3 OCTs ($p<0,05$). On the multiple comparaisons t-test, the Topcon and RTvue were not significantly differents. The bland Altman plots show a moderate agreement but a good correlation between the 3 OCTs. The thinner were the RNFL thickness, the greater were the differences between the devices.

Conclusion This study proved that there were differences in the thickness measurements and a moderate agreement between the 3 devices. SD-OCT are not interchangeable and the patient's follow up should be done on the same device.

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Applications of anterior segment OCT to glaucoma surgery

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Purpose To assess the utility in clinical practice of anterior segment optical coherence tomography (OCT) in glaucoma surgery.

Methods Consecutive cases review of patients diagnosed of primary open angle glaucoma, closure angle glaucoma, pseudoexfoliative glaucoma. Anterior segment 5 Line Raster OCT protocol (Cirrus HD –Spectral Domain Technology) was performed to evaluate the follow-up of glaucoma surgeries (trabeculectomy and drainage devices) of these patients.

Results Anterior segment OCT achieved a correct display of the angle anatomy after surgery. About glaucoma surgery images, it showed a correct display of structures in superficial sclera. However, it showed limitations at the evaluation of structures in deep sclera: space under sclera flap and exact location of the trabecular drainage.

Conclusion Anterior segment OCT is a tool of in vivo diagnostic, that achieves an objective anterior segment evaluation in glaucomatous eyes after surgery. This device shows limitations at the evaluation of deep sclera. However, anterior segment OCT provides clinical information about glaucoma post-surgical anatomy and its functionality.

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Caspase-3 expression in rat lens after in vivo exposure to UVR-300 nm

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Purpose To determine the evolution of active caspase-3 protein expression in albino rat lens after in vivo exposure to low dose UVR-300 nm by immunohistochemistry.

Methods Altogether, 10 Sprague Dawley rats were unilaterally exposed in vivo to 1 kJ/m2 UVR-300 nm for 15 minutes. At 0.5, 3, 7 and 24 hours after UVR exposure, exposed and contralateral non-exposed lenses were removed and processed for immunohistochemistry. Three midsagittal sections per lens were stained. Active caspase-3 labeling was counted and recorded three times in each section.

Results Caspase-3 expression was higher in exposed than in contralateral non-exposed eyes (expressed as a 95% confidence interval for the mean CI[Mean difference] 0.95 = 13.6 ±0.5). The mean difference between exposed and contralateral non-exposed lenses was (CI[Mean difference] 0.95) 13.1 ±9.0, 14.3 ±5.6, 18.4 ±1.9 and 8.8 ±7.2 for the 0.5, 3, 7 and 24 hours groups, respectively. There was no difference in expression of caspase-3 between the 0.5 and 24 hours groups (CI[Mean difference] 0.95 = 4.3 ±7.0). There was a difference between the 3 hours and 7 hours groups (CI[Mean difference] 0.95 = 4.14±2.03). There was a difference when comparing the 0.5 and 24 hours groups versus the 3 and 7 hours groups (CI[Mean difference] 0.95 = 6.21±4.05).

Conclusion Expression of caspase-3 in eye lens increases after UVR exposure. There is a peak of expression between 3 and 7 hours after exposure.

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Evolution of protein concentration in the rat lens after in vivo exposure to close-to-threshold dose ultraviolet radiation

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Purpose To investigate the short term cataract development and protein concentration in the rat lens after in vivo close-to-threshold dose exposure to ultraviolet radiation (UVR) around 300 nm.

Methods Three groups of 10 Sprague Dawley rats were unilaterally exposed to 8 kJ/m2 UVR-300 nm for 15 minutes, and a forth group of 10 rats was kept without UVR exposure as non-exposed control animals. The exposed animals were sacrificed at 1, 3 and 7 days after exposure. Both lenses from all animals were extracted and photographed and the intensity of forward light scattering was measured quantitatively. Whole lens was homogenized and protein concentration was determined spectrophotometrically.

Results All exposed lenses developed cataract. Lens light scattering increased throughout 7 days after UVR exposure. The difference of protein concentration between exposed lens and contralateral non-exposed lens was slightly decreased at 1 day after exposure and then gradually normalized back to baseline within 7 day after exposure.

Conclusion The in vivo close-to-threshold dose UVR induced cataract and protein changes are not paralleled. The altered protein concentration is normalized within 7 days after ultraviolet irradiation.

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Establishment of a lens epithelial cell line from cataract dog

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Purpose The aim of this study is to establish a lens epithelial cells (LECs) line originated from cataract dog.

Methods Anterior capsulorrhexis specimen from a dog (8-year-old male Wire Fox Terrier) naturally developing mature cataracts was obtained prior to routine phacoemulsification cataract extraction. The primary lens epithelial cells were transfected with the expression plasmid DNA encoding replication origin defective simian virus 40 (SV40) large T antigen and then cloned a colony by using glass syrinder.

Results The primary cells proliferated to confluent until three passages. However, the immortalized cells remained proliferative, and this cloned cell line, termed as cdLEC, grew well and could be propagated over 200 times by splitting at 1:20. Functional analysis of Na-dependent vitamin C transporter (SVCT) indicated that the Km value toward ascorbic acid (vitamin C) was 19.9 + 2.8 M, and RT-PCR analysis showed that SVCT2 was observed in this cell line while SVCT1 was not, which was the characteristic of LECs. Western blot analysis and cyto-immunochemistry indicated immortalized cells produced a protein with a molecular weight of 25 kDa, which reacted with an antibody to B-crystallin within the whole cytosol.

Conclusion These results indicate that cdLEC may provide a useful in vitro system for the study of path-physiology of canine cataract.

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Cadmium, copper and lead in cataractous and normal dog lenses

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Purpose This study aims to determine the concentrations of cadmium (Cd), copper (Cu) and lead (Pb) in cataractous and normal dog lens. The possible role of these elements in cataractogenesis has been suggested by reports in humans.

Methods 14 cataracts dogs lenses and a control group of 6 normal clear dogs lenses of different breeds and sex living in same area have been examined. The average ages of the cataractous group are 9.6+/-4,6 years old, while the control group are 4,8+/-2,9 years old. Cataractous lenses were classified as mature. Removed lenses were placed into cleaned PVC tubes and kept frozen below -20°C before being assayed. Cd, Cu and Pb levels of the samples were determined with a Perkin-Elmer atomic absorption spectrophotometer equipped with graphite furnace system using a standard addition technique. The concentrations were calculated in terms of mg/kg dry tissue weight. Statistical method used was Student t test.

Results Cataractous lenses: Cd 0,081+/-0,046; Cu 2,9+/-1,5; Pb <0,05. Normal lenses: Cd 0,062+/-0,035; Cu 3,6+/-3,8; Pb <0,05. No significant differences in Cd, Cu and Pb concentrations related to age and sex have been found at the comparison of normal versus cataractous lens

Conclusion In humans and animals the most likely origin of Cd, Cu and Pb is from environmental contamination. The results suggest that the low concentrations of these heavy metals in cataractous lens in dogs can be related to the fact that: a) dogs have a shorter lifespam than men; b) these elements are not widely spread in the Italian environment; c) the pattern of absorption and storage of these elements could vary among different species.

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Unilateral pediatric cataract of uncertain cause

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Purpose To report the surgical results of unilateral pediatric cataract of uncertain cause and find out factors related to better outcome.

Methods We reviewed the medical records of 39 patients who underwent surgery for unilateral pediatric cataracts of no known cause. All patients underwent primary Intraocular lens implantation, and postoperatively, they were treated for amblyopia with glasses or monocular patch. Postoperative final visual acuity levels greater than 20/30 were considered 'good' Statistical analysis was carried out to determine factors affecting surgical outcome.

Results The mean age was 5.9 ± 1.8 years (range 2.6 to 9.2) at the time of surgery. The mean final postoperative visual acuity was 0.47 ± 0.54 logMAR (range 0.00 to 2.00). In all, 46.2% (18 of 39) achieved a 'good' visual acuity. The 'good' visual acuity was significantly associated with better preoperative visual acuity, smaller amount of preoperative refractive error, smaller amount of preoperative refractive error difference between the operated eye and the fellow eye, and absence of strabismus (p = 0.002, 0.010, 0.008, and 0.014 respectively). Only preoperative visual acuity was significant in the multivariate analysis (p = 0.028). The preoperative visual acuity of 20/160 or better was found to increase the chance of achieving 'good' visual acuity by 8.66-fold (95% CI 1.26 to 59.38).

Conclusion Preoperative visual acuity is the most important prognostic indicator for surgical outcome of unilateral pediatric cataract of uncertain cause.

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Management of IOLs in pediatric cataracts

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Purpose To describe the different possibilities of treatment in pediatric cataract with IOL implantation; analyzing the type of IOL, the position of the haptics AND optic.

Methods Children of different ages underwent cataract extraction with intraocular lens implantation. We analyzed age of detection, age at surgery, cooperation of the patients, uni or bilaterality, presence of associated ocular abnormalities. Postoperatively we studied the evolution of the ocular inflamation during the first weeks, avoiding synechiae and membranes formation using oral prednisolone. Also we studied the visual recovery of the pseudophakic eye trying to avoid ambliopya by oclussion therapy of the fellow eye (in case of monocular cataract).

Results We obtained our best results by implanting an IOL always if possible, unless there is associated ocular pathology (microphthalmos, iris abnormalities,...). Our choice: In children under 2 years of age monofocal "3 pieces" IOL with haptics in sulcus and the optic in the bag or luxated into the vitreous (power undercorrected in 20%). In children between 2 and 4 years of age "3 pieces" IOL in the bag or with the optic into the vitreous. In older children with good preoperative biometric evaluation and good cooperation, specially in monocular developmental cataract, a great option is the use of multifocal IOLs to improve binocularity.

Conclusion In our experience, the best option to manage with pediatric cataract is to implant an IOL after cataract extraction, unless the presence of associated ocular abnormalities make it inadvisable . Visual recovery will be faster than in pediatric aphakic eyes and less "hard". Controversy still persists about the appropiate power of the IOL and how to calculate it.

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Outcomes of phacoemulsification and intraocular lens implantation in cataracts secondary to uveitis

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Purpose Cataract is a common complication of uveitis. Development of cataract depends on factors such as severity or chronicity of the process, steroid treatment and posterior irido crystalline synechiae formation. The aim of our study was to evaluate the results of phacoemulsification and intraocular lens(IOL) implantation in patients with cataracts secondary to uveitis.

Methods We conducted a retrospective observational study of cataract surgeries secondary to uveitis after 3 months of no inflammation. Phacoemulsification and IOL implantation were performed between january of 2004 and 2010. Studied variables were sex, age, type of uveitis, visual acuity before and after surgery, uveitis sequelae and surgical complications.

Results We studied 32 eyes of 21 patients (12 women and 9 men). The average age was 49.19+/-15.4 years. Average preoperative best corrected visual acuity was 0.24+/-0.1 while the final best corrected visual acuity was 0.75+/-0.2. The most common inflammatory process was idiopathic anterior uveitis.Other inflammation processes were Fuchs heterochromic cyclitis or pars planitis. There was no postoperative recurrence of uveitis in 29 eyes(90.6%) during the first month. The most frequent early postoperative complication was corneal edema and the late one was iris atrophy due to pupillary distention. Posterior capsule opacification appeared in 21 cases(66%) during the first six months after surgery. In 79% of patients achieved a final visual acuity from 0.6 to 0.9.

Conclusion Phacoemulsification with IOL implantation is, at this moment,the chosen surgical technique in most postuveitis cataract because it causes less inflammation and provides good visual results.

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Surgery of ectopia lentis

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Purpose Ectopia lentis is a patology with lens dislocation presumably secondary to zonular fiber weakness. Ectopia lentis can occur in isolation, in association with other ocular disorders or as part of systemic disorder. Marfan´s syndrome and homocystinuria are the most frequent cause of heritable ectopia lentis. Marfan syndrome (MFS) is a hereditary connective tissue disorder. Studies of MFS have established the critical contribution of fibrillin-1 deficiency to disease progression through altered cell-matrix interactions and dysregulated TGF-β signalling.

Methods We report four eyes of 4 children aged from 2 years to 4 years with ectopia lentisBoth cases showed bilateral and symmetric lens dislocation with low visual acuity. One of the children was diagnosed of Marfan syndrome.

Results We practised Twenty three gauge two port pars plana lensectomy without intraocular lenses.

Conclusion Pars plana lensectomy is a safe, effective procedure for the management of ectopia lentis. Earlier surgery is indicated to prevent amblyopia and improve visual acuity.Marfan syndrome, homocystinuria, trauma and simple ectopia lentis are the most common caused of pediatric lens subluxation. Ectopia lentis in children continues to be a diagnostic and therapeutic challenge for ophthalmologists. The convencional surgical management of congenital subluxated lenses infrequently associated with a high incidence of complications leading to poor visual prognosis. Surgical intervention is necessary when lens subluxation causes a significant refractive error resulting in amblyopia.

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On the impact of multifocal IOL decentration and tilt on retinal image quality

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Purpose The design of advanced (such as multifocal) intraocular lenses (IOLs) is based on the exact alignment of the optical element with the center of the pupil and its optical axis with the line of sight of the eye. It is the purpose of this study to evaluate the impact of multifocal IOL decentration and tilt on retinal image quality.

Methods A series of patients implanted with multifocal IOLs were evaluated with a Scheimpflug imaging device (GALILEI Dual Scheimpflug Analyzer, Ziemer Switzerland), that was utilised to evaluate centration and tilt of the IOLs. Wavefront aberration was recorded using a retinal ray tracing device (iTrace, Tracey Technologies Houston, USA). Induced high order aberrations were correlated to the orientation of tilt and the location of the IOL.

Results In multifocal IOLs, decentration in recpect to the pupil center is more detrimental to retinal image quality than tilt. Moreover, multifocal IOLs are more sensitive to tilt and decentration than monofocal IOLs in respect to the induced aberrations.

Conclusion Modern imaging technologies in combination with wavefront abberation measurements may elucidate the impact of IOL location in the eye in retinal image quality. In certain cases, such as in diffractive lenses, where wavefront sensing has inherent limitations, retinal image quality may be evaluated by appropriate computer modeling.

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A comparison of remaining refractive error after cataract surgery using different monofocal intraocular lenses

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Purpose The aim of this study was to evaluate the refractive outcomes following cataract surgery using single-piece and three-piece monofocal intraocular lenses (IOLs).

Methods In this retrospective study 114 eyes were enrolled. Monofocal single-piece IOLs were used in group I (Quatrix/Croma., Austria, 61 eyes) and group II (Acrysof IQ /Alcon Laboratories Inc., Texas, 29 eyes) while three-piece IOLs were implanted in group III (Mediconsult A85UV/Mediconsult Intraocular., Germany, 24 eyes). The main clinical outcome parameter evaluated was the remaining spherical equivalent refraction (Remaining SER: post-op SER – target refraction). Kruskal-Wallis non-parametric ANOVA statistic test was used for data analysis.

Results The mean target refraction was -0.52D (SD 0.34). The mean remaining SER in group I, II and III was +0.46D (SD 0.93), +0.25D (SD 0.61) and -0.29D (SD 0.97) respectively. Kruskal-Wallis H test showed that there was a statistically significant difference in the residual refractive error among the different IOL implants (H (2) =11.255, P=.004).

Conclusion According to statistics, single-piece IOL implants Quatrix and AcrySof IQ induced a slight hyperopic shift whereas the refractive outcomes of three-piece implants (Mediconsult A85UV) concurred with the preoperative target. Future prospective studies and a larger number of cases are needed to verify the aforementioned results.

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Evaluation of posterior capsule opacification after cataract surgery using liquifaction method

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Purpose Posterior capsule opacification (PCO) is still one of the most common complication following cataract surgery with IOL implantation. We evaluate the extent of PCO after cataract surgery - torsional phacoemulsification and Liquifaction method removal of the epithelial cells (right eye) and torsional phacoemulsification (left eye). For PCO quantification we use two types of software.

Methods In our prospective clinical study we examine patients 3, 6, 12 and 24 months after surgery, digital retroillumination photographs of the anterior segment, pachymetry, endothelial cell count (ECC) and best corrected visual acuity (BCVA) are obtainedFor evaluation of PCO we use EPCO 2000 software (Evaluation of Posterior Capsule Opacification) and OSCA software (Open-Access Systematic Capsule Assessment).

Results The BCVA two years postoperatively is 0.896 ± 0.13 (right eye), 0.883 ± 0.16 (left eye). Nd-YAG laser capsulotomy one year after surgery underwent one patient (both eyes) and one patient two years postoperatively (right eye).EPCO results - right eye: 0.260 ± 0.198 (3M); 0.259 ± 0.173 (6M); 0.308 ± 0.19 (12M); 0.419 ± 0.252 (24M), left eye: 0.279 ± 0.170 (3M); 0.280 ± 0.153 (6M); 0.333 ± 0.197 (12M); 0.480 ± 0.313 (24M) OSCA results - right eye: 0.599 ± 0.240 (3M); 0.605 ± 0.333 (6M); 0.598 ± 0.256 (12M); 0.655 ± 0.402 (24M), left eye: 0.627 ± 0.403 (3M); 0.635 ± 0.360 (6M); 0.629 ± 0.328 (12M); 0.654 ± 0.452 (24M).

Conclusion The Liquifaction method is save for occular tissue. One year after surgery most cases of PCO is graded as minimal.Supported in part by Charles University Grant Agency, No. 103809

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Light transmission of the human lens and its relation with aging

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Purpose To determine the visible light transmission of the human crystalline lens of persons of different ages, using both solar and incandescent illumination.

Methods The spectral transmission of lens was measured by using the Perkin-Elmer 800 UV/VIS spectrophotometer. With these data we calculated the percentage of visible light transmission for solar illumination, simulated by the CIE D65 illuminant, and for incandescent illumination (A illuminant).

Results The total amount of visible light transmitted by nine crystalline lenses is represented as a function of age: with solar illumination and with incandescent illumination and the comparison between both illuminants.In general, the amount of visible light transmitted by the crystalline decreases with age and, in relative values, this transmission is higher with incandescent illumination (between 2 and 8% higher) than with solar illumination.

Conclusion In general, total transmission of visible light decreases greatly with age. Nonetheless, the case of the transmission of a crystalline lens of a 50-year-old being much lower than that of a 64-year-old has been reported, which indicates that some of the factors that determine the darkening of the crystalline lens may act more intensely in some people than in others. Moreover, a slight improvement in visible light transmission was observed when incandescent light was used instead of solar light. This is because the crystalline lens yellows with age and as incandescent light is basically yellow, it is almost wholly transmitted. However, as solar light is tremendously intense, the absolute amount of light that reaches the retina is always much greater with solar rather than with incandescent illumination.

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Age-induced change in the color of the human crystalline lens

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Purpose To determine the chromatic coordinates of different human crystalline lenses to analyze the age-induced change in the color of the crystalline.

Methods The spectral transmission of nine human crystalline lenses of different ages were measured by using a Perkin-Elmer 800 UV/VIS spectrophotometer. Using these data we calculated the chromatic coordinates of each crystalline lens for both solar and incandescent illumination. The study adheres to the tenets of the Declaration of Helsinki for Research Including Human Subjects and was approved by the Institutional Review Board.

Results The results show a greater saturation of color with the increase of age. In principle, the change tends towards yellow, although for ages of over 70 years it veers more towards orange colors. All the crystalline lenses were more yellow and saturated under incandescent illumination.

Conclusion At the beginning, a young crystalline lens is transparent and its chromatic coordinates practically coincide with those corresponding to solar light. As age increases, the crystalline lens yellows. On the basis of the results obtained, it cannot be claimed that the more yellow a crystalline lens is, the older it is. Our results show that between 40 and 67 years the chromatic coordinates are quite similar, especially under incandescent illumination. However, total transmission of light is more important for vision than the color of the lens and we have found that the age-induced changes in these two parameters do not always coincide. All this shows that the different factors that influence yellowing of the crystalline lens do not act in the same way on everyone and that crystalline opacification does not depend solely on aging.

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Near distance vision with aspherical intraocular lenses in a model eye

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Purpose To determine the image performance of aberration free (AF) and aberration correcting (AC) aspherical IOLs for objects located at near distance in a model eye.

Methods For our simulation we considered 2 AF IOLs (1: Bausch&Lomb SOFPORT, 2: Dr. Schmidt MC6125 AS), 2 AC IOLs 3: Alcon Z9000, 4: Zeiss Invent ZO) and for reference a spherical IOL (5: Dr. Schmidt MC5812). All lenses (nominal refractive power: 22 D) were optimized for objects at far distance at a pupil of 3.0mm and all simulations were done for a pupil of 4.5mm. Image performance was assessed with Strehl ratio and geometrical RMS spot size using optical design software OSLO. The object vergence was increased from 0D:0.5D:3.5D to simulate the capabilities for near distance vision. The Liou Brennan (LBME) and the Gullstrand (GME) model eye were used for simulation.

Results With the LBME for far distant objects the Strehl ratio/RMS spot size was 0.1768/0.0157, 0.2613/0.0131, 0.8978/0.0008, 0.3577/0.0066 and 0.0159/0.0261 for lenses 1 to 5, respectively. For near distant objects (vergence 3D) it was 0.0018/0.0730, 0.0011/0.0579, 0.0004/0.0855, 0.0007/0.0801 and 0.0029/0.0669. With the GME for far distant objects (vergence 0D) the Strehl ratio/RMS spot size was 0.1698/0.0159, 0.2442/0.0134, 0.8651/0.0008, 0.3257/0.0069 and 0.0117/0.0246 for lenses 1 to 5, respectively. For near distant objects (vergence 3D) it was 0.0018/0.0718, 0.0013/0.0747, 0.0003/0.0861, 0.0007/0.0789 and 0.0066/0.0656.

Conclusion As both AC IOLs show the best imaging performance mostly for the LBME as well as the GME for far distance objects, the performance is strongly degraded for near distant objects and even worse than the respective values for AF and spherical IOLs both, for the LBME as well as the GME.

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Simulation platform for evaluation of geometrical and positional changes of lenses during accommodation

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Purpose To build-up an optomechanical eye model to reproduce physiological accommodation as a test environment for assessment of accommodative intraocular lenses (AIOL).

Methods Freshly enucleated porcine eyes were cleaned and glued into an expansion unit at ciliary body level. The cornea was removed using a trephine. After extraction of the crystalline lens with circular capsulorhexis an AIOL was implanted into the capsular bag. Finally, the posterior part of the globe was cut off and a vitrectomy was performed. The expansion unit with the dissected eye was placed in a temperature stabilized cuvette with BSS (35°C) simulating physiological conditions. The ciliary body is expanded to stretch or relax the zonula fibers effectuating pseudophakic accommodation.For a dynamic measurement of accommodation we used:1) A Shack-Hartmann-Sensor for measuring optical performance.2) An optical coherence tomograph (OCT) to measure the shape and relative lens position during accommodation.

Results The setup allows measurement of curvature, relative lens position, optical power and image quality of the IOL for different states of accommodation. Due to optical constraints, simultaneous measurement of 1) and 2) was not possible. Therefore, the cuvette was shifted between both beam paths for each measurement. Within the measurement area (5.5 x 5.5 x 1.6 mm in air) the OCT resolution is limited to 12 µm.

Conclusion The presented setup was considered to analyze the behavior of AIOL during accommodation in terms of change in curvature, position and optical performance. After experimental evaluation of the setup we will standardize and automate the measurement procedure, with the goal of a new AIOL design.

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Pupillometric quantification of residual rod and cone activity in patients with visual loss due to Leber's congenital amaurosis

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Purpose Leber congenital amaurosis (LCA) is a group of genetically heterogeneous retinal dystrophies in which severe visual impairment occurs at infancy or during early childhood. We describe the threshold response function of rods and cones, as determined from pupil responses to colored light stimulation over a range of intensities, in 4 patients with LCA with different gene mutations who each had very poor visual function and non-recordable ERG.

Methods Four subjects with LCA and 10 control subjects underwent computerized pupillography under conditions of dark adaptation. The pupil response to a 1 second red (640 ± 10nm) and blue (467 ± 17nm) Ganzfeld light from -4.0 to 2.0 log cd/m2 was recorded continuously. Pupil responses to low light intensities were used to define the response curve of rods and the rod threshold for blue and red light. When rod-related pupil responses were absent, those obtained from red light stimulation at brighter intensities could be used to estimate cone activity.

Results A rod-related pupil response curve was still preserved and defined in only one patient (RDH mutation) using blue light and the repsonse threshold was -3.1 log cd/m2 . This was almost 2 log-units greater than the mean value in normal eyes (-4.9 log cd/m2 blue light). Residual cone activity in all 4 LCA patients yielded response thresholds of -2.3, -0.9, -0.8 and -2.1 log cd/m2.

Conclusion Pupillometry can estimate residual function and threshold responses of rods and cones in advanced stages of LCA. As such, pupillometry expands the dynamic range of photoreceptor activity that can be objectively monitored, either to follow natural progression or to assess effects of intervention.

Commercial interest

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Analysis of locus 2q13 in Ecuadorian family with keratoconus

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Purpose Keratoconus (KTCN) is described as a non-inflammatory thinning and anterior protrusion of the central cornea which results in altered refractive powers, and loss of visual acuity. The etiology of KTCN remains unknown. Both genetic and environmental factors are associated with the disorder. The purpose of this study was to identify novel genetic factors involved in familial form of KTCN by extensive analysis of multigenerational Ecuadorian family.

Methods A total of 22 individuals from KTCN-019 family were included into this study. Genomic DNA samples of all members of KTCN-019 family were genotyped with highly polymorphic microsatellite markers. After linkage was established, two positional and functional candidate genes, IL1A and IL1B, were examined with polymerase chain reaction amplification, and direct sequencing of all exons, and intron-exon boundaries was performed.

Results The disease susceptibility locus was mapped on 2q13 chromosome in KTCN-019 family. Sequencing analysis of the candidate genes, IL1A and IL1B have revealed numerous alterations in coding and non-coding sequences of both genes including several novel single nucleotide polymorphisms. No mutations segregated with KTCN phenotype have been identified.

Conclusion Analysis of IL1A and IL1B genes revealed no mutations segregating with affected phenotype in large Ecuadorian family, indicating that other genes are involved in KTCN causation in this family.

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Identification of novel germline mutations in the VHL gene in Hungarian von Hippel-Lindau patients

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Purpose Von Hippel-Lindau disease is an autosomal dominantly inherited highly penetrant tumor syndrome predisposing to retinal and central nervous system hemangioblastomas, renal cell carcinoma and pheochromocytoma among other less frequent complications. Our goal was to establish genotype-phenotype correlation in Hungarian von Hippel-Lindau patients.

Methods Fourteen members (9 patients and 5 healthy family members) of 6 unrelated families with type 1 VHL disease underwent clinical and molecular genetic examination. The effect of a novel missense mutation was predicted using molecular modeling.

Results Retinal angioma was detected in seven patients; six patients had central nervous system hemangioblastoma and three patients developed RCC. Molecular genetic investigations detected four novel (c.232A>T, c.340+1G>A, c.163G>T, c.555C>A) and two previously described (c.583C>T and c.472C>G) germline mutations in the VHL gene, including four mutations leading to protein truncation and two missense mutations.

Conclusion RCC only associated to MLTP among our patients, in accordance with previous findings. The novel c.163G>T mutation associated to bilateral RCC and retinal angioma in a 15-years-old male patient, which is the earliest occurrence of RCC in VHL disease reported so far. Molecular modeling of the VHL-Elongin C complex predicted that the c.232A>T mutation responsible for the p.Asn78Tyr amino acid exchange remarkably changes the 77-83 loop structure of the VHL protein destabilizing the VHL protein and the VHL- Elongin C complex. Therefore it is predicted to cause type I phenotype, as seen in our patient indeed. Our results can be useful for genetic counseling and follow-up of VHL patients.

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Anisometropia in population based study: The Mashhad Eye Study

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Purpose To determine the prevalence of anisometropia and its determinants in the population of Mashhad.

Methods In a cross-sectional study in 2008, 4453 residents of Mashhad city between the ages of 1 and 90 years were selected using stratified cluster sampling, of which, 70.4% participated in the study. All respondents had visual acuity and refraction testing. Anisometropia was defined as the absolute interocular difference in the spherical equivalent based on non-cycloplegic refraction. The prevalence rates and 95% confidence intervals (CI) of anisometropia was determined based on cutpoints of 0.5 diopter (D), 1.0 D, and 2.0 D or more, and we used the 1.0D cutpoint to examine associations.

Results After applying exclusion criteria, data from 2947 participants were used in the analyses. Based on cutpoints of 0.5D, 1.0D, and 2.0 D or more, the prevalence of anisometropia was 17.0% (95% CI, 15.1-18.8), 5.6% (95% CI, 4.6-6.6), and 1.7% (95% CI, 1.2-2.2), respectively. The odds of anisometropia showed a significant increase of 2.8% with every year of aging (p<0.001); 2.6% and 2.8% were anisomyopic and anisohyperopic, respectively. The prevalence of anisometropia was directly associated with myopia (p<0.001) as well as a history of ocular trauma (p<0.001). The prevalence of anisoastigmatism was 5.6% and significantly increased with age (p<0.001).

Conclusion The prevalence of anisometropia in the studied population, compared to studies conducted in the Middle Eastern Region and East Asia, is in the midrange. The prevalence of anisometropia is higher at older age, however, children should receive more attention due to the risk of amblyopia. A history of ocular trauma is a risk factor for anisometropia.

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Ocular phototoxicity and altitude among mountaineer guides

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Purpose To evaluate ocular phototoxicity in mountaineer guide in Chamonix, France, exposed to altitude characterized by increased ultraviolet (UV) radiation.

Methods 96 guides working and 90 subjects living in plains, older than 50 years, replied to a questionnaire assessing altitude exposure and wearing protective eyewear. We performed slit lamp examination after pupil dilatation, retinal photography (Topcon) and crystalline lens density analysis (Oculyzer®, Alcon). Student t-test was used to compare the groups and logistic regression to evaluate risks factors in guides group.

Results Guides mean age was 59.8years and 59.1 for control (p=0.39). Guides developed more chronic blepharitis (52.1% vs. 10.6%, p<0.01), pterygium (8.9% vs. 0%, p<0.01), pinguecula (58.3% vs. 21.7%, p<0.001). Their corneal break up time was shorter (4.5secs vs. 7secs, p<0.01). Guides presented more cortical cataract (p<0.01) and cataract surgery (p=0.01). Only 61.5% guides had normal ocular fundus vs. 81.1% in control group (p<0.01). They developed more drusenoid deposit (27.2% vs. 15.6%, p<0.01).Guides group analysis showed that exposure superior to 3000m is risk factor to develop anterior cortical cataract (OR=1.16, p<0.01). Exposition to snow increases risk of maculopathy (OR=1.9, p<0.01). Questionnaire reveals discontinuous eye protection in medium altitude. Wearing ski mask reduces cataract, age related maculopathy and chronic blepharitis risk.

Conclusion Ocular findings highlight the higher incidence of ocular surface pathology, anterior cortical lens opacities and drunenoid deposits. This data emphasize the potential deleterious role of UVs and importance to wear sunglasses even in low to medium altitude but also when climbing.

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The -1562C/T MMP-9 and the -511C/T IL-1β gene polymorphisms in primary open-angle glaucoma patients

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Purpose Matrix metalloproteases (MMPs) play a role in the remodeling of extracellular matrix components (ECM) and the development of primary open-angle glaucoma (POAG). Interleukin 1 (IL-1β) is considered as MMP's transcription upregulating factor. The aim of this study was to evaluate an association of the -1562C/T MMP-9 and the -511C/T IL-1β gene polymorphisms with a risk of POAG in a Polish population.

Methods DNA samples obtained from 196 POAG patients (mean age 70 ± 14) and 256 control subjects (mean age 67 ± 16) were analyzed by restriction fragment length polymorphism of polymerase chain reaction (PCR-RFLP).

Results The comparison of genotypes distributions showed that the -1562C/T genotype (OR 1.69, 95% CI 1.10 - 2.58; P = 0.015) and the T allele (OR 1.57, 95% CI 1.10 - 2.26; P = 0.014) of MMP-9 exhibit a significant increase of the frequency in POAG patients as compared to healthy controls. A statistically significant increase of the frequency was also found for the -511T/T genotype (OR 2.35, 95% CI 1.23-4.51; P = 0.009) and the T allele (OR 1.40, 95% CI 1.06-1.85; P = 0.017) of IL-1β in POAG patients. The analysis of gene-gene interactions of MMP-9 and IL-1β showed a statistically significant increase of the frequency of the C/T-C/T (OR 2.27, 95% CI 1.25-4.10; P = 0.006) and the C/C-T/T (OR 2.23, 95% CI 1.05-4.71; P = 0.033) genotypes in POAG patients group.

Conclusion In conclusion, we suggest that MMP-9 and IL-1β gene polymorphisms may be associated with an increased risk of POAG in a Polish population.This work was supported by grants N N402 375838 and N N402 248936 from Polish Ministry of Science and Higher Education.

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Evaluation of MMP-1 gene expression variants as a risk factor of primary open-angle glaucoma

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Purpose Matrix metalloproteinases (MMPs) have been extensively studied as primary open-angle glaucoma (POAG) risk factors. Recently, several single nucleotide polymorphisms (SNPs) for MMPs encoding genes have been reported in POAG patients. Especially, the –1607 1G/2G polymorphism present in promoter region of MMP-1 gene may affect its expression level. The aim of this study was to investigate the expression level of MMP-1polymorphicvariants in POAG patients group.

Methods In the present case-control study we examined group of 232 POAG unrelated Caucasian patients (mean age 70±14) and 253 age, sex matched controls (mean age 67±16). The –1607 1G/2G MMP1 gene polymorphism was determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). The odds ratios (ORs) and 95% confidence intervals (CIs) for each genotype and allele were calculated. The expression level of the –1607 1G/2G polymorphic variants of MMP1 gene was measured by real time q-PCR.

Results A statistically significant increase of the 2G/2G genotype (OR 1.35; 95% CI 1.05-1.67; P = 0.006) as well as the 2G allele frequency (OR 1.20; 95% CI 1.05-1.37; P = 0.006) of MMP1 was found in POAG patients as compared to healthy controls. We observed statistically significant 8,32 fold higher expression level of the 2G/2G genotype as compared to the 1G/1G wild genotype (P < 0.001), either.

Conclusion In conclusion, we suggest that the expression of the –1607 2G/2G genotype of MMP-1 may be considered as an important risk factor associated with primary open-angle glaucoma.This work was supported by grants N N402 375838 and N N402 248936 from Polish Ministry of Science and Higher Education.

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Clinical assessment and molecular genetics of an autosomal dominant retinitis pigmentosa in a Bulgarian Roma family

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Purpose To make a clinical assessment and molecular genetic analysis in patients with autosomal dominant form of retinitis pigmentosa (adRP) in a Bulgarian Roma family.

Methods Clinical assessment and genealogical analysis in a Bulgarian Roma family suggested the presence of RP with autosomal dominant inheritance with at least 12 affected in 4 generations.Best corrected visual acuity; kinetic Goldmann perimetry; direct and indirect ophthalmoscopy; ERG; fluorescein angiography. The molecular genetic analysis involved screening of 15 known adRP genes using microarray panel of Asper Biotech in the index patient.

Results T in exon 4 of the RP1 gene, leading to an amino acid substitution T373I was found in heterozygous condition.adRP is a severe and genetically heterogeneous retinal degeneration. We present a Bulgarian Roma family with typical clinical symptoms of RP and heterozygous change in the RP1 gene, which has previously been described as a possible disease causing mutation in a Pakistani family with adRP and in homozygous condition leading to a severe arRP in 2 consanguineous families of Pakistani origin.

Conclusion The clinical and genetic analysis of additional affected and unaffected family members is ongoing. This will allow better genotype-phenotype correlations to be made.

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Angioid streaks leading to the discovery of a new mutation in pseudoxanthoma elasticum

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Purpose Discovery of angioid streaks can lead to the diagnosis of pseudoxanthoma elasticum (PXE), an unusual autosomal recessive genetic disorder. We report a new functional pathogenic mutation associated to phenotypic manifestations of the disease.

Methods A 35-year old female was admitted for an etiologic work-up of a diffuse juvenile arteriopathy. Fundus examination evidenced typical peripapillary angioid streaks that led to the diagnosis of PXE, confirmed by genetic analysis of the ABCC6 gene. Our patient was compound heterozygote for two heterozygous mutations: one at exon 24 (c.3421C>T, R1141X), the other at exon 17 (c.2153A>G, D718G) not described before. Among her siblings, her brother and one sister were compound heterozygotes for the two mutations and had vascular symptoms and angioid streaks as well. Her mother was heterozygous for the D718G mutation while her father was heterozygous for the R1141X mutation. Both were asymptomatic.

Results ABCC6 gene implication in PXE was first described in 2000. Pathological mutations are mostly located from exons 23 to 29. The R1141X mutation is already known to be associated with a strong increase in the prevalence of coronary artery disease. Our results highlight that the D718G mutation is functional and may have a pathogenic role mainly due to its segregation with the disease and genetic arguments (Grantham's distance, damaging role related in the Polyphen tool online).

Conclusion Diagnosis of angioid streaks can lead to the diagnosis of PXE confirmed by genetic analysis. Examination of our patients allowed us to describe for the first time a new mutation of the ABCC6 gene (D718G), associated with the classical and recurrent R1141X mutation and with phenotypic manifestations of PXE.

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Multiple mtDNA deletions in Kearns-Sayre syndrome associated with macular dystrophy

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Purpose Kearns-Sayre syndrome (KSS) is a rare disorder resulting from a mitochondrial dysfunction. Classical triad includes chronic progressive external ophthalmoplegia (CPEO), tapetoretinal degeneration and complete heart block. A 48-year-old woman with a clinically and histopathologically confirmed KSS developed a maculopathy resembling an adult-onset vitelliform macular dystrophy in her right eye.

Methods The patient underwent optical coherence tomography (OCT), fluorescein angiography (FA),electroretinogram (ERG), electrooculogram (EOG), visually evoked cortical potentials (VEP)and muscle enzymes determination. A sartorius muscle biopsy was performed. DNA was submitted to Southern blot analysis.

Results The foveal vitelliform lesion remained hypofluorescent because the accumulation of vitelliform material blocks fluorescence. OCT revealed a retinal pigment epithelium (RPE)detachment in the right macula. ERG, EOG and VEP were normal. Serum lactate value was 3.3 mg/dL (normal: 0.63-2.44). Muscle enzymes were normal. Muscle biopsy demonstrated "ragged red fibres" on Gomori-trichome staining. On electron microscopy abnormal aggregation of large and atypical mitochondria were observed. DNA analysis identified the presence of multiple deletions in the mtDNA of a muscle sample, with the common deletion of 4977 bp the most abundant.

Conclusion The retina, in particular RPE, is highly vulnerable to mtDNA defects and decreased oxidative phosphorylation.This is the first report associating KSS to multiple mtDNA deletions and there have been no previous reports of such macular lesion occurring in association with KSS.Ohthalmologists should be aware of the mitochondrial ocular myopathies.

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Retinal dystrophy with macular hyperpigmentation in long chain 3-hydroxy-acyl-CoA dehydrogenase (LCHAD) deficiency

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Purpose LCHAD deficiency is an autosomal recessive inheritance metabolic disorder associated with myopathy, cardiomyopathy, hypoglycaemia, neuropathy and retinal changes as retinitis pigmentosa. It is also related to sudden death. The purpose of this study is to present a case of LCHAD deficiency associated with retinal pigmentary changes.

Methods A 3 year-olds children diagnosed of LCHAD deficiency was examined. Parents were consanguineous. He had several hospitalizations related to hypotonia and lethargia.

Results Fundoscopy examination showed a retinal dystrophy with macular hyperpigmentation and pigmented aggregations and hypopigmentation changes. Both parents and one brother were examined showing no changes in their retinal aspect.

Conclusion Retinal dystrophy in children can be related to metabolic disorders. LCHAD deficiency should always be discarded.

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Benign concentric annular macular dystrophy. Diagnosis in a pediatric case

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Purpose We report a case of a benign concentric annular macular dystrophy diagnosed in childhood during a routine examination. We describe all the ophtlamologic features, complementary tests and the differential diagnosis.

Methods A 5 year old female patient who went to her first ophthalmological examination; her visual acuity (VA) was normal, but we found in the funduiscopy of her right eye an image of annular pigment epithelial atrophy in the macula zone with mottled pigment in the lesion. We appreciated in the left eye funduscopy a less marked alteration of the macular pigment epithelium.

Results The electrophysiological parameters were completely normal, appreciating a bilateral foveal atrophy in the macular optical coherence tomography. We didn't perform perimetry and fluorescein angiography due to early age of the patient. The patient had no relevant family history. This suggests the diagnosis of benign concentric annular macular dystrophy.

Conclusion This is a pattern dystrophy described by Deutman in 1974, with few cases in the literature so far. Inheritance is autosomal dominant and characterized by an hypopigmented ring with respected foveal center. Usually diagnosed in adulthood and initially has a respected VA, so it is important to make a differential diagnosis with other entities to submit a bull's-eye maculopathy, as malarial retinopathy, cone dystrophy and Stargardt disease. May evolve toward greater loss of VA and electroretinogram abnormalities, it is therefore necessary routine checks in these patients.

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Electrophysiologic findings in Greek patients with Stargardt's disease

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Purpose To characterize the clinical and electroretinographic features of Greek patients with Stargardt disease exhibiting mutations in the ABCA4 gene.

Methods We retrospectively reviewed the charts of the patients with the clinical diagnosis of Stargardt disease seen at the department of ophthalmology of the University Hospital of Crete. The diagnosis of Stargardt disease was established based on clinical examination (fundoscopic evidence of retinal flecks) and genetic testing. Parameters evaluated included BCVA, age of onset, findings from fundus photographs, but also findings from the ISCEV standard full field ERG.

Results Twelve patients were included in our study. Median age was 29 years (range: 11-59)and BCVA ranged from 2.0 το 0.2 logMAR. Fundoscopic findings included mild, mottled hypopigmentary changes in one patient, a bull's-eye-appearing macular lesion in four patients and an atrophic macular lesion in seven patients. Of the 12 patients , four patients showed normal scotopic and photopic retinal responses while, eight patients showed abnormal photopic and scotopic function.

Conclusion This is the first report of the electrophysiologic findings of Greek patients with Stargardt disease. Our cohort exhibited a wide range of Electrophysiologic abnormalities. These results provides useful baseline data for the longitudinal monitoring of disease progression.

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Endothelin-1 (ET-1) plasma levels in multiple sclerosis (MS) patients

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Purpose The aim of this study was to estimate endothelin- 1 (ET-1) plasma level in multiple sclerosis patients.

Methods Material was 49 patients (13 males, 36 females, mean age: 40 year, range: 22-62 years) suffering from multiple sclerosis according to McDonalds rule. The healthy controls consisted of 3 males and 28 females (mean age: 38 year, range: 19- 61 years). The protocol was approved by the Ethical Committee of the Postgraduate Medical Education Centre in Warsaw, Poland. Endothelin- 1 (ET-1) plasma levels were determined by ELISA Test (Immuno- Biological Laboratories. Co, Japan with tenderness : 8 fmol/ml). Statistical analysis were performed using the U- Mann- Withney test.

Results Endothelin- 1 (ET-1) plasma levels were significantly decreased in MS patients when compared to age matched controls (P= 0.0075).

Conclusion Statistically significant ET-1 plasma levels difference between examined patients and controls indicates, that vascular dysregulation may exists in MS patients. The outcomes will be discussed.

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Anisometropia and amblyopia in children

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Purpose To asses the quality of life for children with anisometropic amblyopia.

Methods A retrospective study for 53 children (33 girls and 20 boys) performed in ambulatory clinic in 2010. The average age at first diagnosis is 7.1415 ± 2.9317 years old (limits between 2 and 16 years). During the study the average age of children is 9.4943 ± 3.8422 years (limits between 3 and 20 years). Tracking interval is 1 year in 33.95%, between 2 and 5 years in 60.37% and over 5 years in 5.64%. Clinical parameters observed are: sex, age, visual acuity, optical correction, the type of correction (glasses, contact lenses), strabismic deviation and genetic factor.

Results Uncorrected visual acuity average at the right eye is 0.4353 ± 0.3640 and for the left eye is 0.3934 ± 0.3158. Corrected visual acuity average at the right eye is 0.6626 ± 0.3552 and for the left eye is 0.6468 ± 0.3519. Mean objective refraction (in spherical equivalent) at the right eye is -5.8214 ± 4.4651 and -5.52 ± 5.89 for the left eye. The average cylinder value is -0,7783 ± 1,1671 (with a range between maximum = -4.75 and minimum = -1). For 60.37% of patients, cylinder value is less than 0,75. There is a genetic transmission in 23.21% of cases, predominantly in mother (9.43%) and sister (9.43%). In 39.62% of cases there was esotropia. For 11.32% of cases, optical correction was made with contact lenses.

Conclusion 1. As early the diagnosis of anisometropia is made, visual acuity is more easily recovered.2. The average age of diagnosis in the our cases is 7.1415 ± 2.9317, noting that in Romania children are late diagnosed. 3. It is required a collaboration between the pediatrician, an ophthalmologist and the family for an early diagnosis of refraction errors.4. Anisometropic amblyopia can be corrected using contact lenses.

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Retinal nerve fiber layer thickness measured by optical coherence tomography correlates with Expanded Disability Status Scale (EDSS) in multiple sclerosis (MS)

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Purpose To determinate if retinal nerve fiber layer (RNFL) thickness was correlated with Expanded Disability Status Scale (EDSS) score in patients with definite multiple sclerosis (MS)

Methods 74 consecutive patients (extracted from the prospective Lorraine Multiple Sclerosis Registry) were included. A neurological examination with determination of the EDSS score and an ophthalmological examination with visual acuity, visual field testing, and RNFL measurements with optical coherence tomography (OCT3-Carl Zeiss Meditec, Dublin California USA) were performed.

Results Mean age was 44,5 years and 66% were women. EDSS average score was 3. Prior optic neuritis was present in 83% OD and 41% OS. EDSS score was negatively correlated with RNFL thickness (-0,28 p=0.04 OD and -0.2 p<0,1 OS). There were no correlation between RNFL thickness and MS subtype or any of other ophthalmological tests. At the opposite, RNLF thickness was significantly lower among eyes with prior optic neuritis (74 vs 90 OD and 76.8 vs 90.3 micrometers, p<0.01). In addition we did not find any correlation between EDSS and other ophthalmological tests.

Conclusion Our study demonstrates that RNFL thickness is statistically correlated with EDSS score. RNFL thickness measured by OCT appears to be an interesting structural biomarker to detect global axonal loss in MS patients. Larger studies are warranted to confirm if RNFL thickness could serve as a surrogate of EDSS score.

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Simulation and psychosomatic events in ophthalmology

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Purpose The simulation is the act by which one seeks to mimic the symptoms of a disease with some ulterior motive. It occurs in people who seek to obtain compensation (through accident) or a legal or professional advantage.The simulation is to differentiate psychosomatic states requiring expertise neuro-ophthalmological and psychiatric long and complex.

Methods This is a single-center retrospective study, conducted over the past ten years, performed in Picardy to the Eye Clinic St Victor, CHU d'Amiens.We identified 13 patients with suspected nonorganic visual loss.Once these patients are identified, we analyzed their records eye.We illustrate by these observations the diagnostic difficulties in ophthalmology to remove the organic and definitely eliminate nonorganic origin.

Results Among the 13 clinical cases, 8 were referred for low vision, 2 for the deficit of the visual field and 3 for unexplained photophobia. These last three cases were found to be sunglass syndromes.Clinical, electrophysiological, psychosomatic features and testing strategies are discussed.

Conclusion The ophthalmologist may need to see in consultation for patients with eye symptoms whose origin is other than "psychogenic". The challenge is to make the diagnosis with certainty and eliminate organic disease.The ophthalmologist can make use of subjective or objective methods and diagnostic testing that help diagnose simulation.In addition, four pathological traps are often problematic. He must think systematically: Stargardt's disease, optic atrophy, moderate keratoconus beginner, the visual hemi-neglect. Clinical examination and complementary examinations will say will affirm these diseases, which are difficult to diagnose early.

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Frequency of anisocoria in patients with astenopia

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Purpose Anisocoria - an unequal size of pupils. According to literary data, almost 10 % of the healthy population has a difference in diameter of pupils no more than 1 mm in photopic conditions of illumination and in 20 % of cases – in mezopic. Differential diagnostics of physiological and pathological anisocoria frequently causes certain difficulty and in this question the essential help is rendered by modern diagnostic methods of research, including computer pupillography which allow evaluating objectively pupil sizes and its changes on different stimuli.To reveal if anisocoria in patients with astenopia can be found and what kind of anisocoria it is.

Methods 91 patient at the age 7 - 23 y.o. were observed. They had astenopia complaints; some of them had pupil unequal size, no somatic pathology. Pupillography was done by elaborated pupillography devise, blood circulation of the brain was defined by method of computer reoencephalography .

Results 13 % (12) of observed patients had anisocoria. During direct, consensual and accommodative reaction asymmetry of pupil's square have increased on 45,5 %, 51% and 67 % accordingly. Volume of blood supplement in internal carotids had increased values in average on 65 % from age norms. Marked asymmetry was found between right and left a. carotid internal which reached 50 % at 9 patients, and at 3 to 70 % in the given pool.

Conclusion Anisocoria was revealed in 13% of patients with astenopia. Patients who had anisocoria, astenopia and accommodative dysfunction had functional disorders of brain blood circulation.

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Association between non-arteritic anterior ischaemic optic neuropathy and sleep apnoea syndrome

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Purpose To evaluate the association between newly non arteritic anterior optic neuropathy (NAION) and obstructive sleep apnoea syndrome (OSA).

Methods Newly NAION patients underwent polysomnography after a complete clinical examination. The prevalence of OSA in NAION patients was compared to the prevalence previously found in the general population. Other potential risk factors associated with NAION were also identified: cup/disk ratio, optic disk size, hypertension, diabetes, hyperlipidaemia, tobacco smoking and atheromatous lesions of carotid vessels.

Results One hundred twenty one consecutive newly diagnosed patients with NAION were screened consecutively during a 6 year period (2004-2009). Patients with giant cell arteritis (n=9) and patients refusing the polysomnography (n=16) were excluded from the analysis. In the population of 96 NAION patients (61 men and 35 women, mean age 68 ± 9 years, body mass index 27 ± 4 kg/m^2) included in this study, 82 patients (85%) were diagnosed as having OSA (respiratory disturbance index: 39.5 ± 21.8/h). The prevalence of OSA found in this study was significantly higher than that found in an age-matched population (4 -9%, p<0.001) and the risk ratio for a NAION patient to have sleep apnoea was 4.7 compared to the general population (p<0.001). Prevalence of other risk factors was not significantly different between patients with or without OSA.

Conclusion This new prospective study on a large series of NAION patients confirmed that sleep apnoea is the most frequent disorder associated with NAION and should be screened in this population. In addition to a sleep questionnaire, polysomnography should be systematically proposed to patients with NAION.

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Cyclomed® 1% for diagnosis of disturbation of pupillary-accommodative system in patients

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Purpose Differences in pupil reactions in patients with identified accomodative disorders (astenopia, decreasing of visual acuity after loading) in conditions of constant convergence.The aim of the study was to conduct investigation of direct and consensual pupillary reactions on the ashlight, accommodative-convergence reaction on a fixed object with the help of elaborated pupillography device before and after instillation of Cyclomed 1% in both eyes

Methods P – number of heart systoles per min; D – diastolic blood pressure;Cyclomed 1% was applied for diagnoses of pupillary- accommodative system disturbances in 14 patients aged 7–13 with myopia and hypermetropia. We have studied the vision acuity, reserves of accommodation, autorefractometry, pupillography of direct, consensual, pupillary- accommodative reactions before and after instillation of Cyclomed 1% in both eyes. Balance of autonomic nervous system was apriciated by Cerdo index: positive (+) means the prevalence of sympaticus; negative (-) means the prevalance of parasimpaticus.

Results Cyclomed 1% is effective for dilated pupil in 9 patients with sympathycotonic autonomic neuro- system duaring from 1 no 3 days. Cyclomed 1% is not effective in 3 patients with parasympathycotonic autonomic neuro- system.

Conclusion Cyclomed 1% was effective for diagnoses of pupillary- accommodative system disturbances in patients. Cyclomed 1% had been used for myopia decrease and revealing of hypermetropy. Pupillary's diameters were larger in patients with sympathycotonic autonomic neuro- system after using eye-drops of Cyclomed 1%.

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Effects of extreme altitude in retinal and optic nerve head parameters

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Purpose Acute mountain sickness (AMS), the most common form of altitude illness, might represent early-stage high altitude cerebral edema. AMS symptoms are correlated with a higher increase in optic disc swelling. The aims of this study were to measure the peripapillary retinal neve fiber layer (RNFL) thickness and optic nerve head (ONH) parameters following a sojourn to extreme altitude.

Methods Prospective study including three high-altitude expeditions in the Himalayan region. 12 eyes of 6 healthy male experienced climbers underwent baseline and post-expedition ophthalmic examination, including optical coherence tomography (OCT) to measure peripapillary RNFL thickness, ONH parameters, and macular thickness and volume. Lake Louise AMS Scoring System self-report questionnaire estimated AMS severity.

Results Temporal quadrant of peripapillary RNFL showed a significant increased thickness in post-expedition examination (74±17 µm), compared with baseline values (64±12 µm) (p=0.008). Vertical integrated rim area was higher in post-expedition examination (0.65±0.39 mm3). than that in baseline examination (0.51±0.26 mm3) (p=0.012). Likewise, horizontal integrated rim area was significantly higher in post-expedition examination (1.90±0.33 mm2) than that in baseline examination (1.78±0.26 mm2)(p=0.012). The remaining ONH and macular measurements did not show significant differences between baseline and post-expedition examinations.

Conclusion In climbers suffering from AMS, OCT was able to detect subtle increases in the peripapillary RNFL thickness and in some ONH measurements, even in absence of papilledema. These changes might be a sensitive parameter in physiological acclimatization and in the pathogenesis of AMS.

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Relationship between optical coherence tomography and visual evoked potentials in patients with parasellar tumors without chiasmal compression

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Purpose To evaluate the relationship between retinal nerve fiber layer (RNFL) thickness measured by optical coherence tomography (OCT) and visual evoked potentials (VEP) in patients with parasellar tumors without chiasmal compression on MRI examination.

Methods 32 eyes of 16 patients suffering from tumor of sella turcica without any chiasmal compression were included to the study and compared to 59 eyes of 30 healthy patients. Exclusion criteria were any other ophthalmic or general condition that can affect both VEP and OCT measurements. All patients underwent MRI of the head to confirm the diagnosis, retinal nerve fiber thickness measurements with OCT and visual evoked potentials.

Results VEP of patients with parasellar tumors without any chiasmal compression showed no P100 latency prolongation (OD=101,9 ± 6,3ms, OS= 101,2 ± 6,3 ms) in comparison to control group (102,1 ± 4,5ms and 102,5 ± 4,2ms). There was noticed a reduced P100 amplitude in examined patients (OD=10,9 ± 4,8μV, OS=11,6 ± 5,6μV) comparing to healthy subjects (12,3±6,5 μV and 12,1±6,3 μV respectively), however it was not statistically significant (p=0,5 and p=0,8 respectively). Average RNFL thickness in our patients was lower (OD=102,2±8,9μm, OS=101,8 ± 11,5μm) than in control group (104,7 ± 10μm and 104,5 ± 15μm respectively), but the difference was not statistically significant (p=0,8 and p=0,95 respectively).

Conclusion In patients with parasellar tumors without any chiasmal compression both visual evoked potentials and RNFL thickness measurements in OCT showed no significant differences in comparison to healthy subjects.

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Abnormalities of optical coherence tomography and visual evoked potentials in patients with chiasmal compression syndrome

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Purpose To report abnormalities of retinal nerve fiber layer (RNFL) thickness measured by optical coherence tomography (OCT) and visual evoked potentials (VEP) in patients with compressive chiasmal tumors confirmed on MRI examination.

Methods 22 eyes of 12 patients with parasellar tumors causing chiasmal compression syndrome were included to the study and compared to 59 eyes of 30 healthy patients. Exclusion criteria were any other ophthalmic or general condition that can affect both VEP and OCT measurements. All patients underwent MRI of the head to confirm the diagnosis, retinal nerve fiber thickness measurements with OCT and visual evoked potentials examination.

Results Average RNFL thickness in patients with chiasmal compression (OD=96,06 ± 14,2μm, OS=92,4 ± 10,2μm) was significantly lower (p=0.016 and p=0.005) than in normal eyes (OD=104,7 ± 10μm, OS=104,5 ± 15μm respectively). It was noticed also reduced RNFL thickness in nasal quadrants. Visual evoked potentials showed mean P100 latency prolongation in examined patients (OD=112 ± 8,7ms and OS=108,4 ± 7,4ms), which was statistically significant (p<0.001 and p=0.001 respectively) in comparison to control group (103,1± 4,5ms and 102,5 ± 4,2ms respectively).

Conclusion In patients with compressive chiasmal syndrome both RNFL thickness measurements with OCT and visual evoked potentials were significantly changed. These methods provide useful information in the diagnosis of chiasmal lesions.

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Study of retinal nerve fiber layer in obstructive sleep apnea syndrome patients

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Purpose To evaluate the peripapillary retinal nerve fiber layer (RNFL) thickness obtained 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 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 had intraocular pressure less than 21 mmHg and performed at least a reliable standard automated perimetry (SAP). Peripapillary RNFL thicknesses were measured with Cirrus OCT (Carl Zeiss Meditec, Dublin, Ca). After checking for a normal distribution of variables, differences between both groups were tested by Student t test.

Results Age was 50.6 ± 9.3 years in control eyes and 47.8 ± 11.5 years in AOS patients (p = 0.09). Mean deviation of SAP was -0.50 ± 1.0 dB and -1.4± 2.3 dB, in control and AOS patients, respectively (p<0.001). Pattern standard deviation and Visual Field Index (VFI) of SAP were also different between both groups. The RNFL thickness at 7 o'clock position and the average RNFL thickness 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.

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Degeneration of retinal nerve fiber layer in patients with multiple sclerosis. Prospective study with three years follow-up

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Purpose To quantify changes over three years in the retinal nerve fiber layer (RNFL) of patients with multiple sclerosis (MS) and to evaluate if treatments are a protector factor of CFNR degeneration.

Methods One hundred and eighty-eight eyes of 94 MS patients were followed-up during 3 years. All patients underwent a complete ophthalmic examination that included assessment of visual acuity (Snellen chart), colour vision (Ishihara pseudoisochromatic plates), visual field examination, optical coherence tomography (OCT) and visual evoked potentials (VEP). All patients were re-evaluated in a period of 12, 24 and 36 months in order to quantify the changes in the retinal nerve fiber layer (RNFL).

Results Changes were obtained in the RNFL thickness with a 36-month follow-up. There were significant decreases (P<0,05 , t test) in the mean, superior, inferior , nasal and temporal RNFL thickness and macular volume provided by OCT, and in P100 latency of VEP. The greater differences were obtained in the superior and inferior RNFL thickness. Differences were not found between treatments, but untreated patients showed higher degeneration during follow-up in the mean and superior RNFL thickness (p= 0,045 y p=0,024 respectively).

Conclusion Progressive axonal loss can be detected in the optic nerve of MS patients. The analysis of RNFL in OCT can be useful to evaluate MS progression and efficacy of treatments in reduction of axonal degeneration.

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Retinal evaluation by optical coherence tomography in adults with obstructive sleep apnea syndrome

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Purpose Obstructive sleep apnea syndrome (OSAS) is a common sleep and breathing disorder characterized by repeated episodes of hypoxemia.OSAS is associated with persistent neurocognitive injury that may be reflected in structural changes in certain brain regions. The aim of this study is to determine the peripapillary retinal nerve fiber layer (RNFL) thickness, macular thickness and volume by optical coherence tomography (OCT) in adults with OSAS in order to detect axonal injury in this population.

Methods Fourty-nine eyes corresponding to 26 patients (mean age +/- SD: 50.8 +/- 12.7 years; range: 14-75; female/male: 5/21) with newly discovered and previously untreated moderate to severe OSAS (apnea-hypopnea index >15) were compared by OCT with a control group of twenty-two eyes corresponding to 14 age-matched healthy individuals (mean age +/- SD: 52.1 +/- 15.4 years; range: 14-74; female/male: 7/7), measuring peripapillary RNFL thickness, macular thickness and volume, and optic nerve head (ONH) parameters.

Results OSAS patients revealed a significantly lower RNFL thickness in the nasal part of the optic disc (74.6±13.5 µm, range: 47-100) compared to controls (83.2±14.7 µm, range: 56-107) (p=0.015). OSAS patients also showed a decreased macular thickness in the outer nasal ring (250.7±13.6 µm, range: 227-280) compared to controls (265.5±4.9 µm, range: 265-272) (p=0.05). Other OCT measurements did not show any differences.

Conclusion OSAS was associated with a decreased peripapillary RNFL and macular thickness in the nasal quadrants. Therefore, it might be a biomarker of this disease.

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Parkinson's disease and retinal optical coherence tomography

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Purpose The aim of the study was to assess the retinal measurements and optic nerve head (ONH) morphology in patients with Parkinson's disease (PD) and to determine whether there is any correlation among these parameters and the disease´s duration.

Methods Thirty patients affected by PD (mean age 67,3 ± 8,4; range: 49 - 83) were compared with 28 age-matched controls. In all subjects, peripapillary retinal nerve fiber layer (RNFL) thickness, ONH measurements, and macular thickness and volume were measured by optical coherence tomography (OCT).

Results PD patients showed a statistically significant reduction of the overall peripapillary RNFL thickness [95±9µm, range: 73-117] compared with those values observed in control eyes [103±7µm, range:87-117] (p<0.0001, Mann-Whitney U test). Furthermore, a statistically significant reduction of RNFL thickness was observed in nasal [74±20µm, range:18-114](p=0.004), inferior [118±14µm, range:88-147] (p<0.0001) and superior quadrants [120±13µm, range:88-145] in PD patients when compared with controls [84±14µm, range:54-106], [132±14µm, range:101-165] and [125±13µm, range:101-151] respectively (p=0.023; Mann-Whitney U test). The temporal peripapillary quadrant, ONH measurements, macular thickness and volume did not reveal any statistically significant differences between both groups.

Conclusion PD patients show a decreased peripapillary RNFL thickness evaluated by OCT. We also observe that the further evolution of PD, the lower average peripapillary RNFL thickness. Our results suggest that axonal degeneration could be present in the retina of PD patients and that RNFL thickness measured by OCT could be used as a biomarker for early diagnosis and for monitoring PD progression.

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Retinal nerve fiber layer thickness measured by

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Purpose Our study aims to assess retinal nerve fiber layer (RNFL) thickness in patients affected by schizophrenia

Methods Ten schizophrenic patients were enrolled.They were compared with 10 age-matched controls. In all subjects, optic nerve head measurements, peripapillary RNFL thickness, macular thickness and volume were measured by optical coherence tomography.

Results Schizophrenic patients showed an statistically significant reduction of the overall RNFL thickness compared with those values observed in control eyes. We also observed reduced peripapillary RNFL thickness in nasal quadrant in schizophrenic patients when compared with controls. The remaining peripapillary RNFL quadrants, macular thickness and volume did not reveal differences between both groups. No statistically significant differences were observed between control group and schizophrenia patients with regard to ONH measurements, macular thickness and volume.

Conclusion Schizophrenia patients had a reduction of peripapillary RNFL thickness evaluated by OCT. To our knowledge, neither reduced RNFL thickness nor macular thickness and volume have been previously documented in patients diagnosed with schizophrenia. These findings suggest that neuronal degeneration could be present in the retina of schizophrenic patients as previously observed in neurodegenerative disorders.

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Morphological changes in peripapillary nerve fiber in multiple sclerosis patients

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Purpose The aim of this study was to estimate the incidence of lesions in the peripapillary retinal nerve fiber layer in population of patients suffering from sclerosis multiplex

Methods Material of this study consists of 57 subjects (114 eyes) suffering from multiple sclerosis, in observation in our Department of Ophthalmology. In all patients spectral optical coherence tomography of the peripapillary retinal nerve fiber layer was performed by 3D- OCT 1000 (Topcon), glaucoma module, circular around the optical nerve head. Obtained data was analyzed, taking into consideration thickness of the nerve fiber layer in four sectors around the optic nerve head (ONH) and normative database classification (normal, borderline, outside normal limits). Outcomes were classified as borderline or outside normal limits when at least one eye was borderline or outside normal limits.

Results In the obtained OCT results the following data was collected: normal group: 36 (63.2%), borderline group: 15 (26.3%) and outside normal group: 6 (10.5%). The particular numerical data of nerve fiber layer thickness in specific groups will be presented.

Conclusion The percentage of patients with borderline or outside normal results of the nerve fiber layer thickness in the study group was significantly higher than in healthy population, e.g. in persons without glaucoma or sclerosis multiplex. This may suggest the common pathogenetical background of both diseases.

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Frequency of glaucomatous optic neuropathy (GON) in multiple sclerosis patients

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Purpose The aim of this study was to estimate the incidence of structural glaucomatous optic neuropathy (GON) in multiple sclerosis patients.

Methods Material of this study consists of 49 subjects suffering from multiple sclerosis. In all patients scanning laser tomography – HRT (Heidelberg Retina Tomograph), spectral optical coherence tomography of the peripapillary retinal nerve fiber layer (OCT- 3D 1000, Topcon) and clinical stereoexamination was performed in purpose to GON discovering.

Results At least in one eye, GON was observed in 16 (32%) multiple sclerosis patients in HRT(according to Mickelberg classification). 9 patients (18%) with glaucomatous structural changes in HRT had borderline or outside normal results of the nerve fiber layer thickness in OCT. Between these, 4 patients (8%) was demonstrated of GON picture in clinical steroexamination.

Conclusion Outcomes of this study indicate higher frequency of incidence of structural glaucoma changes in multiple sclerosis patients than in normal population.

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Optical coherence tomography in the evaluation of patients with mild cognitive impairment of amnestic type

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Purpose Some cases of amnestic mild cognitive impairment (aMCI) represent the earliest clinically detectable phase of the trajectory toward dementia and Alzheimer's disease (AD).To our knowledge, neither macular retinal thickness nor macular volume have been previously documented in vivo in aMCI patients. The aims of this study were to determine the differences in the retinal nerve fiber layer (RNFL) thickness between aMCI patients and control subjects.

Methods We compared by optical coherence tomography (OCT) 40 eyes of twenty aMCI patients (15 males and 5 females, mean age: 70.4±8.9 years; range: 50-88) to 40 eyes from twenty age-matched healthy controls (10 males and 10 females, mean age: 69.8±6.3 years; range: 58-85), measuring peripapillary RNFL thickness, macular thickness and volume.

Results Overall RNFL thickness was within 94.9 and 128.8 µm (mean: 107.1 ± 7.2 µm) in control subjects and within 32.0 and 102.1 µm (mean: 84.5 ± 11.4 µm) in a-MCI patients. The difference was statistically significant (p=0.0001, Mann-Whitney U test). Peripapillary RNFL thickness evaluated in all the separate quadrants (superior, inferior, nasal and temporal) of aMCI patients was also significantly reduced when compared with that of control subjects. Nevertheless, macular thickness and volume are increased in aMCI patients compared to control subjects. We found no significant correlation between Mini-Mental State Examination (MMSE) scores and OCT values.

Conclusion These findings suggest that neuronal degeneration could be present in the retina of aMCI patients as previously observed in patients with AD.

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The role of suppression in amblyopia

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Purpose This study had three main aims; to assess the degree of suppression in patients with strabismic, anisometropic and mixed amblyopia, to establish the relationship between suppression and the degree of amblyopia and to compare the degree of suppression across the clinical sub-groups within our sample.

Methods Using both standard measures of suppression (Bagolini lenses and ND filters, Worth 4 dots) and a new approach involving the measurement of dichoptic motion thresholds under conditions of variable interocular contrast, we quantified the degree of suppression in 43 amblyopic patients with strabismus, anisometropia or a combination of both.

Results There was good agreement between the quantitative measures of suppression made using the new dichoptic motion threshold technique and measurements made using standard clinical techniques (Bagolini lenses and ND filters, Worth 4 dots). The degree of suppression was found to directly correlate with the degree of amblyopia within our clinical sample whereby stronger suppression was associated with a greater interocular acuity difference and poorer stereoacuity. Suppression was not related to the type or angle of strabismus when this was present or the previous treatment history.

Conclusion These results suggest that suppression may have a primary role in the amblyopia syndrome and therefore have implications for the treatment of amblyopia.

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Prevalence and risk factors of near decompensated heterophoria in a population of university students

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Purpose The aim of this study was to determine the prevalence and risk factors of near decompensated heterophoria in a population of university students.

Methods In a randomized study, 406 students of six schools of Mashhad University of Medical Sciences were selected and classified into symptomatic and non symptomatic groups. Visual acuity (VA), near point of convergence (NPC), Near point of accommodation (NPA), dissociated and associated phoria, suppression, stereopsis, accommodative facility, relative accommodation, accommodative convergence/ accommodation (AC/A ratio and fusional reserves were measured in two groups. The data were analysed by using SPSS software, version 11.5o.

Results The prevalence of symptoms and binocular disorders in students were 41.6% and 21.8% respectively . Of the students,9.1% had near decompensated heterophoria (heterophoria with symptoms). The results of this study showed that VA, NPC, NPA, heterophoria, stereopsis, accommodative facility, relative accommodation, AC/A ratio and fusional reserves were different in symptomatic and asymptomatic subjects and were worsen in students with decompensated heterophoria ($P<0.05$).

Conclusion The results of this study indicated relatively high prevalence of symptomatic students, binocular dysfunction and decompensated heterophoria in university students. Students with decompensated heterophoria failed in more visual skills which can be risk factors for decompensating the heterophoria.

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Peculiarities of accommodative esotropia

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Purpose To study the visual functions and the state of accommodation–convergence–papillary system (ACPS) in children with different forms of accommodative esotropia(AE)

Methods Except of the standard ophthalmological examination the pupillography was performed in 88 patients aged 6-18 years with refractive AE (45), nonrefractive AE (31), combinated AE (12)

Results With optical correction the visual acuity below 0,3 took place of 55,8±7,6% patients with refractive AE, 42,0±18,7% cases with combinated AE, 33,3±9,1% children with nonrefractive AE. Convergence was normal in all cases of refractive and nonrefractive AE, but was weak in 42,8±18,7% patients with combinated AE. Fusion in haploscopic condition was absent in 65,1±7,3% cases of refractive AE, 51,9±9,6% patients with nonrefractive AE and in all cases of combinated AE. Worth´s four dot test showed monocular vision in 88,4±4,9% cases of refractive AE, 85,1±13,2% of combinated AE and 66,7±17,1% of nonrefractive AE. Accommodative insufficiency was inherent to all patients.Pupillography showed narrowing of pupils in all patients in comparison with healthy children. Pupil reaction to light was weakened considerably. The latent periods of the direct, consensual pupillary reaction to light and the latent periods of pupillary reaction after light stimulation and after convergences weakening were increased more than three times as in healthy children.

Conclusion Besides the already known differences in the state of refraction and the value of index AC/A, the These types of AE differ from each other in such functions as visual acuity, fusion power, binocular vision, convergence. Disturbances of pupillary reactions indicate on reduction of lability, increase ACPS's passivity due to functional changes in brainstem.

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Strabismus and amblyopia in Iranian schoolchildren

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Purpose To determine the prevalence of amblyopia and strabismus among the population of school children mashahd, Iran

Methods In a cross-sectional study with cluster sampling, 2510 school children were selected from schools of district one in Mashhad. Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) were recorded for each participant. Amblyopia was distinguished as a reduction of BCVA to 20/30 or less in one eye or 2-line interocular optotype acuity differences in the absence of pathological causes.

Results Of the 2510 selected population, 2150 school children participated (response rate of 85.6%). The prevalence of amblyopia was 1.9% (95% CI: 0.94 - 2.90); 2.1% (95% CI: 0.10 - 3.16) in girls and 1.7% (95% CI: 0.30 - 3.12) in boys (P=0.620). Among myopic, hyperopic andastigmatic students, 3.7%, 27.8% and 6.5% had amblyopia respectively (p<0.001). the causes of amblyopia were 65.9%, 24.4% and 9.8% anisometropia, strabismus and Isoametropic respectively. The prevalence of strabismus was 3.1% (95% CI, 1.3% to 4.3%); 4.2% (95% CI, 3.05 to 5.7%) in girls, and 2.0% (1.3% to 2.9%) in boys(P=0.0011). Strabismus was significantly more prevalent among hyperopic students compared to myopic ones.

Conclusion Results of the present study indicate that, the prevalence rate of amblyopia was in the mid range and the prevalence of strabismus was relatively high. Since refractive errors, especially hyperopia, are responsible for some cases of strabismus, a timely diagnosis andtreatment can prevent a high percentage of cases with amblyopia and strabismus in children.

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Entropion as a complication of the frontalis muscle flap direct advancement

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Purpose The use of the frontalis muscle in a direct attachment is an alternative to the traditional techniques of frontalis muscle flap advancement. This new variant, which is considered the most physiological, shows better functional results, but it may associate entropion as adverse effect.

Methods Through a unique incision on the eyelid crease or making another incision on the superciliar area, a flap of frontalis muscle is created and attached to the tarsal plate with a non-resorbable suture. It is important to attach the flap to the upper third of the tarsal plate for a correct elevation of the eyelid. A lower union otherwise could create long term complications principally residuary progressive entropion, which until now was only seen after traditional techniques of aponeurosis reinsertion of elevator muscle. We present two case reports showing severe ptosis after frontalis muscle flap direct suspension in which a medium third of the tarsal plate union was performed.

Results Both patients showed progressive entropion which needed correction through surgery.

Conclusion To prevent entropion in the frontalis muscle flap direct advancement, the muscle flap should be attached to the upper third of the tarsal plate, which allows physiological distribution of the tractional force in spite of maintaining the vertical vector, preventing the eyelid margin inversion.

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Foreign body granulomas after fadenoperation: a review of seven cases

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Purpose To evaluate and to describe our series of foreign body granulomas and granulation tissue after fadenoperation.

Methods Retrospective monocentric study, from 1997 to 2010, conducted on all the patients who developed a foreign body granuloma or a foreign body granulation tissue histologically proven, after fadenoperation surgery.

Results Seven patients (3 to 10 years old) were included. Incidence of granuloma is evaluated at 1,95 ‰ among all our surgeries of strabismus. All the patients were children. All had been operated of fadenoperation surgery combined with medial rectus recession. Delay of granulomatous formation occurence ranged from 5 months to 5 years. All the patients underwent surgical treatment of granulomatous formations with pathological analysis. We have observed three cases of recurrence after initial surgical removal.

Conclusion Non resorbable suture, ischemia induced by fadenoperation and surgery traumatism may lead to development of subclinical granulomas. Suture extrusion, cause or consequence of granulomatous phenomenon could explain late delay of clinical expression. Granulomas occurred always when both of recession and fadenoperation were realized. This can be explained by increased local inflammation and maybe by the presence of two kinds of suture. Despite surgical treatment, 3 recurrences occured, probably linked to exogenous material persistence within the surgical site. To reduce and to prevent the occurrence of granulomas, using a resorbable suture may be interesting.

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Ocular manifestations in Duane radial ray syndrome

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Purpose To present two related cases with Duane Radial Ray syndrome, ophthalmologic affectation with Duane syndrome and retinal nerve fiber layer (RNFL) hypoplasia.

Methods The first patient (15-years woman) showed Duane syndrome, reduction of visual acuity and pale optic discs. The other patient (12 years woman) presented Duane malformation. Both patients underwent a complete ophthalmologic evaluation with best corrected visual acuity, visual field examination, optical coherence tomography (OCT), scanning laser polarimetry, visual evoked potentials, pattern electroretinogram, and a genetic study.

Results OCT and scanning laser polarimetry showed diffuse decrease of RNFL thickness, mainly left eye, retaining the typical morphology as double hump, in patient 1. Neurophysiology evaluation showed decrease in amplitudes of visual evoked potentials and pattern electroretinogram, and increased latency of P100 component. Neuro-ophthalmologic exploration in patient 2 showed subclinical reduction of RNFL average thickness provided by OCT and increase of P50 and N95 latency by pattern electroretinogram. RNFL average thickness presents reduced scores in both patients, but without glaucomatous morphology.

Conclusion Duane radial ray syndrome, also named Okihiro syndrome, may affect retinal nerve fiber layer development and visual acuity.

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Unilateral mydriasis revealing a neurovascular conflict: a case report

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Purpose To demonstrate a neuro-vascular conflict between the right posterior communicating artery and oculomotor nerve (CN III) revealed by an isolated unilateral mydriasis.

Methods (patient): A right mydriasis without ophtalmoplegia or ptosis was discovered in a 41 years old patient complaining of blurred vision for 6 months. Direct, consensual and accommodation reflexes were absent in the right eye. Slit lamp and fundus examination were strictly normal in both eyes. Cerebral tomography was also normal. After complete ophthalmologic examination (excluding Adie's pupil, with pilocarpine diluted test) and neurological examination, we concluded to a partial CN III palsy reaching the intrinsic component and she underwent an MRI examination including FIESTA weighted images.

Results MRI demonstrated the compression of the right CN III by the right posterior communicating cerebral artery, on its superior median part. Imaging criteria of neuro-vascular conflict were fullfilled: a direct contact, at right angle, at the level of the first millimetres of the nerve and displacing its course. The results of others clinic and paraclinic investigations did not revealed abnormalities, specifically no infectious or inflammatory diseases.

Conclusion We recommend performing an MRI in patients with an isolated and persistent mydriasis.

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Unilateral ischemic optic neuropathy by tacrolimus after liver transplantation

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Purpose To report a case of unilateral optic neuropathy in a patient on treatment with tacrolimus (Prograf®) after liver transplantation.

Methods Case report in a 53-years old woman receiving tacrolimus after liver transplantation, serial neuroophtalmologic exams were performed.

Results 53 years- old woman treated with tacrolimus (Progra®f) after liver transplantation, seen in our clinic concerned by the loss of vision in left eye after several previous chapters of amurosis fugax.She was made a carotid doppler (unaltered) and vertebrobasilar (also normal).We ask that RMN detected mild variable Dandy-Walker, subcortical atrophy, sylvian gaps in deep white matter of probable vascular origin (would microbleeds) and possible osmotic myelinolysis. PCR was elevated and VSG, consistent with pathology data accompanying the patient. Blood analysis showed alterations also be explained by what was happening.Vitamin B12 and folic acid were normal.Serologic tests for Brucella, Borrelia, syphilis, Epstein-Barr virus, cytomegalovirus, herpes simplex and zoster were negative.Normal coagulation. Following these studies was diagnosed by non-arteritic NOIA and tacrolimus treatment was added to adiro® 100 mg.The vision was 20/20 in right eye and amaurosis (no light perception) in OI. Had a pupillary afferent deffect in left eye. PIO of 15 mmHg in both eyes. Camera anterior large and transparent crystal. Fundus slight optic nerve pallor in the left eye.OCT with great thinning of the RNFL in the left eye and normal right eye

Conclusion Tacrolimus is an immunosuppressive agent useful in hepatic transplantation which may be associated with ischemic optic atrophy.

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Loss of visual acuity following bariatric surgery for morbid obesity in three sisters

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Purpose Bariatric surgery are various weight loss surgery options, that can originate deficiencies of Vitamin A, D and K as well as iron-deficiency anemia and diminution of calcium and zinc. These nutricional changes can generate a loss of visual acuity after the surgical treatment. The purpose of this study is to describe three cases of visual acuity loss after bariatric surgery.

Methods Three sisters underwent a bariatric surgery for morbid obesity. All of them complained visual acuity loss months after surgery.

Results All the patients shown optic nerve atrophy. Biochemical alterations were presented in all of them, showing diminution of both liposoluble and hydrosoluble vitamins..

Conclusion Bariatric surgery could generate visual acuity loss. Vitamin deficiency must be controlled to avoid retinal and optic nerve changes and atrophy.

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A case of chronic relapsing inflammatory optic neuropathy (CRION)

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Purpose The chronic relapsing inflammatory optic neuropathy (CRION) is a recurrent optic neuropathy not associated with any demyelinating or systemic desease, characterized by the need for prolonged immunosuppressive therapy to prevent relapse.

Methods We report the case of a 32 year old man who presented three episodes of optic neuritis in the left eye over a period of 8 months. Each episode remitted quickly with intravenous steroids and resorted after gradual withdrawal thereof. The initial visual acuity in left eye was counting fingers, had relative afferent pupillary defect and diffuse edema of the optic nerve. All systemic examinations were normal (analytics, and serology tests, imaging studies, lupus anticoagulant, ECA and autoimmunity tests).

Results After CRION suspected, corticosteroid treatment was decided at a dose of 1mg/kg/day maintained in decreasing doses associated with azathioprine, and response to treatment was favorable, with no new episodes. Actually, visual acuity is 7/10 , there are palidness optic disc and inferior visual field lost in perimetry due to optic neuritis.

Conclusion CRION is a recurrent optic neuritis, corticoid dependent, not associated with any neurological deficit or autoimmune disease. Severe visual loss, associated with persistence of pain after onset of visual loss and frequent recurrences should make us suspect this entity.

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Is tractography coupled with the retinotopy obtained by functional magnetic resonance imaging feasible at 1,5 Tesla to study the optic radiations?

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Purpose to evaluate the feasibility and to compare the results of different algorithms of tractography by diffusion weighted (DWI) magnetic resonance imaging (MRI) coupled with retinotopy by functional MRI (fMRI) at 1,5 tesla, to study the optic radiations.

Methods one healthy subject had: (1) a fMRI with visual stimulations by sectorial contrast alternating checkerboard patterns (2) a DWI MRI and (3) anatomical acquisitions. Optic radiations were tracked by both deterministic and probabilistic algorithms, using anatomical and functional data.

Results the optic radiations reconstructions agreed with literature data. The deterministic reconstruction algorithm is conceivable in current practice, and can correctly tracked the optic radiations with a good view of the Meyer loop, unlike the probabilistic reconstruction algorithm, whose post treatment is long and results disappointing.

Conclusion tractography coupled with the retinotopy is feasible at 1,5 tesla to study the optic radiations with deterministic reconstruction algorithm but not with probabilistic algorithm.

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An unusual optic neuropathy: interest of imaging and conservative treatment

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Purpose Interest of imaging of an unusual optic neuropathy case report and to perform a conservative treatment.

Methods A 17 year-old girl was referred for a 3 months progressive visual loss. No personal or family history was noticed. At ocular examination right VA was 3/10 P14 OR and 10/10 P2 OS. At fundus optic disc was discolored with optic neuropathy. At examination she showed a large unilateral visual field loss possibly mimicking ocular manifestation of multiple sclerosis. OCT was performed. MR Imaging revealed a high signal and a right optic nerve sheath meningioma, with unilateral optic disc mild atrophy. Stereotactic fractionated radiotherapy treatment was decided and applied twice at one month interval. After 3 years follow-up tumor was non active with a visual improvement at 4/10 P5 OR.

Results This clinical presentation of an optic neuropathy can mimic ocular defect in multiple sclerosis but the imaging allow the diagnosis of the meningioma. Saeed study underlines the interest of stereotactic treatment in optic nerve sheath meningioma. A conservative treatment is of interest and visual improvement of our case was obtained with stable tumor.

Conclusion Unusual presentation of optic neuropathy systematically must benefit of an imaging with accurate definition. Primary radiotherapy for patients with optic nerve sheath meningioma is associated with long-term improvement of visual acuity and few adverse effects.

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The distribution of retinal thickness in healthy eyes and its use in the objective analysis of optical coherence tomography (OCT) scans

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Purpose OCT provides quantitative data but interpretation remains subjective. We have developed a statistical method to detect abnormal retinal thickness in OCT scans.

Methods High resolution macula topography maps, which were identified as normal by a retinal specialist, were exported from a spectral domain OCT/SLO machine. A Matlab® algorithm was written to perform image registration to a model macula. A reference map was constructed for each eye consisting of mean thickness and standard deviation at each point. Kurtosis and skewness were calculated. To analyse pathological scans areas > 2 SD from the mean were deemed abnormal.

Results 151 left eye scans and 112 right eye scans were analysed. The mean foveal thickness was 190.7 microns (SD 1.8) for the left and 189.2 microns (SD 1.6) for the right. Skewness and kurtosis were assessed over the macula. The mean skewness was 0.34 (-0.39 to 0.39) for the left and -0.0154 (-0.45 to +0.45) for the right. The mean kurtosis was 0.95 (SE 0.39, range -0.8 to 0.8) for the left and -0.0324 (SE 0.45, range -0.90 to 0.90) for the right.20 abnormal scans from patients with diabetes were aligned with the reference maps. The mean percentage area of abnormality >2 SD was 28%, 2-3 SD was 8%, 3-5 SD was 7%, 5-10 SD was 8% and >10 SD 5%. There was a linear correlation of area >2 SD with areas 3-5 SD (R2 = 0.65) and 5-10 SD (R2 = 0.73) indicating that larger lesion area is associated with greater oedema.

Conclusion The data show a normal distribution of retinal thickness in healthy eyes. A quantified image of statistical abnormality in a diseased eye can be generated which is helpful for standardising interpretation.

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Cytokine concentration in aqueous humor of eyes with diabetic macular edema

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Purpose To measure cytokine concentrations in aqueous humor of eyes with diffuse diabetic macular edema.

Methods The study included a study group of 23 patients with diffuse diabetic macular edema and a control group of 22 patients undergoing cataract surgery were compared. Cytokine concentrations were measured in aqueous humor samples using a Luminex xMAP suspension array technology.

Results In the study group as compared to the control group, significantly higher concentrations were measured for epidermal growth factor (EGF)(P<0.001), human growth factor (HGF)(P<0.001), intercellular adhesion molecule-1 (ICAM1) (P<0.001), interleukin 1a2 (IL1a2)(P=0.04), interleukin 6 (IL6)(P=0.001), interleukin 8 (IL 8)(P<0.001), interferon-gamma induced protein (IP10)(P=0.004), monocyte chemoattractant protein-1 (MCP-1)(P<0.001), monokine induced by interferon gamma (MIG)(P<0.001), matrix metalloproteinase 1 (MMP1)(P=0.02), matrix metalloproteinase 9 (MMP9)(P<0.001), plasminogen activator inhibitor 1 (PAI1) (P<0.001), placenta growth factor (PlGF) (P<0.001), tissue growth factor beta (TGF-ß) (P=0.003), vascular cell adhesion molecule (VCAM)(P<0.001), and vascular endothelial growth factor (VEGF)(P<0.001). Retinal macula thickness was significantly associated with the concentrations of the EGF, ICAM1, IL3, IL6, IL8, MCP-1, MIG, MMP9, TGF-ß, PlGF, VCAM, and VEGF. In multivariate analysis, macular thickness remained to be significantly associated with the concentration of ICAM1 (P=0.006;r=0.40).

Conclusion Numerous cytokines are associated with the presence and the amount of diabetic macular edema. Among these cytokines, ICAM1 was the most significantly associated with the disease parameters.

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Experimental study of distinguishing small retinal haemorrhages from dust artefacts using HLS colour space

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Purpose Many ophthalmologists consider it difficult to distinguish small retinal heamorrhages of early diabetic retinopathy from dust artefacts on fundus cameras.

Methods Photographs of the fundi of five patients with diabetic retinopathy were taken. Paint Shop Pro v. 8.0 was used to measure HLS colour spaces of both hemorrhagic area and the area around the heamorrhage at two locations of each photograph. We constructed the experimental device, which has an illumination optical system and a photographic optical system separated by a mirror having a hole with 4 mm diameter. The device consists of a canon EOS 50D camera, an EF 50mm f/1.8-2 camera lens, a Speedlite 270EX flash, an object lens, four double-convex lenses, two aperture stops and four artificial eyes. The eye ground is a half sphere made of polythene terephthalate painted by four mat colour sprays: red, white brown, ochre and yellow. Five fragments of house dust on the object lens were photographed under each artificial eye. Paint Shop Pro 8.0 was used to measure the HLS colour spaces of dust artefacts and the area around the artefacts.

Results The evaluation space of house dust was calculated using the HLS data obtained from the experimental device. Hue was red, −7.1±16.9; white brown, −5.7±7.4; yellow, 3.4±1.6 and ochre 0.3±2.3. Lightness was red, 10.7±3.4; yellow, 9.9±3.0; ochre, 9.5±1.8 and white brown, 8.2±2.1. Saturation was red, 25.5±23.5; white brown, 22.6±12.2; yellow, 15.1±12.3 and ochre, 5.0±2.8.

Conclusion The lightness of the HLS colour space helped in distinguishing dust from heamorrhage in all colour spectra. However, hue and saturation could distinguish dust from heamorrhage only under certain conditions.

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New cyanine dye for ILM staining

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Purpose To investigate the biocompatibility and staining properties of a new cyanine dye (DSS: 3,3´-Di-(4-sulfobutyl)-1,1,1´,1´-tetramethyl-di-1H-benz[e] indocarbocyanine).

Methods Dye concentrations of 0.5%, 0.25% and 0.1% were evaluated (osmolarity between 290 and 295 mOsm). Toxicity was assessed using a colorimetric test measuring the inhibition of ARPE 19 cell, human primary RPE cell and human Müller cell proliferation. Exposure time was 30, 60, 120 and 300 seconds. Indocyanine green (ICG) (0.5%, 0.25% and 0.1%) served as a control. Besides staining of porcine and human lens capsule, internal limiting membrane (ILM)-staining was assessed by applying 0.25% and 0.5% DSS over the macula in two human post-mortem eyes.

Results The dye DSS did not reveal any toxicity on ARPE-19, primary human RPE cell and human Müller cells proliferation in all concentrations and exposure times investigated. The absorption maximum is found at 591 nm, the even more bathochromic fluorescence proceeds with a common Stokes' shift where maxima at 620 and 660 nm with a quantum yield of 32% were found. The fluorescence is sufficiently hypsochromic and the fluorescence quantum yield high enough for an easy visual detection. The contrast and staining properties at the ILM was excellent because of matched optical properties and allowed for a controlled removal of the ILM during surgery. No penetration into deeper retinal layers was noted.

Conclusion Our results indicate that this new cyanine dye DSS may represent an alternative for ILM staining due to its matched absorption concerning visibility and fluorescence qualities as well as its good biocompatibility. The dye is superior compared with ICG where there is no matching of the UV/Vis spectra.

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Acute intraocular pressure after intravitreal injections, what is the mechanism?

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Purpose To evaluate the mechanism of acute intraocular hypertension after intravitreal injections (IVI) of anti-VEGF therapies.

Methods A prospective study was performed to evaluate the IOP increase immediately after IVI of 0,05ml ranibizumab in 50 patients. We have also studied the correlation between IOP immediately after IVI and axial length, then with lens status. Moreover we have analysed the anterior chamber anatomic changes (anterior chamber volume and irido corneal angle), measures were taken before and 5mn after IVI by scheimpflug camera from Oculyzer® (Alcon).

Results The IOP peak immediately after IVI was higher than 45 mmHg in 67,3% of patients. It was transient, decreasing after 15mn and returning to baseline in all patient after 45 mn. We found no statistically significant difference between pseudophakic eyes (n=30) and phakic eyes (n=20, p=0.80). No correlation was found between the axial length and the IOP spike (r=0.042, p=0,85). The mean change for the anterior chamber volume (ACV) is mild (0,33 mm3).The ACV increased in pseudophakic eyes (+15,64 mm3, +7,7%), but decreased in the phakic eyes (-7,24 mm3, -4,4%). The mean change for irido corneal angle (ICA) is not significant (-1,61°), it decreases in phakic eyes (-2,97°, -7,2%) versus a quite neutral effect in pseudophakic eyes (+0,78°, + 1,5%).

Conclusion The IOP spike is not correlated either with axial lengh or with lens status. ACV and ICA variations are different according to the lens status but remains mild. These results enhance the importance of the scleral biomechanical properties, and highlight an unpredictable peak. This could be an argument to propose a systematic prophylactic hypotensive treatment before IVI.

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Intravitreal bevacizumab (Avastin®) in treating macular oedema associated with central retinal vein occlusion

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Purpose To report the response following intravitreal bevacizumab(IVB) therapy in macula oedema associated with central retinal vein occlusion(CRVO).

Methods Clinic charts of consecutive patients with macula oedema secondary to CRVO were retrospectively reviewed. Data from ophthalmological examination, Visual acuity, OCT (optical coherence tomography) fundus fluorescein angiography were recorded. All patient received one intravitreal bevacizumab 1.25mg/0.05ml at baseline and retreatment was on prn (pro re nata) basis.

Results Twenty-five eyes of 25 eyes of 25 patients with a mean age of 73.1±12.1 were reviewed. Average time between diagnosis and initiation of IVB was 9.3±8.2weeks(range=0-52weeks). Follow up was 12 months. All patients were treatment naïve. Mean baseline visual acuity and central retinal thickness(CRT) was 32.5±7.2ETDRS letters and 625±240µ respectively. The mean change in in vision at month 1, 3, 6 and 12 was + 4.5(p=0.10), +9.6(0.051), +11(p=0.062) and 13.6(p=0.049) ETDRS letters respectively. The mean change in CRT from baseline at month one was -209µ(p=0.056) and -335µ(p=0.009), -263µ(p=0.03) and -258µ(p=0.022) at month 3, 6 and 12 respectively. Mean number of injection was 3.4 at month 6 and 5.2 at month 12. There were no complications recorded.

Conclusion Treatment of macula oedema secondary to CRVO with IVB resulted in improvement of visual acuity and significant decrease in macula oedema over 12 follow up.

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The dexamethasone drug delivery system for the treatment of retinal venous occlusion with cystoid macular edema

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Purpose To report our case report with sustained-release dexamethasone 0.7 mg intravitreal implant (Ozurdex®; Allergan, Inc., Irvine, CA) in retinal vein occlusion with macular edema.

Methods A 67-years old female patient with recent retinal vein occlusion with macular edema treated with sustained-release dexamethasone 0.7 mg intravitreal implant was performed. On initial examination, the right best-corrected visual acuity (BCVA) was 0,3. Right fundoscopy revealed dilatation and tortuosity of the retinal veins and 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.

Results The patient was treated with two intravitreal ranibizumab injections but two moths later the visual acuity was 0,2 and then we treated with sustained-release dexamethasone 0.7 mg intravitreal implant and six moths later the right BCVA was improved to 0.7. Funduscopy and optical coherence tomography confirmed reduction of edema and tolerability of the implant was assessed.

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. 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

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Retinal vein occlusion: treatment by series of 3 ranibizumab IVT

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Purpose To evaluate the functional, anatomical, vascular flow, anti- exudative effects of intravitreal injections(IVT) for Retinal Vein Occlusion ,by a protocol with 3 Ranibizumab IVT series, and the recurrences frequency at 3 years evolution.

Methods 17 eyes of 17 patients with Retinal Vein Occlusion received intravitreous Ranibizumab, 3 times, every 4 weeks in an inductive treatment. The next injections depended on the follow-up results and were done by series of 3. First and 2 months' interval follow-up exams included ETDRS visual acuity (VA), complete ophthalmic examination, optical coherence tomography (OCT), and fluorescein angiography (FA). VA and OCT were done before each IVT. We want to evaluate the incidence of this protocol on the exudation and frequency of recurrence and so on the number of IVT needed.

Results VA improved in 16 eyes, stabilized in 1. Diffuse edema was 53% normalised ,total thickness was 60% less in the average follow-up, cysts 100% disappeared in 75% cases, in 60% were diminished in size , volume and number, by OCT. At Angiography, no leakage in 65% cases, cystoids macular edema disappeared, vascular abnormalities diminished. Most of patients had good functional, anatomical results, with few IVT needed, no scars in the retina. Inductive treatment was sufficient in 5 cases, needed 2 IVT Series in 27% cases, failed in no cases. This protocol was compared ,discussed .

Conclusion The results with improved visual acuity, reduction of exudation at OCT, vessel's leakage and structure normalized at FA, suggest this protocol, with series of 3 Ranibizumab IVT, seems effective, more retinal protective. This protocol seems attractive, specific indication criteria and its indication must be optimized.

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Responce to intravitreal bevacizumab for macular edema following central retinal vein occlusion in patients with pseudoexfoliation syndrome

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Purpose To evaluate efficacy of intravitreal 1.25mg Bevacizumab in patients with pseudoexfoliation sindrome (PEX) and macular edema (ME) secondary to central or branch retinal vein occlusion.

Methods A retrospective study was performed on 168 patients with central retinal vein occlusion (CRVO) and branch retinal vein obstruction (BRVO) with significant decreased visual acuity (VA) due to ME. To evaluate the role of 1.25mg bevacizumab in patients with PEX, were created two groups: the first group – 21 patients with CRVO or BRVO and clinical diagnosis of PEX (mean age 74.5 [range 63 - 87]) and the second group – 21 patients with CRVO or BRVO with no clinical signs of PEX (mean age 72.7 [range 60 -85]). All patients were analyzed for the best corected VA and optical coherence tomography changes of the central macular thickness.

Results A clinical diagnosis of PEX was present in 21 of 168 patients (12.5%), 17 (81.0%) of them had a CRVO and 4 (19.1%) – BRVO. The average of initial VA in the first group was 0.16 (SD±0.19), in the second group – 0.18 (SD±0.19). In the second group the VA after intravitreal injection of bevacizumab was significantly better (0.49 (SD±0.33)) compared to the first group (0.29 (SD±0.26)) (Mann-Whitney test, p=0.043).Mean central retinal thickness decreased from 696.9µm (SD±261.9) to 261.0µm (SD±154.2) in the first group and 636.5µm (SD±236.9) to 254.5µm (SD±167.2) in the second group.

Conclusion Pseudoexfoliation syndrome is significantly more common in eyes with central retinal vein occlusion compared to branch retinal vein occlusion. Pseudoexfoliation syndrome could be counted as one of the factors damaging functioning of the neurosensory retina.

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Design and rationale of COMO, a 12-month study that compares the safety and efficacy of dexamethasone intravitreal implant versus ranibizumab in branch retinal vein occlusion

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Purpose The DEX implant 0.7 mg and ranibizumab have not been directly compared in a randomized trial in branch retinal vein occlusion (BRVO). Inclusion of different patient populations in the GENEVA[1] and BRAVO[2] trials also prevents an indirect comparison. Duration of disease and visual acuity at baseline have been shown to impact outcomes following treatment. BRAVO recruited patients with a shorter duration of macular oedema (ME) and lower best corrected visual acuity (BCVA) at baseline than GENEVA. Sub-analysis of GENEVA showed a greater BCVA improvement which peaked at day 60 (17.8 letters, p=0.002) and was sustained out to day 180 (14.4 letters, p=0.138).[3]

Methods This Phase IV, multinational, randomized, 12 month study directly compares DEX implant 0.7 mg with ranibizumab in BRVO with ME for <90 days. Recruitment will begin in 2011 and circa 400 patients will be enrolled and randomized (1:1). Stratification will be according to BCVA.

Results The primary endpoint is the mean change in BCVA from baseline to month 12 in the intention-to-treat population using a non-inferiority analysis. Secondary endpoints include other measures of visual acuity and quality of life.

Conclusion The results of this first head-to-head comparison of DEX implant 0.7 mg with ranibizumab will have implications for future practice.References1.Haller JA, et al. Ophthalmol 2010;117(6):1134-46.2.Campochiaro PA, et al. Ophthalmol 2010;117(6):1102-1112.3.Allergan data on file. GENEVA sub-analysis.

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Analysis of gene expression in ischemic neuroretinas: genome-wide screen discriminating occlusion versus laser effects in rats

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Purpose Identification of genes differentially expressed in rat neuroretinas submitted to experimental acute BRVO, to laser treatment, or to light exposure

Methods Using an in vivo experimental model of BRVO in rat retinas, we induced acute ischemia by argon laser photocoagulation of venous sites near the ONH in the right eye of one group of animals. In a second group, right eye retinas were exposed to laser treatment at sites located between major vessels. A third group of animals had their right eye exposed to light through a slit lamp. Untreated left eyes served as controls in each animal. Total RNA was extracted from neuroretinas, 30 min and 6 h post treatments, and processed for global gene analysis with Affymetrix microarrays. Genome-wide comparison of transcriptomes was then performed

Results At 30 min, data did not reveal any sequence differentially expressed for the 3 treated groups. At 6 h, light exposure was definitively excluded as an impacting factor. However, the expression of 627 and 113 sequences changed, respectively post BRVO and post laser treatment. When comparing transcriptomes of both groups, we identified, respectively, 396 and 21 genes specifically modified. Interestingly, around 80 genes, all upregulated, were common to both groups.The majority of differentially regulated genes encode proteins involved in different aspects of a large number of complex pathways, among which we retained: inflammation, angiogenesis, apoptosis and neuroprotection

Conclusion Microarray analysis revealed changes in gene expression bearing similarities to results from other ischemia models. Furthermore, it revealed that laser treatment may have unreported and specific impacts on retina's metabolism

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Central retinal vein occlusion: visual acuity correlates with focal electroretinogram but not with optical coherence tomography

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Purpose Central retina vein occlusion(CRVO) is a retinal vascular disorder associated with various degrees of retinal ischemia leading to macular oedema and visual acuity loss. The standard method to detect and measure the macular oedema is the Optical Coherence Tomography(OCT). The focal electroretinogram (FERG) is a part of the electroretinography that investigate functionally the macula.The aim of our study was to investigate the relationship between visual acuity, morphologic aspects and functional results in CRVO.

Methods We examined 24 eyes affected by CRVO. All the patients had complete survey comprehending ETDRS visual acuity(VA), FERG, OCT. The FERG was performed via ERG dome, using a background light of 300 cd/m2 and a led stimulus alternating at 5,1 hz. The OCT values of macular volume and thickness, the a and b wave values of latency and amplitude were collected and analyzed. The results were matched with 19 eyes not affected of the same sample and with 20 eyes of healthy subjects. Multiple statistical relationship analysis of the r and p were done by mean of Kruskal-Wallis test. The sensitivity and specificity were analyzed with Roc curve.

Results We do not found correlations between VA and OCT macular volume and thickness. A significant correlation with VA was found in a and b FERG amplitudes between the CRVO group, healthy subjects and the healthy eyes of CRVO group and also between the healthy eyes of CRVO and healthy subjects.Significant sensitivity and specificity (72.1 and 80 respectively) were found in Roc curve

Conclusion In our study functional alterations of the FERG correlate and probably precede VA loss

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Intravitreal ranibizumab for retrofoveolar neovascular age related macular degeneration, in pseudovitelliform and/or drusenoid pigment epithelium detachment shape

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Purpose To evaluate the functional, anatomical, vascular flow, effects of intravitreal Ranibizumab injections for retrofoveolar neovascular Pseudo vitelliform and/or Drusenoid pigment epithelium detachment (PED) Age Related Macular Degeneration (AMD), at 3 years 1/2 evolution.

Methods 48 eyes of 40 patients, 15 men, 25 women, with neovascular Pseudo vitelliform(35 eyes) and/or Drusenoid PED (13eyes) AMD. Patients received intravitreous Ranibizumab, 3 times, every 4 weeks in an inductive treatment, the next injections (IVT), depending on the follow-up results, were done by series of 3 IVT. First and 2 months' interval follow-up exam included ETDRS visual acuity (VA), complete ophthalmic examination, fluorescein and infracyanine (ICG) angiography, and optical coherence tomography (OCT).VA and OCT were done before each IVT.

Results VA improved in 52% cases. Angiographic leakage disappeared in 78% cases, reduced about 75% in 40% cases. At ICG ,vascular flow, vessel's diameter were 2/3 time less in 45% cases, low-flow in 83% cases .Diffuse edema was normalized in 60% cases , pigment epithelial detachment(PED) was less dense in most of cases, by OCT. No ocular or systemic side effects observed.Better contrast Inductive treatment was sufficient in 24 cases, needed 2 IVT Series in 40% cases, failed in 1 case. In few cases, retinal and pigment epithelium atrophy was induced, Drusenoid PED disappeared. Discussion is open.

Conclusion The results, with generally improved visual function, lack of fluorescein leakage, low neovascularisation's flow in ICG, reduction of exudation on OCT, suggest Series of 3 Ranibizumab IVT Protocol seems effective, in those usually poor resort considered cases.

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Effect of subtenon injection of natural leucocytic interferon-α for treatment of age-related choroidal neovascularization

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Purpose To evaluate the effect of subtenon injection of natural leucocytic interferon-α (IFN-α) on visual acuity (VA), macular thickness (MT) and membrane size in patients affected by type II age-related choroidal neovascularization (CNV) refractory to intravitreal injection of bevacizumab

Methods 20 patients (male:female=8:12; mean age: 77.7±6.6) were evaluated, including best-corrected visual acuity (BCVA), fluorescein angiography, indocianin angiography and SD-OCT, preoperatively and after 1 month and 4 months following the last injection. Patients received a parabulbar subtenonian injection of IFN-α (1x106 UL/ml, Alfaferone, AlfaWassermann) 3 times a week for 4 consecutive weeks.

Results BCVA, expressed in LogMAR, significantly improved after the first month (0.88±0.49vs0.65±0.52; p<0,001), and was stable at the third visit (0.60±0.52 p<0,001). SD-OCT showed a significant reduction in MT (485.05μm ±129.5 vs 391.00μm ±125.47; p<0.001). After 4 months, MT was slightly increased, but it was still significantly lower than the baseline (405.20μm±151.03 p=0,04). Fluorangiographic images showed a significant reduction in membrane size (1.79 mmq ±1.26 vs 1.18 mmq ±1.10 p=0.003) and the result was stable at the follow up visit (1.01 mmq ±1.17 p=0.002). No adverse advents were recorded.

Conclusion IFN-α, with its immunomodulatory, antiproliferative and antiangiogenic actions, was effective in improving VA and reducing MT and membrane size. Randomized controlled studies will be useful to illustrate the effect of parabulbar IFN-α alone or in combination with other intravitreal therapy for the treatment of CNV.

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Idebenone prevents retinal pigment epithelial cells from oxidative stress and apoptotic cell death by stabilizing BAX/Bcl-2 ratio

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Purpose Age related macular degeneration is one of the leading causes of blindness. Oxidative stress plays an important role in the pathogenesis of this disease. This study investigates the possible anti-apoptotic and cytoprotective effects of idebenone on retinal pigmentepithelial cells (ARPE19) under oxidative stress.

Methods ARPE19 were treated with 1 to 100 μM idebenone. Cell viability (tetrazolium dye-reduction assay and live-dead assay) and expression of BAX and Bcl-2, two key modulators of apoptosis, and their mRNA were determined after 48 h and after H2O2 treatment.

Results Idebenone concentrations from 1 to 20 μM showed no toxic effects ARPE19. Doses of 5 and 7.5 μM were most effective in increasing cell viability after H2O2 treatment. Further more RT-PCR and Western blot analysis yielded an increased expression of Bcl-2 and a decrease of BAX compared to those cells that were treated with H2O2 only.

Conclusion In this study idebenone reduced oxidative stress and apoptotic cell death in cultured ARPE19 in vitro. Our results suggest that idebenone may help to protect these cells in vivo, and therefore might be helpful in preventing the progression of geographic atrophy in age related macular degeneration.

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Long – term results of intravitreal bevacizumab (Avastin®) injection for choroidal neovascularisation secondary to angioid streaks

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Purpose To evaluate the efficacy of long term intravitreal bevacizumab (Avastin) treatment for choroidal neovascularisation (CNV) associated with angioid streaks.

Methods 65 year old woman with bilateral active CNV secondary to angioid streaks was treated since October 2006. Photodynamic therapy (PDT) was used for primary treatment, after – intravitreal bevacizumab (1,25mg) was injected 20 times in each eye, average 1,4 months interval was between each session. Treatment efficacy assesment based on VA (visual acuity) (Snellen chart), fluorescence angiography (FA) and optical coherence tomography (OCT) was performed pre- and post- treatment before and after each injection.

Results The follow-up of the patient lasts for 55 months. BCVA (best corrected visual acuity) of both eyes before treatment was 0,6. The patient received 3 PDT with verteporfin (Visudyne) into left eye and later 40 intravitreal bevacizumab injections (20 into each eye) for 41 months. During the whole follow-up BCVA of the right eye decreased from 0,6 to 0,3 and left eye improved from 0,6 to 0,8. The CNV size remains stabile, low activity of FA was observed in both eyes. Central retinal thickness (CRT) decreased from 351 μm to 324 μm in the right eye and from 191 μm to 166 μm in the left eye. At the last follow-up on FA no further leakage was observed. No injection-related complications or drug-related side effects were observed.

Conclusion CNV associated with angioid streaks can respond to treatment with PDT and bevacizumab. CRT reduced and stabilisation of visual acuity was achieved.

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Premacular haemorrhage in a patient with leukaemia

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Purpose Blood dyscrasia has been associated with premacular haemorrhages. The combination of severe anaemia and thrombocytopenia has been hypothesised to cause reduced coagulability and loss of endothelial cell integrity, allowing blood leakages through the jeopardised endothelial barrier.

Methods Prospective, interventional, single case report. A 20-year-old man, treated with chemotherapy for acute lymphoid leukaemia, is referred with a sudden loss of vision in his left eye (LE). Funduscopic examination revealed a sharply demarcated, dome-shaped premacular haemorrhage, with approximately one diameter-disk of size. The spectral-domain OCT(SD-OCT) scan showed that the cleavage plane of blood accumulation was located under the internal limiting membrane (sub-ILM). Considering the location and the size of the haemorrhage we decided to perform a conservative management with periodic checks.

Results Four months later, the macular haemorrhage had been reabsorbed and vision had improved. The SD-OCT scan revealed the total absorption of blood, with signs of thickening of the internal limiting membrane.

Conclusion Therapeutic options in premacular haemorrhages (conservative management, laser membranotomy or vitrectomy) should be established on an individual basis, considering in each case, the underlying disease, bilaterality of the process, duration and severity of bleeding, lens transparency, age and general condition of the patient.

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Association between retinal vessel diameters and different types of diet

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Purpose To study the relationship between retinal vessel diameters and different types of diet.

Methods The Inter99 study comprised an age- and sex-stratified sample of 13,016 participants residing in 11 suburban municipalities of the south-western part of Copenhagen County. Of 6784 subjects aged 30-60 years who volunteered to participate in the main study, a subgroup of 970 subjects participated in the eye study. We investigated the relation between fundus photographic retinal vessel diameters and different types of diet (represented in scales, range 1-9) as a risk factor for cardiovascular disease and diabetes. Vessel diameters were expressed as central retinal artery equivalent diameter (CRAE), central retinal vein equivalent diameter (CRVE), and artery-to-vein diameter ratio (AVR). Data were analysed using multiple regression analysis.

Results A significant association was found between CRAE and different types of diet (p=0.026), and between CRVE and different types of diet (p=0.001). After adjusting for age and blood pressure, which influence retinal vessel diameters, significant association between CRVE and different type of diet persisted, which was not the case in association between CRAE and different type of diet (p=0.234).

Conclusion In the Inter99 study, retinal vessel diameters are associated with risk factors for cardiovascular disease and diabetes, such are different types of diet.

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Clinical manifestations of reticular pseudodrusen in Korean patients

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Purpose To clarify the clinical characteristics of reticular pseudodrusen(RPD) in Korean patients.

Methods The study was designed as retrospective, observational, consecutive case series. A total of 255 eyes of 130 patients diagnosed with RPD were evaluated. RPD were diagnosed by characteristic fundus findings, using multimodal imaging tests. Age related macular degeneration(AMD) was determined by the International Classification and Grading System.

Results The mean age of the patients was 72.6±9.0 years(range, 43-92). Most of the RPD patients had the disease in both eyes(97.7%), with a female preponderance(86.2%). All of the 3 patients with unilateral RPD had shown neovascular AMD in the eye without RPD. AMD was found in 183 eyes(71.8%); early AMD in 115 eyes(45.1%), geographic atrophy(GA) in 41 eyes(16.1%), and neovasuclar AMD in 27 eyes(10.6%). The mean age was 73.7±9.2 years(range, 58-92) in the RPD group and 69.9±11.7 years(range, 43-90) in the control group repectively, and there was a statistically significant difference between these two groups($p<0.05$). Classic choroidal neovascularization (CNV) was found in 13 eyes (48.1%), and occult CNV was found in 14 eyes (51.9%) in the neovascular AMD group.

Conclusion Clinical manifestation of RPD in Koreans did not differ significantly from those described in Caucasians. However, our study demonstrated a higher rate of bilaterality, lower prevalence of AMD, and higher prevalence of GA in RPD patients than those previously reported. Ethnical differences may be associated with these findings and further studies are required.

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Correlation between exudative age-related macular degeneration and pseudoexfoliation syndrome

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Purpose To evaluate the correlation between exudative age related macular degeneration (AMD) and pseudoexfoliation syndrome (PEX) in patients receiving Bevacizumab therapy for AMD.

Methods Consecutive 200 patients with exudative AMD treated with Bevacizumab at Vilnius University Hospital between December 2010 and March 2011 were included into the study. Each patient's data was recorded only once. Those with retinal occlusive disease were excluded. The results were statistically analysed by SPSS 19.0 program.

Results 135 (67.5%) females and 65 (32.5%) males were studied. The mean age was 73.9 (SD=0.6) years. The difference between the mean age of female and male patients was statistically not different (74 and 73.3 years respectively). The prevalence of PEX in the treated as well as in the controlateral eye was 15.5% (31 patients), binocular PEX was in 32% of the eyes, in all there were 15.0% eyes with PEX. There was no statistically significant correlation between the type of AMD and frequency of PEX, but the frequency of PEX in eyes with AMD was twice larger than in controlateral eyes without AMD: Odds ratio was 1.96 (95% CI: 0.4-8.6). No correlation was found between sex, AMD type and PEX.

Conclusion In our study exudative AMD was found more often in female patients. PEX was found more often in eyes with AMD.No statistically significant differences between frequency of PEX and type of AMD were found. Further studies are necessary to achieve statistically significant results.

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Subtenon injection of natural leucocytic interferon-α for treatment of diabetic macular edema

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Purpose To report the effect of subtenon injection of natural leucocytic interferon-α (IFN-α) on visual acuity (VA) and macular thickness (MT) in diabetic macular edema (DME).

Methods 3 patients affected by diabetic macular edema refractory to intravitreal injection of bevacizumab received a complete ophthalmic examination including best-corrected visual acuity (BCVA)and spectral domain ocular coherence tomography (SD-OCT) before and after 1 week, 1 month and 4 months of a cycle of 3 parabulbar subtenonian injections in a week of IFN-α (1x106 UL/ml, Alfaferone, AlfaWassermann).

Results BCVA and MT significantly improved after a week in patient 2 (male, age 66): 20/50 vs 20/30 and 498μm vs 237μm. The result was stable during the third and fourth visits (299μm and 254 μm). BCVA and MT improved after a week in patient 1 (male, age 64): 20/40 vs 20/32 and 467μm vs 244μm, respectively; BCVA was stable during the follow up period, but MT increased significantly (610 μm and 603μm during the third and fourth visits). BCVA improved in patient 3 (female, age 75) after one week (20/50 vs 20/32) and was stable during the follow up period, but she had only a little improvement in MT (533μm, 483μm, 498μm and 493μm during the 4 visits).

Conclusion BCVA improved in all the patients, and was stable after 4 months. MT greatly improved in two patients after 1 week but only in one patient was the result stable. IFN-α, with its immunomodulatory, antiproliferative and antiangiogenic actions, was effective in improving VA and reducing macular thickness in DME. Randomized controlled studies will be useful to understand how long the effect of IFN-α lasts, how many injections are needed and which patients might have the best results.

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Increased IL-6 levels in the vitreous of proliferative diabetic retinopathy (PDR)

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Purpose To assess the activity of HIF-1alpha and NF-kappaB transcription factors and inflammation markers (IL-6 and IL-8) in the vitreous of patients suffering from proliferative diabetic retinopathy.

Methods Twenty seven patients were enrolled for the study. The severity of retinopathy was classified (0, 1, 2, 3, 4) and the activity of neovascularization was graded (0, 1, 2, 3, 4) intraoperatively. Samples were collected during surgery and the NF-κB and HIF-1alpha and transcription factors activity and expression levels of IL-6 and IL-8 were measured.

Results The majority of samples fell into the retinopathy classes 3 (n=12) or 4 (n=13). Neither the level of IL-6 increased from 68.9 + 46.8 pg/ml to 102.7 + 94.1 pg/ml and IL-8 from 165.1 + 136.0 pg/ml to 521.0 + 870.9 pg/ml (mean + SD, non-significant change: normality test followed with Mann-Whitney Rank Sum Test). According to the neovascularization activity the samples fell into the grades 1 (n=7), 2 (n=12) or 3 (n=7). In IL-6 there was a statistically significant increase ($p<0.05$) from grade 2 to 3: 58.6 + 40.3 pg/ml and 158.4 + 102.5 pg/ml, respectively (Kruskal-Wallis One Way ANOVA on Ranks followed with Dunn's Method). The level of IL-8 was in grade 1: 118.0 + 62,4 pg/ml, in grade 2: 192.3 + 127.1 pg/ml and in grade 3: 884.3 + 1161.0 pg/ml (statistically non-significant change). There was a statistically significant Linear Regression between IL-6 and IL-8 ($P<0.001$): IL-6 = 51.88 pg/ml + (0.092 * IL-8), $r=0.772$. Increased activity of the HIF-1alpha and NF-κB transcription factors were not observed.

Conclusion IL-6 is a candidate to indicate activity of neovascularization process in PDR. It might be a new molecular therapeutic target to regulate innate immunity response in vitreous.

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Proliferative diabetic retinopathy: from screening to treatment

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Purpose To assess if the guidelines for referral and treatment of proliferative diabetic retinopathy (PDR) in the English National Screening Programme are being followed in Tower Hamlets Diabetic Retinopathy Screening Service(THDRSS). The guidelines mandate that all patients with PDR must be seen within 2 weeks in an eye clinic and should be treated within 4 weeks if needed. This can potentially decrease blindness related to PDR in the underprivileged population of Tower Hamlets of East London, UK.

Methods During the period from 01/04/2010-31/03/2011, 34 patients were diagnosed with retinal changes characteristic of PDR at THDRSS. All patients were referred to Moorfields Eye Hospital (MEH). The times between screening and referral and referral to treatment were measured. Images were reviewed if there was a discrepancy between screening and clinical diagnosis.

Results All patients were referred to MEH on the same day of screening. Five patients did not attend any appointments given and were referred back to THDRSS and education on eye health. The remaining 29 patients were examined at MEH within 6 weeks from screening but only five (17.24%) were examined within the recommended 2 weeks. Half of those requiring laser for PDR were treated on the day of the first consultation and the other half within 4 weeks. Three patients had asymmetrical disease and these were confirmed to be retinal vein occlusions.

Conclusion Referral guidelines were followed by THDRSS with 100% of the patients referred on time. Guidelines for timely treatment of PDR patients were followed at MEH. This may contribute to the prevention of severe complications from PDR in this population. The delay between screening and first appointment will warrant further investigation.

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Combined cataract surgery with anti-VEFG agents in patients with quiescent proliferative diabetic retinopathy with no macular edema

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Purpose The study of visual acuity and the course of diabetic retinopathy after combined cataract surgery and injection of ANTI-VEGF agents in diabetic patients with quiescent proliferative diabetic retinopathy without macular edema.

Methods The study included 22 patients with quiescent proliferative diabetic retinopathy with no macular edema aged 62-75 years of both sexes (15 men and 7 women). The preoperative visual acuity was of 1/10 to 4/10 and the time monitoring the patients after cataract surgery was 18 months.

Results The visual acuity improved in all patients and follow up of 18 months showed that only one patient developed macular edema after 6 months who was treated with subsequent monthly infusions of Anti-VEGF (4.5%). At a percentage of 72.7% (16 patients), visual acuity improved and at a rate of 22.8% (5 patients), visual acuity remained unchanged

Conclusion The combination of cataract surgery and Anti-VEGF helps in the greater improvement of visual acuity and of proliferative diabetic retinopathy.

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Intrasession reproducubility of retinal nerve fibre and macular thickness measurements using Cirrus® Fourier-domain OCT in DM patients without retinopathy

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Purpose To evaluate the intrasesion reproducibility of retinal thickness and retinal nerve fiber layer (RNFL) measurements in type 1 diabetic subjects without retinopathy using Cirrus Fourier-domain optical coherence tomograph (OCT) (Carl Zeiss Meditec, Inc)

Methods 35 patients with diabetes Mellitus (DM) type 1 underwent 3 scans through Cirrus-HD in the same session, separated for 3 minutes between each scan. Each scan included 2 adquision protocols: "Macular Cube 512 x 128" and "Optic Disc Cube 200 x 200". Descriptive statistics, analysis of variance, intraclass correlation coefficients (ICCs) and coefficients of variation (COV) were calculated for nine areas corresponding to the Early Treatment Diabetic Retinopathy Study an for macular volume, and for quadrants and RNFL clock hours sectors.

Results Mean retinal thickness was 298,14 ± 12,76 µm at the first scan, 296,97 ± 12,75 µm at the second scan, and 296,86 ± 12,03 µm at the third scan. Coefficients of variation ranged from 0,7% to 2,2%. Intraclass correlation coefficients ranged from 0.622 to 0.972. Mean RNFL average thickness were 97,28 ± 9,26 µm at the first scan, 96,38 ± 9,98 µm at the second scan, and 95,91 ± 10,11 µm at the third scan. COV ranged from 1,9% to 5,5%. ICC ranged from 0.823 to 0.987. No significant differences were found except in macular central thickness.

Conclusion Retinal and RNFL thickness measurements obteined using Cirrus OCT were highly reproducible in type 1 DM patients with low intrassesion variabilities, so it can be consider a valid device for measuring retinal and optic nerve parameters in these patients.

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Diabetic retinopathy screening with computational support

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Purpose Diabetic retinopathy (DR) is among the most common causes of blindness in the developed world. Since many patients retain normal vision and may experience only minimal reduction despite the presence of a severe, sight-threatening disease, screening and early detection of DR is highly recommended. Our purpose was to develop an automated DR screening system to gain computational support for high throughput screening activities.

Methods Detection of microaneurysms (MA) - the most important indicators and the earliest signs of DR - and of other lesions (exudates, vascular structures, etc.) have been assembled in an ensemble-learning based framework, which has been tested on 1200 images of the Messidor database.

Results Images were classified as having DR or non by the MA detector only with 95% sensitivity, 51% specificity and 76% accuracy. By including other lesions, our system reached 89% sensitivity, 82% specificity and 85% accuracy.

Conclusion Our system has sensitivity/specificity values for the MA step comparable to or better then other automated systems available, as tested in the Retinopathy Online Challenge, where it is currently ranked as first. MA detection remains a key component in automated DR screening, but detection of other DR lesions can lead to further improvement. This work was supported in part by NKTH, TECH08-2, Hungary DRSCREEN project and the NIHR BMRC in Ophthalmology (TP).

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Cytokines and adhesion molecules in proliferative diabetic retinopathy: high vitreous concentration of IL-6 and IL-8, but not of adhesion molecules in relation to plasma concentrations

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Purpose Inflammatory markers have been observed in vitreous in diabetic retinopathy, but the increases may be predominantly due to leakage than due to intraocular production. We assessed vitreous concentrations of adhesion molecules and cytokines in proliferative diabetic retinopathy (PDR) and non-diabetic controls (C) in correlation to corresponding plasma levels. The purpose of the study is to differentiate intraocular production from breakdown of the blood retinal barrier.

Methods The study population was 38 patients with PDR undergoing vitrectomy. Group C consisted of 16 subjects vitrectomized for macular hole or epiretinal membrane. Vitreous and plasma concentrations of six adhesion molecules (sE-Selectin, sICAM-1, sICAM-3, sPECAM-1, sP-Selectin, sVCAM-1) and eleven cytokines (IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12(p70), TNF-α, TNF-β, IFN-γ) were detected by the flow-cytometry based Multiplex assay (Bender).

Results IL-6 and IL-8 were 26-fold and 6-fold higher in vitreous than in plasma in PDR, respectively. Vitreous concentrations of IL-10, sPECAM-1, sE-selectin, sICAM-1 and sVCAM-1 were higher in PDR than C. However, concentrations of adhesion molecules in vitreous in PDR were less than 10 % of corresponding concentrations in plasma. Also anti-inflammatory IL-10 was lower in vitreous than in plasma and vitreous IL-10/IL-8 ratio significantly lower in PDR than in C.

Conclusion There is an active role of cytokines IL-6 and IL-8 in proliferative diabetic retinopathy, which might be due to their intraocular production. Furthermore, there is an imbalance between inflammatory and anti-inflammatory cytokines in vitreous.

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Retinal photoxicity related to xenon light

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Purpose To describe the anatomical and functional changes observed after surgery, in three patients with idiopathic macular hole, who developed retinal toxicity related to Xenon light.

Methods Three eyes (3 patients), two females and one male, underwent three-port pars plana vitrectomy with internal limiting membrane (ILM) peeling and fluid-gas exchange. In all cases we used a new Xenon light during surgery with an intensity power ranging between 50 and 75%. In order to facilitate ILM peeling, Indocyanine Green (ICG) (0.05%) was used in one case and Brilliant Blue G (BBG) in two cases. Full clinical examination, with determined Best Corrected Visual Acuity (BCVA), fundus examination, retinography and Optical Coherence Tomography (OCT), were performed prior and after surgery. Fluorescein angiography (FA) was also performed in all cases after surgery.

Results One week after surgery, the macular hole was closed in all cases and it remained stable during follow-up. One month later, BCVA was lower than before surgery and we observed changes in retinal pigment epithelium at the posterior pole. These changes were more intense three months later: retinal atrophic areas combined with patches of hyperplasia of the RPE in the macular area. The FA confirmed the diagnosis of retinal phototoxicity. Similar changes were observed at six months, one, two and three years later in all cases with a final BCVA lower than 1/10 in all eyes.

Conclusion The light we use to perform vitrectomy may cause photoxicity. As we used two different dyes during surgery, and previously we had operated more than two hundred cases of macular hole with ICG and halogen light without problem, we postulate that changes observed in these cases could be due to Xenon light, independently of the use of different dyes.

Commercial interest

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Changes in the retinal vessel diameter, retinal nerve fiver layer thickness, and optic disc after vitrectomy

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Purpose To investigate the retinal vascular caliber, retinal nerve fiver layer thickness, and optic disc changes in patients after pars plana vitrectomy.

Methods We examined 40 eyes in 40 patients who had undergone unilateral pars plana vitrectomy at before and 3 months, 6 months after operation. The diameters of central retinal arteries and veins were measured on retinal photographs. The central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE) were calculated using the revised Parr-Hubbard formula. Retinal nerve fiver layer thickness was obtained using Stratus optical coherence tomography. Cup-to-disc vertical ratios of optic disc was evaluated using stereo optic disc photo

Results There were no significant differences between both eyes before operation. Cup-to-disc vertical ratios of optic disc significantly increased for 3 months and 6 months post-operatively ($p<0.01$, $p<0.01$) and there was significant difference between operation eye and fellow eye at the same period ($p<0.01$, $p<0.01$). The changes of CRAE and CRVE in operation eye were significantly larger than fellow eye at 6 months post-operatively ($p<0.01$, $p<0.01$). The retinal nerve fiver layer thickness showed no significant changes.

Conclusion Whereas no retinal nerve fiver layer thickness decrease was observed, vitrectomy induced changes in Cup-to-disc vertical ratios of optic disc and retinal vessel diameter for significant periods following surgery.

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Aspirin® is not a risk factor of haemorrhagic complications during or after surgery of primary rhegmatogenous retinal detachment

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Purpose To evaluate the hemorrhagic risk of treatment by acetylsalicylic acid, during the management of primary rhegmatogenous retinal detachment(RD).

Methods This comparative prospective case control study included a cohort of 322 patients from a prospective cohort of 835 patients with primary rhegmatogenous RD. After exclusion of patients with RD secondary,74 patients were included in the hemorrhagic group and patients without hemorrhagic complications were randomly selected in order to reach a 1:3 case (control population, n=248). Univariate and multivariate analyses were performed to identify risk factors of perioperative bleeding.

Results Univariate analysis showed that the presence of initial vitreous hemorrhage, size of breaks, number of breaks, pars plana vitrectomy (PPV) and the number of cryotherapy impacts were significantly associated with perioperative bleeding. Independent risk factors of perioperative hemorrhage were the number of cryotherapy sessions (odds ratio =1.12 [1.06; 1.20], 95% CI), transscleral drainage (OR =4.22 [1.62; 10.98]), and PPV (OR =3.39 [1.36; 8.47]). The occurrence of bleeding complications was associated with a lower single-operation anatomical success rate. There was also a trend toward an association between bleeding complications, the total number of RD recurrences, and final visual acuity.

Conclusion Aspirin was not an independent risk factor of hemorrhagic complications during and after surgery of primary rhegmatogenous RD. The bleeding risk is instead associated with surgical factors such as PPV, cryotherapy, and subretinal fluid drainage.

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Intravitreal ranibizumab in the treatment of subretinal neovascularization in a case of punctate inner choroidopathy

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Purpose To report a case of a subretinal neovascular membrane in a bilateral retinal lesions compatible with punctate inner choroidopathy (PIC) treated with intravitreal ranibizumab obtaining excellent results.

Methods A 28-year old woman suffering loss of visual acuity with her left eye, who presented an image suggestive of subretinal neovascular membrane in her left eye and bilateral retinal lesions compatible with punctate inner choroidopathy(PIC).

Results In this situation it was decided to initiate treatment with intravitreal ranibizumab in OD,(monthly for a total of three injections). The visual acuity improved to 20/30 after 1 st injection. One month after the third injection, the BCVA was 20/20 and remained stable. During the year the patient has been followed in our department were no new symptoms or signs of activity.

Conclusion The differential diagnosis must be made between PIC and the rest of "white dot syndromes" and the presumed ocular histoplasmosis syndrome (POHS). Angiogenic drugs may be a good alternative for the treatment of such diseases when they develop a subretinal neovascular membrane.

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Pivotal role for SD-OCT in the diagnosis of acute zonal occult outer retinopathy

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Purpose Acute Zonal Occult Outer Retinopathy (AZOOR) is characterized by an acute partial loss of outer retinal function with corresponding visual field defects and electroretinographic (ERG) abnormalities in one or both eyes. Spectral domain optical coherence tomography (SD-OCT) findings are described as a key to the early diagnosis of AZOOR in a patient.

Methods A 25 -year-old man developed acute painless central vision loss together with photopsia in the right eye (RE). He underwent a full ophthalmological work-up including fluorescein and ICG-angiography, SD-OCT, specialized imaging, visual field testing (VFs) and electrophysiological testing.

Results On initial evaluation visual acuity was 15/10 in both eyes. Fundoscopy revealed a subtle loss of the foveal reflex with very limited foveal mottling in the RE. Fluorescein and ICG-angiography were unremarkable. Static and kinetic perimetry showed an absolute scotoma inferotemporal of fixation and a slightly enlarged blind spot in the RE. Most remarkable were the inner/outer segment boundary defects visible on SD-OCT. One month later, small changes were observed on infrared imaging and reduced responses were seen on multifocal ERG corresponding to the scotoma on VFs. A full-field ERG and EOG were normal. The unilateral scotoma stabilized over the next 2 months.

Conclusion AZOOR is a rare condition with subtle and often vague signs and symptoms, which makes diagnosing it quite a challenge. The added value of SD-OCT is that it allows identification of specific inner segment/outer segment boundary defects at presentation.

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Diabetic retinopathy and type 2 macular telangiectasia

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Purpose To establish the severity and progression of diabetic retinopathy (DR) and maculopathy (DMac) in patients with both Type 2 macular telangiectasia (MacTel) and diabetes mellitus (DM) and relate these to characteristics of MacTel.

Methods MacTel is a bilateral retinal disease affecting central vision. The MacTel Project enrols from 27 sites around the world; those in the study have multiple imaging performed yearly. Colour fundus, fluorescein angiographic, OCT and autofluorescence images were graded at the Reading Centre of Moorfields Eye Hospital, UK for characteristics of MacTel, DR and DMac; diabetes status and clinical data were obtained from the co-ordinating centre (EMMES). Grading for DR and DMac was on 7-field stereo images for baseline, and 3-fields for follow-ups using ETDRS standards.

Results The mean age of MacTel patients at diagnosis was 57±9 years. Diabetes was diagnosed in 188 out of 555 MacTel patients enrolled. MacTel patients with DM had an average HbA1c of 6.9±1.4%. Over 70% of patients had no DR at baseline. Only one patient developed mild and one moderate non-proliferative DR during the over 3 years follow-up. Only one patient developed DMac requiring laser treatment. MacTel patients with DM had significantly lower visual acuity at baseline (No DM 70.3±0.7 letters, DM 65.±1.6; p=0.02). MacTel patients with DM progressed significantly more on NEI-VFQ and on OCT characteristics at the fovea, such as foveal empty cavities and neuroretinal changes (all $p<0.05$). Progression of the severity of MacTel was significantly modified by DM ($p<0.05$).

Conclusion DM has a clinically meaningful impact on visual functioning and progression of MacTel. Further study is required to understand the relationship between the two diseases.

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OCT as sensitive indicator of geometric fundus deformities

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Purpose To emphasize the contribution of optical coherence tomography in detecting geometric fundus deformities

Methods Seven cases of geometric fundus deformities are evaluated retrospectively with regard to OCT (Heidelberg Spectralis), B-scan ultrasound, fundus imaging, direct ophthalmoscopy and functional examinations, among them acuity, color vision and various perimetric techniques.

Results Patients were referred to our hospital because of unexplained reduction in visual acuity or loss within their visual fields, or were identified as being affected from geometric fundus deformity on routine exam. OCT provided the first-at-hand finding leading towards the explanation of abnormal visual function, or was the first to point incidentally to a geometric fundus deformity. Ophthalmoscopy (incl. an estimate of paraxial optic path length) and fundus imaging ranked next, whereas B scan ultrasound provided affirmative data. Among functions, visual fields were more often affected than acuity. There were no defects in color vision.

Conclusion OCT profiles of the posterior pole of the eye provide a sensitive indicator of geometric fundus deformities, thus leading to an understanding of otherwise unexplained defects of visual function.

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Reproducibility and differences between Cirrus® and Spectralis® Fourier-domain OCT in epiretinal membranes

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Purpose To evaluate the ability of Fourier-domain (FD) OCT to detect retinal alterations in epiretinal membrane (ERM) eyes. To test the intra-session reproducibility of macular thickness measurements in ERM and healthy subjects using Cirrus and Spectralis OCT.

Methods Two hundred and nine of 209 subjects (87 ERM patients and 122 healthy subjects) underwent three macular scans by the same experienced examiner using Cirrus and Spectralis OCT . Differences between healthy and ERM eyes were studied. The relationship between average thicknesses with both instruments was evaluated. Repeatability was studied by intra-class correlation coefficients and coefficients of variation (COV) for the nine areas corresponding to the ETDRS.

Results Macular thickness increase was detected in ERM eyes for all OCT parameters ($p<0.05$). Macular average thickness was 338.45 and 431.99 μm in ERM eyes using Cirrus and Spectralis, respectively. Changes in the morphology of the retinal layers were detected using both OCTs. Macular average thickness in ERM eyes as determined by both OCTs was correlated ($r= 0.678$; $p<0.001$), but differences were statistically significant ($p=0.044$). In ERM eyes, measurements showed a mean COV of 2.96% using Cirrus, 2.21% using Spectralis and 0.99% using Spectralis progression feature. Intra-class correlation coefficients were higher than 0.919.

Conclusion Significant differences exist in macular thickness measurements between Cirrus and Spectralis despite the high correlation of measurements between the two instruments. Fourier-domain OCT can be considered a valid device to detect alterations in ERM patients.

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Reproducibility of retinal thikness measurements in patients with age-related macular degeneration using Fourier–domain optical coherence tomography

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Purpose To assess the reproducibility intraoperative macular thickness measurements using optical coherence tomography, spectral domain (spectralis, Heidelberg Engineering, Germany) in patients with wet AMD and to evaluate differences in reproducibility with optical coherence tomography (Stratus, Carl Zeiss Meditect Inc, USA).

Methods Prospective observational study and cross-sectional study included 30 eyes of 30 patients with exudative AMD. All of them were dealt with macular status by fast-track protocol posterior pole with spectral domain OCT (Spectralis OCT) and time domain OCT (Stratus OCT). Each patient underwent 3 consecutive scans each of the scanners and performed by the same observer to compare the reproducibility of both devices. We evaluated the central macular thickness in macular different areas described in the ETDRS (Early Treatment Diabetic Retinopathy Study).Statistics was performed descriptive analysis of variance and calculated the intraclass coefficient of correlation (ICC) and coefficients of variation

Results The thickness of the retina was highly reproducible for all ETDRS areas with OCT Spectralis with values of ICC and VOC better than the Stratus OCT. VOCs spectralis were obtained with less than 5% indicating a high reproducibility and the ICC greater than 0.9.

Conclusion Reproducibility of retinal thickness measurements with optical coherence tomography spectral domain is almost perfect, there are few differences in intraobserver assessments. The values are higher than getting with time-domain OCT .Fourier domain OCT is a valid and highly reliable device for diagnosis and monitoring of retinal diseases such as wet AMD.

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Retinal manifestations in catastrophic antiphospholipid syndrome

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Purpose We present a case report with an ocular vascular event and multiple organ thrombosis and dysfunction in the presence of antiphospholipid antibodies.

Methods We report a case of a 79 years old female related visual loss in left eye. She had a venous occlusion and vitreous haemorrhage. In two weeks presented a maculopapular, bullous skin lesions on the legs, rapidly followed by widespread cutaneous necrosis and skin ulceration on all the limbs showing the tendons tissues of the heels. Later, she had an extension of thrombotic events to other vessels in the body. With medical treatment, there was initially a small functional improvement and then a general degradation in 10 weeks, followed by the death of the patient secondary to sever pulmonary emboli in the intensive care unit.

Results It was found histopathologic evidence of multiple small-vessel occlusions, and laboratory confirmation of the presence of antiphospholipid and anticardiolipin antibodies, in high title. It was refractory to anticoagulation, steroids and immunomodulation treatment

Conclusion Catastrophic antiphospholipid syndrome is an autoimmune disorder characterized by a rapidly progressive life-threating disease. Catastrophic occurs when three or more organ systems are affected by thromboses in a very short time less than a week. Roughly 50% of these patients have systemic lupus erythematosus. The overall mortality of this desvasting syndrome is about one-half.

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Presence of contracting cellular elements at the border of stage III and IV macular holes

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Purpose Myofibroblasts play a major role in the production of retractile phenomena causing contraction or shrinkage of the epiretinal membranes (ERM) in proliferative vitreoretinopathy, diabetic retinopathy or idiopathic macular epiretinal membranes. The presence of a-smooth muscle actin (a-SMA)-positive myofibroblasts and of ED-A fibronectin (FN), one of the main inducers of myofibroblastic differentiation was studied in internal limiting membranes (ILM) removed during macular hole surgery.

Methods Samples of ILMs following macular hole surgery in 9 eyes were collected. Double immunofluorescence staining with antibodies recognizing a-SMA and ED-A FN followed by confocal microscopy analysis as well as electronic microscopy were performed.

Results a-SMA and ED-A FN were detected in ILM removed in stage III and IV macular holes. ED-A FN was expressed in close relation with a-SMA-positive myofibroblasts predominately located close to the border of the macular hole area. Distally to the hole area the ILM specimens were a-SMA and ED-A FN negative. No a-SMA staining was observed in ILM specimens of stage II macular hole specimens.

Conclusion Scanning electron microscopy indicated that cellular migration was not apparent around the macular hole in the early stage of the development of this pathology.Cellular elements expressing contractile properties related to a-SMA, typical of myofibroblasts differentiation, appear to be present at late stage macular holes.

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Laser and surgery treatment of retinoschisis

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Purpose To find new methods to cure retinoschisis.

Methods Observed:130 patients. In1and 2 stages of process there were 80 patients (80 eyes). For these cases we used our method – step-by-step progression – beginning laser coagulation around the macula and toward the periphery retina. We used diode laser. Radiation power: 350mW-850mW, wavelength: 0,83 mm, exposition 0,2 s, spot diameter: 150-200mm. In 3 stage there were 50 patients (50 eyes), but in 3 stage laser coagulation was used only in 27 cases. In 23 cases we used surgery because these patients had new retina ruptures with traction by vitreous body. Before operation laser coagulation around macula zone and along the vessels. For surgery a segment-oval silicone sponge implants was used. This implant is constructed with unilateral protuberant surface that affords to get sufficient press roller to blockade any schisis holes in eye retina. Application method of segment oval consists: implant lies on sclera on its convex surface and is fixed by several nodulous sutures in projection of retinal ruptures. Implant is not strengthening out in length but is applanated toward retina. It is possible to blockade large gigantic ruptures, dialysis and group of ruptures in retina. We did not drainage intraretinal fluid; repeated laser-coagulation in 7 days after operation

Results 1-2 stages of retinoschisis after 4 session of laser coagulation we observed complete cysts delimitation outside macular zone. Complete intraretinal fluid resorption was achieved in 2 years.

Conclusion Full fluid resorption was observed in 15 patients in 3 stage of retinoschisis after 5 sessions of laser coagulation. In 12 patients of 3 stage we observed complete cysts delimitation outside macular zone. In 23 cases of 3 stage operations ended with good results

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Fluorescein angiography based classification of retinopathy of prematurity

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Purpose To select fluorescein angiography (FA) signs detected in Retinopathy of prematurity (ROP) in order to propose a new classification.

Methods From December 2009 to December 2010, 15 patients affected by ROP (stage 2 or 3, zone 2, no plus) were evaluated at San Matteo Hospital(Pavia) and Maria Vittoria Hospital (Torino) along with their FA exams by an expert in paediatric retina diseases. Among the multiple FA features in ROP, we considered: ischaemic area posterior to the shunt, leakage at the vascularised/avascularised junction (v/av j) and peripheral plus (vessel tortuosity just beyond the v/av).

Results Patient group characteristics were: Mean Gestational age: 25 weeksMean Weight at Birth: 657 gMean Age at ROP diagnosis: 30 weeks Considering the described criteria, we were able to detected a new class of ROP patients; they were all described as type 2 ROP on the basis of fundus examinations, while FA characteristics permitted to:

- Identify a more aggressive subtype of ROP type 2, in need of a sudden treatment

- Plan FA based laser administration which involved the ischaemic area near the shunt All the patients in the study received a laser treatment with favourable structural and visual outcome.

Conclusion FA classification allows to advance and/or improve laser administration in FA selected patients with retinopathy of prematurity.

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Ocular surface evaluation in children presenting ongoing ocular allergy

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Purpose To evaluate in a retrospective study ocular surface impairment and tear osmolarity in children presenting ongoing ocular allergy. Tears are necessary for continued health of ocular surface and tear osmolarity is considered a key point for tear film impairment and ocular surface damage.

Methods Our retrospective study included 20 children (mean age 11 yo, range 6 to 17 yo) of two groups that presented at ocular consultation of our hospital. Group a, 10 children with ongoing ocular allergy, group b 10 control children who had been tested but finally did not present any sign of allergy or dry eye. All the children underwent a tear osmolarity measure prior to complete ocular consultation to be aware of influencing results by the examination. The tear osmolarity measure was obtained with the Tear Lab Osmolarity System (OcuSense). A complete ocular examination was also performed. So the type of ocular allergy was diagnosed.

Results In group a, all the children presented clinical signs of on going ocular allergy with conjunctival redness, follicles and/or papillae. In two cases severe keratitis was present. In group b no ocular signs of conjunctiva anomalies were found. Mean tear osmolarity in group b, was 305mOsm/l and in group a, was 316mOsm/l. Tear osmolarity appeared higher in the ocular allergy group than in the non symptomatic children. Younger children had a higher measure of tear osmolarity.

Conclusion In adults 305mOsm/l is a cut-off value for dry eye. In our study this measure appears similar to adults but could be higher in youngest children. In children with ocular allergy, higher measure of tear osmolarity indicates an ocular surface damage that is underestimated. Tear osmolarity can be useful to manage ocular surface disease in children.

• 402 / 4175
High resolution images of the tear film lipid layer: effect of the blink cycle

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Purpose Deficiency of the lipid layer causes evaporative dry eye. We have therefore developed a high-resolution microscope to investigate lipid layer structure and how it may relate to evaporation and the blink cycle.

Methods The microscope images a 200 um diameter spot at the center of the cornea, with a resolution of about 1 um. Time after a blink is also recorded. Over 10,000 images of at least "fair" quality were recorded from 375 subjects including dry eyes and normals.

Results 1. Within about 0.1 seconds after a blink, lipid layer reflectance was less than at later times, implying that lipid thickness was lower. In this early interval, cloud-like patches of lipid were more often seen than at later times; they were surrounded by darker (thin) lipid. 2. Some structures in the lipid layer were very fluid, showing pronounced shape changes in a fraction of a second, whereas other structures were stable, with no evident change over several seconds.

Conclusion 1. Immediately after a blink, the lipid layer tends to be thin and often has an unusual appearance. 2. At later times, some structures vary rapidly in shape, indicating that the lipid layer is fluid with a low viscosity. Other structures are stable, suggesting that the lipid layer can have a gel-like structure.

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Altered corneal nerve morphology and epithelial wound healing in experimental lacrimodeficient dry eye

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Purpose To analyze the morphological changes of corneal nerves and its influence on corneal epithelial wound healing in a lacrimodeficient dry eye model in the guinea-pig.

Methods Corneal nerve architecture and the rate of corneal epithelial wound healing were studied in guinea-pigs to whom the main lacrimal gland was removed 4 weeks before (dry eye) and in control animals. Eyes were fixed, cryoprotected and incubated with neuronal class III Beta-tubulin antibody. Epithelial migration rate (EMR) and estimated time of healing (ETH) were calculated for 2mm-diameter epithelial corneal debridations stained with fluorescein, photographed regularly until complete closure and analyzed with image processing software.

Results Density (16±6 vs 27±11 nerves/mm2) and length (115±45 vs 186±74 µm) of subbasal nerves decreased significantly in dry eye. Subbasal nerves were less branched and tortuous. Epithelial nerve terminals were also reduced. EMR decreased significantly (63±4 vs 110±1 µm/h) and ETH increased significantly (38.6±1.8 vs 20.1±0.1 h) in dry eye.

Conclusion The morphological appearance and the decreased density, length and branches of corneal subbasal nerves are suggestive of corneal nerve degeneration at 4 weeks after lacrimal gland removal. Lacrimodeficient eyes presented also a slowing-down in corneal epithelial wound healing suggesting an early trophic defect consecutive to nerve damage.(Supported by: SAF2008-00529, CSD2007-00023, BFU2008-04425, BFU2009-07793 and RETICS RD07/0062/0012 from Ministerio de Ciencia e Innovación, Spain, and the Leonardo da Vinci Lifelong Learning Program.)

• 404 / 2377
Mechanical reinforcement of the cornea with an intrastromal insitu photopolymerised implant

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Purpose A photo-polymerisable hydrophilic material (PEG/Irg) has been previously evaluated in terms of biocompatibility and toxicity in a series of laboratory animals. It was the purpose of this study to evaluate the bio-mechanical effect of lamellar implants created from PEG/Irg in porcine cadaver eyes.

Methods Twenty porcine corneas where removed along with a 3 mm corneoscleral rim, de-epithelialised and mounted on an artificial anterior chamber. The pressure was maintained at 22 mmHg hydrostatically. In each cornea, a circular lamellar pocket (7mm diameter) was created manually. Thirty microliters of PEG/Irg in liquid form were injected in each pocket. A rigid contact lens was pressed on top of the cornea and the excessive quantity of PEG/Irg was leaked out of the pocket. The cornea was then irradiated with UV light (390nm, 4mW/cm2) and the PEG/Irg underwent a polymerization and the associated phase transition to form a rigid film. Mechanical measurements were performed by means of a purposely-developed device featuring a stepping motor and a load cell. By keeping the pressure constant the role of corneal stiffness is isolated. The force as a function of indentation was recorded for each specimen before and after the in-situ creation of the PEG/Irg film.

Results The mean slope of force versus indentation for the reinforced group was 166.72 (±74.14) and the mean slope for the non-reinforced group was 116.94 (±21.16). The two-tailed P value equals 0.0033, equally meaning that the difference between those two groups was statistically different.

Conclusion According to the results, there was a significant biomechanical reinforcement of the cornea following the in-situ creation of the polymer film.

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Long-term results of simultaneous topo-guided photorefractive keratectomy followed by corneal collagen cross-linking for keratoconus

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Purpose To present the long-term results after simultaneous photorefractive keratectomy (PRK) followed by corneal collagen cross linking (CXL) for keratoconus

Methods In this prospective case series, 26 patients (31 eyes) with progressive keratoconus were included. All patients underwent customized topography guided photorefractive keratectomy (PRK) immediately followed by corneal collagen cross linking with the use of riboflavin and ultraviolet-A irradiation. Epithelium was removed by transepithelial phototherapeutic keratectomy (t-PTK) in all cases

Results Mean follow-up was 19.53 +/- 3.97 months (range 12 to 25 months). Mean preoperative spherical equivalent (SE) was –2.3 +/- 2.8 diopters (D) while at the last follow up examination was significantly ($p<0.001$) reduced to -1.08 +/- 2.41 D. LogMAR uncorrected (UDVA) and corrected distance visual acuity (CDVA) were significantly reduced by 0.46 and 0.084 LogMAR units, ($p<0.001$) at the last follow up examination. Mean steep and flat keratometry readings were reduced by 2.35 D ($p<0.001$) and 1.18 D ($p=0.013$) at the last follow-up examination

Conclusion Simultaneous topo-guided PRK followed by CXL seems to be an effective and safe treatment without any complications in our series of keratoconic patients

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Topical application of autologous adipose-derived mesenchymal stem cells (AdMSCs) for persistent sterile corneal epithelial defect

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Purpose To report a patient with post-traumatic persistent sterile corneal epithelial defect treated with topical application of autologous AdMSCs.

Methods A 35-yr-old man was referred to our clinic for treatment of post-traumatic persistent corneal epithelial defect previously treated as infection. 1 yr before CxL was performed for keratoconus stabilization. Examination showed a central corneal epithelial defect with stromal opacification and thinning. Corneal sensitivity was decreased, while corneal scraping cultures were negative for bacterial or fungal infection. Despite conventional treatment (patching, artificial tears, soft contact lens & autologous serum) no corneal epithelial healing progress occurred 50 days after injury. A PKP was scheduled due to risk of corneal perforation. While waiting for graft, we proposed to the patient the alternative treatment of autologous AdMSCs. IRB was obtained and approved from the Hospital.

Results Corneal epithelial healing process was started 10 days after topical application of MSCs, isolated through liposuction. 1 month later, complete corneal epithelial healing was observed. 1 yr later, corneal epithelium remained intact with mild anterior stromal opacification. The patient's current UCVA lies between 6-7/10.

Conclusion Topical application of autologous adipose-derived MSCs seems to promote corneal epithelial healing in a patient with persistent sterile corneal epithelial defect refractory to other treatments. Differentiation or trans-differentiation of MSCs into corneal epithelial/stromal cells and/or production of trophic factors could be possible mechanisms behind the corneal healing process.

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Late-onset diffuse lamellar keratitis associated with cataract phacoemulsification

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Purpose Diffuse lamellar keratitis (DLK) is characterized by the presence of a diffuse inflammatory infiltrate localized at the laser in situ keratomileusis interface, with a non-infectious etiology. Most cases of DLK occur within the first week following surgery but late-onset DLK has been associated with inflammatory conditions such as iritis, viral keratoconjunctivitis or interstitial keratitis; and it can occur even years after LASIK.

Methods Prospective, interventional, single case report. A 67-year-old male patient, who had undergone bilateral LASIK 13 years earlier, developed an episode of DLK on the third day of the postoperative-cataract surgery on his left eye (LE). Slit-lamp biomicroscopy and optical coherence tomography (anterior segment mode) were performed to demonstrate the presence of highly-reflective multifocal infiltrates and the absence of fluid at the flap interface. The patient was treated with intensive topical corticosteroids.

Results Treatment with topical 1.0% prednisolone acetate was instituted and continued for months, with improvement in patient symptoms and visual acuity.

Conclusion This is a case of DLK with an extremely delayed onset, which emphasizes the importance of following-up of these patients not only in the early postoperative period.

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Ligneous conjunctivitis. Response to topical cyclosporine and mitomycin

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Purpose We report a case of a 50-years-old female referred for pseudomembranous conjunctivitis in the left eye(LE) that is unresponsive to conventional antibiotic treatment, presenting continual recurrence of the membranes after extraction.

Methods Left eye showed hyperemia with yellowish-white pseudomembranes adherent to the tarsal conjunctiva.The extraction of the membranes lead to relapse within a few days.She was treated with antibiotics and topical anti-inflammatory without improvement.

Results The culture was negative.We associated systemic steroids and excision of the membranes with topical mitomycin.Pathological anatomy confirmed the diagnosis of ligneous conjunctivitis,so topical cyclosporine A is added,but persisted upper tarsal pseudomembrane.At this time,repeated injections of mitomycin were performed at the upper eyelid,with remarkable clinical improvement.After months of gradual withdrawal of treatment,the disease remited leaving a retraction in the upper eyelid.

Conclusion Ligneous conjunctivitis is a rare form of chronic conjunctivitis characterized by recurrent formation of conjunctival pseudomembranes-rich fibrin.It begins in childhood as a bilateral conjunctivitis that does not respond to conventional treatments,with yellowish-white pseudomembranes that progress to form woody masses that replace the normal mucosa.Its pathogenesis is unknown,but recently has been associated with type I plasminogen deficiency.These patients may have lesions on other mucous membranes.Treatment consists of topical antibiotics and anti-inflammatories as well as heparin, cyclosporine and topical mitomycin, or the recent addition of topic plasminogen.The visual prognosis is closely related to corneal involvement present in 30% of cases.

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Fourier-domain OCT and keratoconus

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Purpose Optical coherence tomography (OCT) is an optical imaging technique that provides high resolution, cross-sectional, in vivo, noninvasive measurements of the eye. The OCT is widely used in ophthalmology, especially in retina and neurophthalmology. For the study of anterior segment, Visante® OCT has so far been the most widespread, with the disadvantage of high cost and lacks posterior pole module.Currently one of the posterior pole tomographs, Cirrus HD-OCT (Carl Zeiss Meditec Inc., Dublin, CA), has introduced an anterior segment high-resolution module.

Methods We describe the use of Cirrus HD-OCT (Carl Zeiss Meditec Inc., Dublin, CA) and its application in Keratoconus, a prevalent pathology. We present several images of anterior segment Cirrus HD OCT. We can appreciate its use in the study, analysis and follow-up of the keratoconus, as well as for the evaluation of the corneal status aftersurgical treatments.

Results Cirrus HD allows the measurements of corneal thickness and show the thinning process,it shows the corneal ectasia,the presence and quantification of hydrops, defines the exact depth of the placement of intracorneal rings and the visualization of them, the tunnels of implantation, the condition of the epithelium in the main incision, the condition of the keratoplasty seeing the donor-recipient interface, etc.

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• 410
Topical treatment with 0.05% cyclosporine for subepithelial infiltrates secondary to adenoviral keratoconjunctivitis

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Purpose To evaluate the treatment with topical 0,05% cyclosporine A (CsA) in patients with subepithelial corneal infiltrates secondary to adenoviral keratoconjunctivitis.

Methods 4 patients (8 eyes) before and after treatment with CsA 0.05% eyedrops twice daily were prospectively examined. All patients had been treated with topical corticosteroids previously without improvement. The objective data recorded included best-corrected decimal visual acuity, intraocular pressure and evaluation of severity of SEIs (improved, stable, or worse).

Results 1 male and 3 females, mean age of 45 +/- 10 years, were included. Mean follow-up on CsA was 12 months +/- 4 months. The mean best-corrected decimal visual acuity before and after treatment was 0.8 +/- 0.25 and 1.0 +/- 0.28, respectively. 3 patients showed clinical improvement, and 1 was stable during the treatment period. Patients reported reduction in the severity of symptoms before and after the treatment. Most of the patients reported no foreign body sensation, glare, or other side effects with topical CsA treatment. Overall, patients noted an improvement in vision and satisfaction with CsA treatment.

Conclusion Topical CsA 0.05% is a safe and effective alternative treatment in patients with SEIs who do not respond to other treatment modalities or have unwanted side effects from topical steroids.

• 411
Corneal biomechanical properties in myopic LASIK

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Purpose Describe and quantify the effect of myopic LASIK on corneal biomechanics considering the preoperative hysteresis

Methods In 126 eyes with myopia and myopic astigmatism the Ocular Response Analyzer (ORA) was used to measure corneal hysteresis (CH), corneal resistance factor (CRF), Goldman-correlated intraocular pressure (IOPg), and corneal-compensated IOP (IOPcc) before and 3 months after LASIK. We divided the sample into three groups based on the values of CH (mmHg) preoperative: G1 (30 eyes) CH 7.5-9.5, G2 (66 eyes) 9.5-11.5, G3 (30 eyes) >11.5.

Results After LASIK, there was a reduction in mean CH (ΔCH; G1:0.98 G2:1.51 G3: 1.81), CRF (ΔCRF; G1:2.35 G2:2.46 G3:2.83), IOPcc (ΔIOPcc; G1: 3.26 G2:1.74 G3: 1.75) and IOPg (ΔIOPg; G1: 5.01 G2:3.92 G3: 4.31) in three groups. However, there was no statistically significant difference between the groups in the percentage change of CH (G1: 13% G2: 14.6% G3: 15%) and CRF (G1: 25% G2: 23% G3: 24%). While the percentage decrease in IOPcc (G1: 18% G2: 10.5% G3: 11.5%) and IOPg (G1: 31% G2: 25% G3: 27%) was statistically different. Was find a significant correlation between ΔCH and ΔCRF with microns of ablation (r =- 0.406, r =- 0.616) and spherical equivalent (r = 0.405, r =- 0.599).

Conclusion LASIK surgery decreases the corneal hysteresis and corneal resistance factor. The percentage decline of corneal hysteresis and corneal resistance factor after LASIK surgery was no different between the three groups based on the preoperative hysteresis. Although there is a correlation between variations of the CH and CRF, with microns of ablation and the refractive error corrected.

• 412
Peripheral corneal ulceration associated with rheumatoid arthritis

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Purpose To report a case of a patient with rheumatoid arthritis (RA) and associated peripheral corneal ulceration.

Methods A 60 year old woman with RA diagnosed 15 years ago, and under immunosuppressive therapy (IV abatacept 250 mg / month), demonstrated blurring of vision in her right eye. Visual acuity was 6 / 10 in the right eye and 10 / 10 in the left eye. Slitlamp examination revealed a paracentral superior corneal melt in the right eye. Anterior chamber reaction was 2+. Laboratory investigations revealed negative Extractable Nuclear Antigens (ENA) Screen ELISA Test, negative anti-Sm antibodies, positive serum IgG and IgA reactivities, and IgE and IgM within normal levels. Evaluation for the underlying connective tissue disease revealed highly elevated Rheumatoid Factor and C-reactive protein (CRP) (955 IU/ml, normal range: 0-20 IU/ml, and 1.59 mg/dl, normal range: 0-0.8 respectively). The patient underwent extensive treatment with topical tobramycin and lubricants and oral prednisolone 60 mg/day with tapering doses, and methotrexate p.os. 15 mg / week was added.

Results The condition was improved within a few days after the initiation of prednisolone treatment. Re-epithelization occurred one week after the onset of the treatment and only punctate fluorescein dye uptake was detected in the margins of the lesion.

Conclusion The effective control of the underlying disease and early diagnosis of the dry eye syndrome in RA patients may prevent serious corneal complications, such as corneal ulceration, which are difficult to treat. The initiation of treatment with steroids and immunosuppresants was found to halt the progression of keratolysis and assist re-epithelization.

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Clinical and ultrastructural feature of a cornea with pellucid marginal degeneration

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Purpose Pellucid marginal degeneration (PMD) of the cornea is a rare ectatic disorder which typically affects the inferior peripheral cornea in a crescentic fashion. We report clinical, histological and ultrastructural PMD cornea.

Methods A 57 year old female was diagnosed with PMD and keratoconus in the right eye, and PMD in the left eye. Uncorrected vision was: OD 5/200 with pinhole 20/400; OS 20/100 with the pinhole to 20/70. The patient underwent lamellar keratoplasty in the right eye and the excised cornea was processed for light and electron microscopiy.

Results Four months post-operatively uncorrected vision in the right eye was 20/160 improving with the pinhole to 20/60. Ultrastructure of the peripheral and central parts of the cornea was similar to each other. The epithelium was irregular and most of the basal epithelial cells were vacuolated. Hemidesmosomes were broken at various places. Bowman's layer was degenerated and absent or replaced by collagenous panus. Lamellae in the anterior and middle stroma were thin and undulating. Numerous microfilaments were aggregated at the inter-lamellar junction. The collagen fibrils (CF) were running in random directions in the anterior and middle stroma.

Conclusion Our observation of disorganisation and degeneration of CF suggestes that PMD could be related to malfunctioning in the synthesis of CF due to a disorder in keratocan, a luecine rich proteoglycan. Cross linking treatment should be considered for treatment in early stages of the disease.

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Analysis of factors affecting corneal endothelial cell loss after penetrating keratoplasty

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Purpose To evaluate the factors affecting corneal endothelial cell loss after penetrating keratoplasty in the long term follow up.

Methods Donor age, post-mortem time, storage time, underlying disease, elevation of IOP after surgery, underlying glaucoma, trephine size were analyzed in 76 eyes. Post operative corneal endothelial density was measured after 1, 3, 6, 12 months. Patients who experienced graft rejection were excluded.

Results Donor age and endothelial loss was correlated in total patients (t-value=1.98) but post-mortem time, storage time was not statistically significant (t2<2). Endothelial cell loss was more severe in bullous keratopathy patients group than keratoconus patients group but it was not statistically significant (p-value=0.154). The number of antiglaucomatous eye drops showed positive correlation with decline rate of endothelial cell (t-value=1.975). Existence of glaucoma which was diagnosed before surgery did not statistically influence endothelial cell loss. And In bullous keratopathy patients group, inverse correlation between endothelial cell loss and trephine diameter was observed (t-value=-2.859).

Conclusion Old donor age, small trephine size in bullous keratopathy, post operative IOP elevation are risk factors for increased endothelial cell loss following PKP.

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Use of hypo-osmolar riboflavin for corneal cross-linking in thin keratoconic corneas

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Purpose To evaluate the efficacy of UVA collagen cross linking (CXL) on thin keratoconic corneas with previous application of hypoosmolar riboflavin solution.

Methods Twelve eyes of 12 patients with progressive keratoconus and a corneal thickness of less than 400 µm without the epithelium, were submitted to collagen cross-linking after the application of an hypoosmolar riboflavin solution. We instilled one drop every 5 seconds for 2 or 4 minutes to increase corneal thickness up to a minimum value of 400 µm. Pachimetry measurements were taken every 30 seconds to verify the effect on corneal stroma.

Results Mean corneal thickness improved in most cases with reduction of the mean K-value of the keratoconus and no progressionwas observed at six and twelve months after CXL. One year after treatment no scarring lesions in the stroma were observed and all corneas were transparent. Improvement of visual acuity was significant in three patients (25%), low but detectable in seven patients (51%) and no modifications of visual acuity were observed in two patients (24%).

Conclusion Hypoosmolar riboflavin solution showed to be useful to allow CXL procedure in keratoconic corneas with low stromalthickness. No progression of keratoconus was observed six months and one year afer CXL., no developing of stromal scars and patients showed good stability of visual acuity delaying time of surgery.

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Protective antioxidant system disorders in myopic patients

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Purpose The early revealing of the antioxidant system disorders in myopic patients is extremely important for correction and prevention of dystrophic changes in retina and sclera of the eye. One of the most powerful intracellular antioxidants is glutathione (S.M. Cohen, 1994; Paula S. Samiec, 1998). Connected SH and S-S – groups represent tiol and disulfide bonds in protein structures. As a whole concentration levels of these groups can be considered now as important link of antioxidant protection. To evaluate the protective antioxidant system in patients with myopia by the concentration levels of free and connected SH and S-S – groups in tear liquid in patients with myopia of different degree the work was conducted.

Methods 34 children aged 8 - 14 years with myopia of different degree and control group of the same age (10) were examined. Except ophthalmologic observations free and connected SH and S-S – groups in tear liquid were defined by spectrocolormeter Spekol-210 wave length 356 nm and 412 nm accordingly.

Results It was established that levels of connected SH and S-S – groups in tear liquid had tendency to increase in average on (4, 8 – 14, 5) % in dependence of myopic degree. Free SH- groups content in tear of children with high myopia was lower in comparison with control group on 28% (54,2 ± 5,5) u., P<0,05.

Conclusion Free SH- groups content in tear of children with high myopia was significantly lower than in children of other groups. It confirmed that protective antioxidant system abilities are weakened in myopia and that they decrease with myopic severity.

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Ocular surface epithelial thickness evaluation with spectral-domain optical coherence tomography in patients with dry eye syndrome

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Purpose To use spectral-domain optical coherence tomography (SD-OCT) to measure corneal, limbal and bulbar conjunctival epithelial thickness in patients with dry eye syndrome.

Methods A total of 111 eyes of 56 subjects were enrolled in 3 groups: (1) young control (YC group), < 40 years; (2) middle-aged control (MAC group), > 40 years; (3) patients with dry eye syndrome (KCS group). The central corneal epithelium (CE) thickness, and the limbal (LE) and bulbar conjunctival epithelium (BCE) thickness in four quadrants were measured using a SD-OCT. All patients underwent a complete examination of the ocular surface including Schirmer test, TBUT and fluorescein staining.

Results The ocular surface epithelial thickness was not significantly different between the YC and MAC groups. CE thicknesses were not significantly different between the KCS (49.0 ± 4.1 µm) and control groups (48.3 ± 2.9 µm in YC and 48.8 ± 3.0 µm in MAC). The mean LE thickness was significantly lower in the KCS group (77.3 ± 17.2 µm) compared to the MAC group (84.3 ± 10.1 µm, p=0.031). The mean BCE was significantly thicker in the KCS group (50.4 ± 11.1 µm) compared to the MAC group (42.2 ± 7.9 µm, p=0.005). In the KCS group, the BCE thickness was significantly higher in the superior and inferior quadrants compared to nasal and temporal. The mean BCE thickness was significantly higher in ocular surface severity grades 3 and 4 (53.3 ± 12.1 µm) compared to grades 1 and 2 (45.7 ± 7.2 µm) (p=0.031).

Conclusion SD-OCT can provide a non invasive in vivo evaluation of ocular surface epithelial thickness. Limbal and conjunctival epithelium thicknesses were modified in dry eye patients whereas aging seemed to have no effect.

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Analysis of factors affecting the decrease of endothelial cell density of imported donor corneas

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Purpose To evaluate the difference between corneal endothelial cell density at the moment of preservation and keratoplasty in imported donor corneas, and analyze the correlated factors of the difference.

Methods Eighty-seven corneas imported between March 2009 and February 2011 were evaluated. Corneal endothelial cell density at the moment of preservation was obtained from the medical record and was measured just before the keratoplasty.

Results All of the corneas showed decrease of endothelial cell density. Mean endothelial cell density of imported donor corneas at the moment of preservation and keratoplasty was 2789±235 cells/mm2 and 2592±254 cells/mm2(p=<0.001). Mean endothelial cell loss was 197±148 cells/mm2, which was significantly correlated with preservation to surgery time, death to surgery time and preservation period more than 7 days(p=0.042, p=0.045, p=0.036 respectively).

Conclusion Decrease of death to surgery time and keratoplasty before 7days of preservation period are needed for better surgical outcome.

• 419

Efficacy of amnion membrane transplantation (AMT) on corneal surface in annular abscess and anterior uveitis

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Purpose To determine the effect of amniotic membrane transplantation (AMT) on a patient with an annular abscess with a stromal defect of the cornea and anterior uveitis. To determine the effect of amniotic membrane transplantation (AMT) on a patient with an annular abscess with anterior uveitis.

Methods In June 2010 a transplantation of amniotic membrane was performed on a patient suffering from an annular abscess with a stromal defect of the cornea and anterior uveitis. On examination objective findings show a mixed hyperemia with conjuctival chemosis and corneal opacifications, a hypopyon reaching a level of 4 mm and the presence of posterior synechiae, as well as opacities in the vitreous body. We also established corneal epithelial disruption, detected with fluorescein staining of the eye.

Results One month after the AMT a significant improvement was established. We observed epithelization of the cornea, disappearance of the ciliary hyperemia, closure of the stromal defect , resorption of the hypopyon, of the corneal opacifications and opacities in the vitreous body. There was a partial presence of posterior synechiae. The inflammatory process was overcome. Three months after the AMT a semi-transparent leucoma was observed and an increased visual acuity was registered. We inspected solitary posterior synechiae.

Conclusion The AMT was efficient, has manifestive anti-inflammatory effects and could be successfully applied in cases of sever inflammation processes, anular abscess, corneal defects and anterior uveitis.

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A retrospective comparison of enhancement rate between low myopic astigmatism and high myopic astigmatism in patients treated with femtosecond LASIK

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Purpose To analyze the retreatment rate between patients with low myopic astigmatism versus patients with high myopic astigmatism; all of them treated with Femtosecond Laser- Assisted Sub-Bowman Keratomileusis (FSBK).

Methods To analyze the retreatment rate between patients with low myopic astigmatism versus patients with high myopic astigmatism; all of them treated with Femtosecond Laser- Assisted Sub-Bowman Keratomileusis (FSBK).

Results The preoperative mean data were:Group I: Sphere was –3.98 +/- 2.09. Cylinder was –0.44 +/- 0.3 and best corrected visual acuity (BSCVA) was 1.15 +/- 0.1.Group II: Sphere was –3.66 +/- 2.54. Cylinder was –2.41 +/- 0.87 and BSCVA was 1.00 +/- 0.1.Three months after FSBK:The mean postoperative uncorrected visual acuity (UCVA) remained slightly higher in group I (1.08 +/- 0.2) than in group II (0.88 +/- 0.2) with p +/- 0.001. The mean sphere was + 0.02 +/- 0.4 in group I and + 0.11 +/- 0.5 in group II (p +/- 0.009), and the mean cylinder was statistically significant superior (p +/-0.0001) in group II (-0.55 +/- 0.6) than in group I (-0.11 +/- 0.2). This is correlated with the retreatment rate found, which was 26.9% (110 eyes) in group II and 6.48% (28 eyes) in group I (p +/- 0.0001).

Conclusion In patients with primary myopic astigmatism treated with FSBK, we found an statistically significant higher rate of enhancements in eyes with high myopic astigmatism (26.9 %) than in eyes with low myopic astigmatism (6.48 %).

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Ocular surface changes and corneal sensitivity in keratoconus

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Purpose This study aims to describe ocular surface, tear function, corneal nerve and sensitivity in patients with keratoconus.

Methods Thirty-one patients diagnosed as having asymmetrical KC (31 keratoconus eyes, and 31 subclinical keratoconus eyes) and 31 normal control subjects (one eye) were studied in a prospective, cross-sectional study. The subjects underwent routine ophthalmic examinations, corneal topography, corneal sensitivity measurements, Schirmer test, conjunctival impression cytology, and tear osmolarity. Western blot analysis and Immunofluorescent staining with monoclonal antibodies for Class III β-tubulin in corneas of keratoconus and normal were done.

Results The mean corneal sensitivity and Schirmer test values were significantly lower in eyes of keratoconus and subclinical keratoconus compared with control. Conjunctiva of keratoconus and subclinical keratoconus had significantly higher grades of squamous metaplasia and goblet cell loss compared with normal. Corneal nerves were significantly decreased in eyes of keratoconus and subclinical keratoconus compared with control.

Conclusion Whatever the keratoconus-related factors might be, we found marked changes on the ocular surface that affected not only the corneal, but also the conjunctival epithelium. The loss or decreae of trophic effects of corneal nerves due to primary or secondary events with the progression of keratoconus may plays a role in the pathogenesis of the ocular surface change in keratoconus.

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A case of lattice corneal dystrophy due to the L527R mutation in the TGFBI gene in Korea

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Purpose The purposes of this study are to report the first case of LCD type with different phenotype in each eye.

Methods A 67-year-old Korean female patient who was otherwise in good medical health presented with gradual impairment of vision over the previous 1 year. After informed consent was given, slit lamp biomicroscopy and genetic analysis were performed. All the exons from the entire coding regions of stromal corneal dystrophy related genes, TGFBI, CHST6 and M1S1 genes, were directly sequenced to determine if there were any mutations.

Results Relatively thick lattice lines that extended from limbus to limbus in the superficial stromal layers were observed in the right eye by slit lamp biomicroscopy, whereas gray-colored nodular deposits deep in the central stroma were observed in the left eye. We could not find lattice lines in the left eye or any nodular deposits in the right eye. We detected a heterozygous point mutation, CTG CGG (c.1580 T>G: Leu527Arg in exon 12 by IC3D classification) in codon 527 of TGFBI.

Conclusion Given that we identified a Korean patient with lattice corneal dystrophy due to the L527R Mutation in the TGFBI Gene, although this mutation is very rare, LCD type may occur in individuals of races other than Japanese.

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Changes in expression of matrix metalloproteinases 12 and 19 in corneal epithelial cells after UV irradiation

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Purpose Matrix metalloproteinases (MMPs) are zinc-binding endopeptidases that degrade various components of extracellular matrix. MMP-12 participates in macrophage migration and MMP-19 is involved in regulation of angiogenesis. Based on our previous findings dealing with the coincidence of the concentration of proteolytic enzymes with the severity of corneal injury induced by UV irradiation, the aim of this study was to investigate the effects of UVA and UVB rays on expression of matrix metalloproteinases 12 and 19 in the corneal epithelium.

Methods In the first group of rabbits the corneas were irradiated with UVA lamp (365 nm, once a day during 4 days, and a dose per day 1.01 J/cm2). In the second group of rabbits the corneas were irradiated with UVB lamp (312 nm, once a day during 4 days, and a dose per day 1.01 J/cm2). Matrix metalloproteinases 12 and 19 were examined on cryostat sections immunohistochemically by using sheep polyclonal anti-MMP-12 and anti-MMP-19 antibodies.

Results Results show that as compared to normal corneas, UVA rays did not change the expression of MMPs studied in the corneal epithelium. In contrast, UVB rays induced overexpression of both MMPs in corneal epithelial cells. The expression of MMP-12 was more pronounced in irradiated corneas than the expression of MMP-19.

Conclusion In conclusion, UVB rays (not UVA rays) evoked increased expression of MMPs in irradiated corneas. Results point to the suggestion that overexpression of these MMPs due to UVB-exposure might mediate previously found angiogenesis and neutrophil migration through the UVB-irradiated cornea and thus contribute to the development of abundant inflammatory response.

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Anti-inflammatory mechanisms of mapracorat, a novel selective glucocorticoid receptor agonist, in human conjunctival fibroblasts

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Purpose Mapracorat (BOL-303242-X; ZK 245186) is a selective glucocorticoid receptor agonist (SEGRA), under clinical evaluation for the treatment of inflammatory eye and skin diseases. It is structurally distinct from glucocorticoids and NSAIDs. Data suggest an improved side effect profile of this compound compared to traditional glucocorticoids. This study was to determine its anti-inflammatory mechanisms.

Methods Primary human conjunctival fibroblasts (HConF)were challenged with IL-1ß and Luminex technology or ELISA was used to determine the effect of mapracorat on IL-1ß-induced cytokine, prostaglandin E2 (PGE2) and matrix metalloproteinase (MMP) release in the presence or absence of mifepristone (RU-486), a glucocorticoid receptor antagonist. The effect of mapracorat on IL-1ß-induced cyclooxygenase-2 (COX-2) expression was assessed by Western blotting. Dexamethasone was used as the control.

Results IL-1ß induced release of multiple cytokines, including IL-6, IL-8 and monocyte chemotactic protein-1 (MCP-1), and of PGE2 and MMPs (MMP-1 and MMP-3), as well as the expression of COX-2. Mapracorat inhibited cytokine, PGE2 and MMP release as well as COX-2 expression in a dose-dependent manner with comparable effectiveness as dexamethasone. The inhibition of cytokine and PGE2 release was fully or partially reversed by mifepristone.

Conclusion Mapracorat acts as a potent anti-inflammatory agent in HConF by inhibiting multiple intracellular mediators. The fact that mapracorat is effective on inhibiting PGE2 pathway suggests that it may reduce post-surgery pain. Clinical significance of these findings needs further investigation.

Commercial interest

• 425 / 4344
Skin tattoos and the development of uveitis

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Purpose To report a case of recurrent non-granulomatous anterior uveitis associated with tattoo inflammation.

Methods A 28-year-old female presented to our ophthalmology department with a sharp shooting pain, photophobia and redness in both eyes but more pronounced in the right eye. A bilateral anterior uveitis was noticed. Simultaneously she experienced a rash at the site of her skin tattoos. The patient had her skin tattooed quite extensively at the chest, the back and around the umbilicus, between 13 years and one year ago.

Results Investigations for causes of anterior uveitis, including general and infectious serologic testing, ACE, HLA-B27 and chest X-ray were normal. Clinical pneumological examination, thoracic CT and abdominal ultrasound showed no arguments for sarcoidosis. A tattoo biopsy showed a granulomatous response of lymphocytes and histiocytes around tattoo pigment, there was no histological evidence for sarcoidosis.

Conclusion Tattoo granulomas can be a manifestation of sarcoidosis but may also be a delayed hypersensitivity reaction to pigment containing metallic tattoo compounds. The association of recurrent anterior uveitis with swelling of skin tattoos is an unusual occurrence. Similar cases of uveitis associated with tattoo inflammation have been reported in the literature.

• 426 / 4345
Acute retinal necrosis. 3 case reports

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Purpose To present three case reports of acute retinal necrosis (ARN) syndrome and discuss the aspects of diagnosis, treatment and prognosis.

Methods Retrospective analysis of clinical, laboratory, photographic and angiographic records of three immunocompetent patients with acute retinal necrosis syndrome.

Results Two male 22 and 36 years old and one female 25 years old patients had typical clinical symptoms of ARN syndrome: sudden decrease of vision acuity, eye pain, multiple areas of peripheral retinal necrosis, occlusive vasculitis, opticopathia, anterior uveitis and vitritis. Serum Ig G antiviral (VZV, HSV, CMV) titers were the basis for the etiological diagnosis. After applying systemic antiviral and steroid therapy, a rapid improvement of symptoms with the development of pigmentation in the areas of retinal whitening was observed in all patients. Retinal detachment occurred in 2 male patients and was successfully treated.

Conclusion Acute retinal necrosis syndrome is one of the vision threatening diseases for immunocompetent patients with poor prognosis. Early diagnosis and urgent antiviral therapy is therefore of vital importance for visual outcomes. Long term follow-up is necessary due to high risk of retinal detachment.

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Slowly progressive corneal opacification in a patient with known mucocutaneous leishmaniasis and HIV

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Purpose To present a case of corneal opacification and anterior uveitis in a patient with systemic Leishmaniasis

Methods Case report

Results A 40-year old HIV-positive patient was already followed for conjunctival involvement in systemic Leishmaniasis. Treatment with Glucantime was effective, but had to be stopped because of acute pancreatitis. A switch to Ambisome was made, but did not result in complete resolution.Slow appearance of corneal stromal opacities was also noted at this time. In January 2011 the patient consulted in emergency and was diagnosed with bilateral acute anterior uveitis as well as manifest progression of the stromal opacification. Regarding the inflammation, a good initial response was obtained with topical prednisolone acetate. However, a slumbering reaction remained present in the anterior chamber and an increase of the keratic precipitates was noted. On tapering of the steroids, several relapses occurred.The intrastromal opacities were still increasing, resulting in worsening visual acuity. An in-vivo confocal microscopy of the cornea was performed and showed presence of cystic structures in the stroma, possibly related to intracorneal presence of the parasite. Because of insufficient response of the anterior chamber reaction to topical steroids, anterior chamber tap was performed and PCR showed positive for Leishmania.A tentative treatment with intrastromal and intracameral injection of Amphotericin B was initiated.

Conclusion We report an atypical ocular presentation of Leishmaniasis, with proven presence of the organism in the aqueous humor, and presence of the cystic structures on in-vivo confocal microscopy. A tentative treatment with intrastromal and intracameral injection of Amphotericin B was initiated.

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Meganuclease-mediated inhibition of HSV1 infection

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Purpose Current anti-viral treatments of Herpes simplex virus type 1 (HSV1) inhibit the viral replication but impair neither the viral cycle at its early stages nor the latent form of the virus. Latent HSV1 virus could be addressed by rare cutting endonucleases, such as specific meganucleases.

Methods Co-transfections with plasmid expressing I-CreI variants cleaving target sequences and GFP were performed using Lipofectamine on BSR cells for 48 hours. After infection for 8h with SC-16 at different MOIs (Multiplicity Of Infection) ranging from 0.1 to 8, cells were incubated with i) HSV1 rabbit antibodies and ii) with phycoerytrine (PE) conjugated goat anti-rabbit IGg secondary antibodies. Fluorescence-activated cell sorting (FACS) analysis was performed. The ratio of infected cells among transfected (GFP+) and non transfected (GFP-) cells were counted and an antiviral index was calculated.

Results GFP+ and GFP- cells were both well represented in all experiments, with an average GFP+ cell frequency of 0.63 over 90 transfections (standard deviation: 0.20). A strong inhibitory effect was observed at MOIs of 0.1 and 0.5, with 4 to 7 times less infection among GFP+ cells than among GFP- ones. This effect was however not detected by a MOI of 2.

Conclusion Meganuclease proteins in BSR cells inhibits the replication of HSV1, at moderate MOIs, inducing a significant reduction of the viral particules. This qualifies meganucleases as a new class of antiviral agent, with the potential to address replicative as well as latent DNA viral forms. Specific meganucleases may thus be used in the future with the aim of controlling recurrent herpetic keratitis.

Commercial interest

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Effect of SOCS1 overexpression on RPE cells activated by cytokines

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Purpose Retinal pigmented epithelium (RPE) cell activation by cytokines plays an important role in autoimmune uveitis development. The aim of this study was to investigate if Suppressors of Cytokine Signaling (SOCS1) overexpression in RPE cells can modulate this activation.

Methods SOCS clone and control clone were isolated after stable transfection of APRE-19 with plasmids containing or not the SOCS1 gene. qRT-PCR was used to measure SOCS1 mRNA expression. Clones were stimulated by IFNγ or/and TNFα. Membrane expression of MHCII and CD54 was measured by flow cytometry, IL-8 secretion by ELISA and (P-)STAT-1 and IκBα expression by Western Blot.

Results We found a stable high expression of SOCS1 in the SOCS clone as compared to the control clone or native ARPE cells. This SOCS1 overexpression strongly decreased IFNγ-mediated STAT-1 phosphorylation, MHCII induction and CD54 upregulation. On the contrary, SOCS1 overexpression had no effect on TNFα-mediated IκBα degradation, IL-8 upregulation, but weakly inhibited CD54 upregulation. During simultaneous IFNγ and TNFα stimulation, SOCS1 overexpression canceled the inhibitory effect of IFNγ on TNFα-induction of IL-8 secretion.

Conclusion SOCS1 overexpression can block IFNγ but have almost no effect on TNFα activation of retinal pigmented epithelium cells. Those data suggest that SOCS1 overexpression might only affect certain cytokine pathways important in autoimmune uveitis development.

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Loiasis. approach to a form of ocular parasitosis

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Purpose We report the case of a 37 year old male from Guinea referring foreign body sensation in his right eye intermittently for 5 years. The slit lamp examination revealed a creeping worm under the conjunctiva. The microbiological analysis after surgical removal confirmed that it was an adult form of Loa-Loa.

Methods The anterior segment examination demonstrates the existence of a structure cordoned mobile moves creeping under the superior bulbar conjunctiva of his right eye. Given the findings are applicable to the surgical removal under local anesthesia of a worm 6 cm in length.

Results Microbiological study confirms the diagnosis of Loa Loa in their adult form (female).

Conclusion : Loiasis is a parasitic disease endemic in Africa. Recognition of the condition must be due to increased African migration to Spain. Surgical removal of adult Loa loa worms from the subconjunctival space only the ocular Improves Symptoms. An interdisciplinary approach (ophthalmology, infectious disease and parasitology) for a systemic work-up and treatment is usually required.

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Demodex infestation in the normal population, blepharitis patients and among people who work with microscopes

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Purpose Aim of the study was to estimate the prevalence of Demodex spp. infections of lid margin in Polish population

Methods 264 individuals were enrolled in the study. Patients were divided into four groups. First two groups consisted of young people (mean age 22 years) and seniors (mean age 66 years). The third group was made up of people who work with microscopes. Forth group consisted of patients with diagnosed blepharitis. From every individual 3-4 lashes were epilated from upper and lower lid margin of each eye and examined under the microscope for Demodex mites.

Results The lowest number of infected individuals was observed in the young group- only 5%, the highest in blepharitis patients- 74% infected. Among microscope users (mean age 44 years) 30% were infected, in senior group (mean age 66 years) also 30% were infected.

Conclusion Demodex mites are etiological factors of blepharitis. There is a significant correlation between Demodex spp. infection and the age of the examined individual. People who work with microscopes are in a risk group for Demodex infection of lid margins.

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ICAM-1 and HLADR expression on conjunctival epithelial cells in patients with Graves' orbitopathy and Graves' disease - preliminary report

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Purpose The objective of the study was to evaluate wheather an assessment of conjunctival epithelium expression of HLA-DR and ICAM-1 could be helpful as an early marker of local inflamation in the eye and the orbital tissue.

Methods Specimens for flow-cytometric evaluations of ICAM-I and HLADR expression were collected by impression of ocular surface from 8 eyes with Graves' diaseas without signs of active Graves' orbitopathy (CAS ≤ 4), from 8 eyes of patients with active Graves' orbitopathy (CAS ≥ 4) and from 14 normal speciments without any ocular surface disorders.

Results Decreased fluorescence of ICAM-1 on conjunctival epithelium cells was detected in patients with active Graves orbitopathy vs. patients with Graves wihout orbitopathy. There was no correlation between the CAS and NOSPECS values and the expression of ICAM-I and HLADR expression on conjuctival epithelium.

Conclusion Results of this preliminary study confirm that conjunctival epithelial cells may abnormally express ICAM-1 on conjunctival epithelium cells in active ocular surface disorder like Graves orbitopathy. Nethertheless, since the number of the examined patients needs to be enlarged the study needs further examination.

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Mutations in the BAP1 gene in uveal melanoma

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Purpose Uveal melanoma (UM) is the most frequently occurring intraocular malignancy in adults. UM has a strong tendency to metastasize to the liver. There are no effective therapies for metastatic disease resulting in a tumour-related death in about 45% of UM patients within 15 years after the initial diagnosis. Monosomy of chromosome 3 is the most frequent found chromosomal aberration in UM and is predominantly found in metastasizing tumours. Chromosome 3 losses can be detected by karyotyping, FISH or DNA based techniques as QPCR/MLPA and Array CGH. We use a combination of FISH and SNP arrays to select patients for a dendritic cell therapy trial.Recently, inactivating somatic mutations were identified in the gene encoding BRCA1-associated protein 1 (BAP1) on chromosome 3p21.1 in metastasizing tumours. In a retrospective series of UMs we will determine the sensitivity and specificity of mutations in BAP1 and compare these with the currently used predictive standard of monosomy.

Methods We will use targeted multiplexed Next Generation Sequencing to determine mutations in the BAP1 gene.

Results Our results will follow shortly.

Conclusion Conclusions will be drawn when all the results are known.

• 434 / 3367
Preclinical study of a glycoengineered anti-human CD20 antibody in murine models of primary cerebral and intraocular B-cell lymphomas

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Purpose Primary cerebral lymphomas (PCL) and primary intraocular lymphomas (PIOL), related to the systemic diffuse large B-cell lymphoma family, are highly aggressive tumors, with poor prognosis and any specific therapy. Despite good results obtained with chemotherapy, many patients relapse and new therapeutic strategies are needed. PCL and PIOL are characterized by the presence of CD20+ lymphomatous B-cells and as such are eligible for therapy with anti human CD20 antibodies.

Methods In this study, we evaluated the efficiency of LFB-R603, a promising glycoengineered anti-hCD20 monoclonal antibody that displays a high affinity for FcgRIIIa (CD16) receptors, when injected intumoraly. We used a murine lymphomatous B cell line transfected with the human CD20 gene to generate two syngeneic murine models of PCL and PIOL

Results After a single therapeutic injection of LFB-R603 mAb, a strong anti-tumor response was noted against the PCL and a less pronounced response in the PIOL model. This was linked to an inhibition of tumor growth and infiltration with CD8+ T-cells in both models. Interestingly, therapeutic effects were much better than those obtained with the Rituximab used as a reference.

Conclusion These in vivo results confirm the potential of the LFB-R603 mAb as an innovative therapeutic approach for the treatment of PCNSL tumors.

• 435 / 4162
Juvenile xanthogranuloma of the iris treated with proton beam radiotherapy.

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Purpose To report a case of juvenile xanthogranuloma of the iris treated with proton beam radiotherapy.

Methods An 18-year-old male presented in October 2010 with blurred vision of the left eye. Clinical examination showed a hyphaema. A yellow-pink tumour was noted in the temporal aspect of the iris. Ultrasonography showed the tumour to have a low internal reflectivity, measuring 7.8mm by 6.4mm in basal diameter with a thickness of 1.4mm. The lesion was noted to be extending to the pars plana. Incisional biopsy showed the tumour confirmed a diagnosis of juvenile xanthogranulomatosis. Treatment with topical steroids was unsuccessful. The patient was therefore treated with proton beam radiotherapy, comprising 18 Gy delivered in four fractions, penetrating to 4mm. Margins of 8mm around the lesion were also treated.

Results The patient was followed up in March 2011 where significant tumour shrinkage was observed on slitlamp examination. The response to treatment was confirmed on ultrasound. There were no new lesions and no evidence of anterior chamber activity. The patient remains under review.

Conclusion Proton beam therapy is an effective alternative local treatment for this condition.

• 436 / 4164
Superselective intra-arterial chemotherapy complications in advanced retinoblastoma

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Purpose The purpose of this study is to report the complications of superselective intra-arterial chemotherapy with melphalan in children undergoing treatment for advanced intraocular retinoblastoma.

Methods 49 eyes of 43 children with advanced intraocular retinoblastoma (Reese-Ellsworth Group Vb or International Classification Group D) were treated with superselective intra-ophthalmic artery infusion of melphalan. 22 eyes of 43 children were first diagnosis. 27 eyes of 43 children had previously failed traditional management with systemic chemotherapy and focal therapies and underwent intra-ophthalmic artery infusion of melphalan as an alternative option to enucleation. Serial complications RETCAM images were collected.

Results Ophthalmic artery cannulation was successfully performed in 49 eyes of 43 patients. 9 eyes out of 43 (20.9%) patients were enucleated. 4 eyes out of 43 (9.3%) patients were lost to follow-up. No severe systemic side effects occurred. Grade III neutropenia was seen in 3 patients (0.6%). No transfusions were required. 25 (58.1%) patients developed eyelid hyperaemia, 10 (23.2%) frontal region skin rash, 12 (27.9%) emiptosis, 6 (13.9%) eyelid edema, 2 (4.6%) frontal alopecia, 2 (4.6%) eyelashes loss, 2 (4.6%) chorioretinal atrophy, 1 (2.3%) acute ischemic optic neuropathy, all resolved spontaneously. 1 case (2.3%) with permanent ptosis underwent surgery. 1 case (2.3%) presented Roth's spots.

Conclusion Ophthalmic intra-arterial infusion with melphalan is a promising globe-conserving treatment option in advanced retinoblastoma cases with minimal systemic side effects.

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Anterior segment OCT and histopathologic data in conjunctival, limbal and subconjunctival tumours

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Purpose To show the use of anterior segment optical coherence tomography (AS-OCT) in conjunctival, limbal, subconjunctival tumors and to compare the data with histopathologic specimens.

Methods 15 patients (15 eyes) with conjunctival, limbal and subconjunctival lesions were examined using AS-OCT (Visante OCT 2.0, Carl Zeiss Meditec, Dublin, CA). Eyes were scanned using Anterior Segment Single, High Resolution Corneal and Raw Image modes. Gray-scale, OCT Color and Rainbow Color images were analyzed using built-in software. All tumors were excised and histopathologicaly examined.

Results In all small tumor cases AS-OCT allowed to see the deeper lesion structure with complete penetration. In conjunctival melanoma, papilloma, subepithelial naevus and pterygia cases AS-OCT showed tumor structure, layers and extension clearly. Underlying cornea was also visible. In larger and solid tumors (squamous cell carcinoma, fibroma and lipoma) anterior surfaces were hyper-reflective, but the deeper structures of the lesions were incompletely penetrated. However, in all cases it was possible to differentiate cystic lesions from solid lesions. Histopathologic examination revealed the diagnosis and in small tumors confirmed the AS-OCT data showing tumor epithelium and underling layers.

Conclusion AS-OCT may be a useful non-invasive diagnostic tool for the evaluation of ocular surface tumors in selective cases. AS-OCT may give useful information before planning the surgery.

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Squamous cell carcinoma (SCC) of the caruncle, with clinical presentation of an inflammatory mass.

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Purpose The presentation of 2 cases with a very rare adenoidlike SCC of the lacrimal caruncle, clinical referred with a inflammation mass apparent as an abscess.

Methods The tissue of a lacrimal caruncle is arising as well as from skin as mucous and adnexal structures, where in most of the patients only benign laesions could be developed. In our cases inflammation and malignant tumours were found. The diagnosis were made clinical, by imaging methods, (as coherence tomography scan (CT), and ultrasound) and histological analyses. In both cases good differentiated squamous cell carcinomas of the right caruncle were characterized

Results Although in the literature very rarely found, the adenoid type of SCC is described as a less malignant type but in our cases with inflammation a more aggressive behaviour was demonstrated during the follow-up. Both patients refused orbital exenteration and radiotherapy was performed. However in the second patient, at a later stage, an exenteration was done for a recurrence and extension to the nose and sinus, she died several months later.

Conclusion The very rarely published adenoid caruncle SCC , which first was presented in two cases as an

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Adenocarcinoma of the retinal pigment epithelium: clinicopathological case report

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Purpose Adenocarcinomas of the retinal pigment epithelium (RPE) are rare adult tumors, treated with enucleation or surgical excision. We present a child with an adenocarcinoma of RPE, treated with protontherapy.

Methods A 10-year-old girl with loss of vision had a pigmented macular tumor, diagnosed as hamartoma. Five years later, tumor growth led to a transvitreal incisional biopsy.

Results Histopathology and immunohistochemistry were compatible with an adenocarcinoma of the RPE. The tumor was irradiated. After 5 years of follow-up, the tumor is under control and the patient presents no distant metastases.

Conclusion Adenocarcinomas of the RPE can simulate a combined hamartoma of the retina and RPE. Diagnosis can only be established after biopsy. Protontherapy is a valid therapeutic alternative.

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Unexpected ectopic thyroid tissue in the orbit: a clinical case report

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Purpose To present clinical case report of the benign ectopic thyroid tissue in the orbit.

Methods 75-year-old woman with a slowly growing, painless, elastic tumor in the left inferior –lateral part of the orbit complained about diplopia, eye globe protrusion and dislocation medialy-superiorly. Symptoms were progressing for two years. Head magnetic resonance imaging (MRI), tumor excision and histopathological examination of the obtained specimen were performed.

Results Head MRI showed 18x14 mm in size, non-homogenic, contrast accumulating mass with well defined margins in the inferior –lateral part of the orbit. Gross examination of the excised mass revealed grey color, round tumor, covered by connective tissue. Histologicaly tumor was well circumscribed, composed of micro-/ macrofolicules with colloid. Folicular epithelium had no atypical changes. These criteria support diagnosis of ectopic thyroid tissue with slight signs of goiter. In the National Pathology Registre it was found that one year before patient had thyroidectomy and histological diagnosis of nodular thyroid hyperplasia and follicular adenoma was established. Possibility of follicular carcinoma metastasis to the orbit was rejected reviewing both cases by three pathologists and only usual Hematoxylin/Eosin method was used for staining.

Conclusion There are rear case reports of ectopic thyroid tissue. To our knowledge this is the first description of thyroid tissue with signs of goiter in the orbit.

• 441

Epiretinal membranes in a patient with Scheie's syndrome diagnosed using a high-resolution SD-OCT

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Purpose To report a case of a young woman with Mucopolysaccharidosis I-S (Scheie's Syndrome) having bilateral epiretinal membranes (ERMs) which have been confirmed by the use of a high resolution spectral-domain optical coherence tomography (Spectralis SD-OCT).

Methods A 28 year-old female, diagnosed with Scheie's Syndrome since 8 years old, was examined in our department. For the last 6 years she has been receiving weekly intravenous laronidase. In manifest refraction the patient achieved a visual acuity of 20/40 OD and 20/32 OS with a high hyperopic spherical equivalent correction (+7.50D, OU). Slit-lamp anterior segment examination showed the presence of diffuse corneal haze in both eyes which obscured retinal view. During dilated fundus examination she complained of severe photophobia. An OCT examination using the Spectralis SD-OCT (Heidelberg Engineering, Germany) was performed to evaluate the retinal pathology.

Results The SD-OCT examination revealed the presence of epiretinal membranes in both eyes without any signs of macular edema.

Conclusion In patients with mucopolysacharidosis I the view of retinal abnormalities with the use of a slit-lamp biomicroscope could be difficult due to corneal haze and severe photophobia. SD-OCT examination is an alternative method to investigate the presence of epiretinal membranes or other retinal pathology in such cases.

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Initial experience of a nationwide ruthenium-106 and iodine-125 ocular brachytherapy service in Ireland

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Purpose St. Lukes Hospital, Rathgar, Dublin 6, Ireland has recently implemented an Ocular Brachytherapy Service using both Ruthenium-106 and Iodine-125 plaques. This work will summarize the initial experience of the hospital in these treatment modalities and provide information on some of the challenges experienced by a new centre performing this technique. Outline plans for the future of the service will also be presented.

Methods Between September 2010 and June 2011, twenty six patients received a plaque treatment at St. Lukes Hospital. Six of these were Iodine-125 cases, while twenty used Ruthenium-106. A multi-disciplinary pre-planning procedure using BEBIGs "Plaque Simulator" software identifies treatment durations. This group consists of a Physicist, Consultant Ophthalmologist and a Consultant Radiation Oncologist with the goal of fitting both plaque insertions & removals into designated weekly theatre slots. Following this, a comprehensive plancheck analysis is performed. Post-treatment, a delivered plan is generated by a Physicist and signed by the clinical team.A yearly delivery of Ruthenium plaques is scheduled; information is given on plaque types, number of uses and plans for Year Two. NPL calibrations were used as a second-check in Year One with an in-house method involving a stereotactic diode proposed for Year Two.

Results Nine months into the program, tumour regression in the initial patients is already being observed. Procedures have been streamlined to satisfy designated theatre slots where possible and to maximise throughput of patients. A second-check calculation procedure for Ruthenium plaques has been devised; however the long-term plan proposes a greater proportion of Iodine treatments due to the timing flexibility this provides.The in-house method of calibration shows promise, however further investigations are required before it is suitable for clinical use. This work is ongoing.

Conclusion An Ocular Brachytherapy service has been successfully implemented in St Lukes Hospital that is providing both Ruthenium-106 and Iodine-125 treatments to patients across the Republic of Ireland. As the service matures and further intra-departmental training takes place, the facility will be well prepared to handle both an increase in capacity and complexity while performing treatments to a high standard.

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Orbital involvement in multiple myeloma

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Purpose To present the case report of a patient with multiple myeloma who develops orbital infiltration in the left side due to the myeloma.

Methods A 53-year-old male with the diagnosis of IgA-kappa multiple myeloma 3 years ago, stage III B in the staging system of Durie and Salmon, who has increased the volume in the left upper eyelid region in recent months. On examination the patient had moderate ptosis without affecting the pupillary axis, exophthalmos of 22.5 mm, hypotropia in primary position of gaze and limitation of supraversion left eye. Radiological and histological findings confirmed the existence of orbital extension of multiple myeloma at the supero-internal quadrant.

Results The patient has received several lines of chemotherapy treatment and autologous bone marrow transplantation without systemic or orbital improvement. Because of its systemic poor condition has been rejected surgical treatment and radiotherapy to the orbital level.

Conclusion Although orbital involvement is rare and there are few reports in the literature, a patient with multiple myeloma who presents proptosis and / or increased the orbital volume, we must consider orbital infiltration by myeloma however, definitive diagnosis is histological.

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Atypical inflammatory myofibroblastic pseudotumor of the etmoidal sinus extending into the orbit

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Purpose To report a case of an atypical inflammatory pseudotumor of the paranasal sinuses with bony invasion extending into the orbit .

Methods Case-report.

Results A 71-year old man presented with slowly progressive painless diplopia followed by unilateral proptosis of the left eye with a slight edema of the upper eyelid. Visual acuity was 0.4 with a relative afferent pupillary defect . Abduction and depression of the left eye were limited. Imaging showed an orbital tumor around the obliquus superior with lateral displacement, possible infiltration of the superior and medial rectus, involvement of fossa pterygopalatinum , sinus etmoidalis, sphenoidalis and maxillaris , intracranial extension through the fissura orbitalis superior, bone erosion and sclerotic bone reaction. Endoscopic ethmoïdal, maxillary and orbital biopsies discovered a inflammatory myofibroblastic tumor. Blood parameters showed eosinophily. ANCA and CRP were negative.Discussion: In the literature three cases of orbital myofibroblastic tumors have been described but never with bone invasion. Only a few sinus inflammatory pseudotumors with bony erosion have been reported. Central nervous system myofibroblastic tumors give a dura based mass-formingan en plaque pattern. Two cases with orbital involvement have been described.

Conclusion : This eroding sino-orbital inflammatory myofibroblastic tumor is a new finding mimicking a malignant tumor.

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Extraskeletal chondroma of the palpebral conjunctiva : a case report

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Purpose To report one rare case of soft tissue chondroma of palpebral conjunctiva.

Methods A 34-year-old female presented with one year history of a slowly enlarging painless mass arising in the left eye. There was no history of trauma or any medical problems. Physical examination revealed a placoid mass of the upper palpebral conjunctiva of the left eye. It was firm, round with 3.0mm diameter and not infiltrative with good-defined margins.

Results Excisional biopsy revealed a white hard tumor with no pus. Histological examination showed a neoplasm composed pilosebaceous glands and fibrous connective tissue with focal cartilage. The histopathology report was benign chondroma. At one month follow-up, the patient was asymptomatic without infection and any evidence of recurrence.

Conclusion This is one rare case of chondroma of palpebral conjunctiva. And no other cases were reported before in literature.

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Incidence of eyelid cancers in Singapore - a 13-year review

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Purpose To determine the epidemiology of patients with eyelid malignancies in Singapore from 1996 to 2008

Methods The Singapore Cancer Registry has been collecting epidemiologic data of all cancers seen in Singapore since 1968. The epidemiology of eyelid cancers diagnosed from 1968 to 1995 have previously been reported by Lee et al. The data of all eyelid cancers from 1996 to 2008 was retrieved for analysis. The age standardized incidence rates and age-specific incidence rates were calculated and the results were compared to the previous study

Results There were a total of 160 male patients (48%) and 173 female patients (52%). The average annual age-standardised incidence rate among male Singapore residents was 5.2 per 1,000,000 and 5.1 per 1,000,000 among female Singapore residents. Between 1996 to 1998, the average annual rate for females was 6.6 per 1,000,000, compared to 3.9 between 2005 to 2008. The most common cancer was basal cell carcinoma (82%), follwed by sebaceous adenocarcinoma (11%) and squamous cell carcinoma (4%)

Conclusion The annual age- standardized incidence rates for male residents have remained relatively stable. The rates for female residents have showed a steady decline over the last 13 years. The rates for males are generally higher than for females. Basal cell carcinoma dominates the incidence trends. These expanded epidemiological characteristics serve to provide ophthalmologists and epidemiologists with a foundation to monitor future disease patterns in Singapore and provide a basis for comparison with other selected populations elsewhere

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Treatment of an infantile hemangioma with propanolol

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Purpose Angiomas are common vascular tumors in children. Only 10-15% should be treated by any vital consequences, functional or aesthetic complications. Classically, oral corticosteroids were the preferred treatment for this type of injury. We present the results obtained after treatment of an eyelid angioma in an infant with oral propranolol.

Methods Infant 6 months old, was referred to our clinic for purple injury which had gradually increased in size, in the right lower eyelid.Underwent imaging studies (MRI), which together with the clinical features led to the diagnosis of eyelid hemangioma without intraorbital extension, so it was decided to start treatment, under pediatric control with 2 mg / kg / day of oral propranolol suspension in two doses.

Results Three months after starting treatment we found a partial regression of the lesion. Complete resolution occurred after 8 months. During this period there were no adverse reactions or complications to treatment with propanolol.

Conclusion Treatment with oral propranolol is currently an effective and safe alternative in the management of infantile hemangiomas.

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Treatment and visual outcome in orbital and palpebral hemangiomas of infancy

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Purpose To study the relationship between the location of orbital and palpebral(eyelid) hemangiomas and ocular problems in children and the interventions needed to prevent or reduce the severity of visual impairment.

Methods This study included 12 cases (10 female and 1 male;age range:1 day to 5 months old at first evaluation;mean age 2,5 months)of eyelid and/or orbit hemangiomas gathered over a 6 year period (2005-2011).Ultrasonography and magnetic resonance imaging(MRI)identified these lesions to be:palpebral in 2 cases, palpebral and orbital involvement in 9 cases.Pediatric and ophthalmological evaluation(orthoptic examination,visual acuity determination with Teller Acuity Cards,refractometry and fundus opthalmoscopy)were performed in all cases.

Results The mean follow-up was 36 months (range 11-63 months)Treatments for infants and children with hemangiomas obstructing the visual axis included oral steroid administration(9 cases);in 1 case a surgical treatment was associated.4 cases developed amblyopia and 1 case strabismus.Treatment of early amblyopia through selective patching part-time patch occlusion of the uninvolved eye and early prescription of astigmatism correction was performed.10 children achieved normal vision at last evaluation.

Conclusion In our study 10 patients treated for visual impairment and available for long-term follow-up showed an excellent functional outcome with no residual amblyopia.In most cases,early intervention to address hemangioma-related visual disturbances can lead to a good functional outcome. Intervention typically involves medical debulking of the hemangioma(using oral steroids)combined with the treatment of early amblyopia through selective patching and/or optical correction with refractive lenses.

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Cationic oil-in-water emulsions protect and restore function of the injured ocular surface

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Purpose Ocular surface damage is a consequence of tear instability arising from numerous inciting events: preserved eye drops, contact lens wear, systemic medications, environment and age. While unpreserved eye drop reduce iatrogenic toxicity they do not restore the deficient tear film which leads to ocular surface injury. Cationic oil-in-water emulsions have been shown to restore and reduce evaporation of the tear film. We studied the effect of cationic emulsions (Cationorm® and Catioprost®) in established animal models of ocular surface injury.

Methods Acute toxicity and local tolerance were evaluated in rabbits. Healing properties were assessed in a rat model of corneal scraping. Abrasions were treated for 5 days, and corneas were evaluated clinically and histologically. Conjunctival function was assessed by goblet cell (GC) count and MUC5 immunostaining. The kinetics of ocular surface healing was assessed in an in vitro scraping assay.

Results Neither Cationorm® nor Catioprost® induced toxicity as evidenced by clinical and confocal microscopy scoring. Catioprost® was well tolerated, with a reduced (-42%) occurrence of hyperemia when compared to Xalatan®. In rats, Catioprost® improved healing, protected GC and maintained normal MUC5 secretion. In vitro, the cationic emulsions improved cell migration and maintained MUC4 expression.

Conclusion Cationic emulsions were well tolerated. In contrast to preserved and unpreserved ophthalmic drops, cationic emulsions promoted healing, restored function of injured ocular surface, and protected against ocular surface injury. The findings suggest that cationic emulsions by augmenting the tear film may benefit patients with ocular surface disease.

Commercial interest

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Ghrelin expression in the rat's eye

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Purpose The purpose of this study was to evaluate the ghrelin's ocular tissue distribution in the adult rat's eye and to confirm previously reported data, describing the identification of ghrelin's mRNA in the iris posterior epithelium and in the ciliary body non pigmented epithelium.

Methods Adult Wistar rats were sacrificed through an intraperitoneal injection of sodium pentobarbital and both eyes were immediately enucleated and processed for cryostat sections and indirect immunofluorescence protocol. Slides were incubated with anti-ghrelin, anti-histone H3 (positive control) and with 2% NGS (negative control) at 4ºC for 48 hours and then with secondary antibody containing a fluorescent tag during 1 hour. After incubation slides were examined under a fluorescence microscope.

Results We observed immunolocalization of ghrelin in the rat's ciliary body epithelium. Its major label was in the inner part of that epithelium facing to the stroma of the ciliary processes. This peptide was not localized in the posterior segment, naamely in the retinal pigmented epithelium.

Conclusion Ghrelin is locally produced in the eye, mainly in the ciliary processes. Based on these findings, we can conclude that this peptide may play a role as a local regulator of the aqueous humor dynamics and ciliary muscle kinetics.

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Cystoid macular oedema in a phakic eye treated with bimatoprost for presumed normal tension glaucoma

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Purpose We report a case of a patient with presumed normal tension glaucoma and cystoid macular oedema induced by treatment with bimatoprost. It has been reported that topical bimatoprost is not associated with structural or clinical macula changes in phakic eyes with glaucoma. In discordance our case is of CMO in a phakic patient treated with bimatoprost.

Methods A 56 year old phakic lady with no previous medical history was started on bimatoprost to both eyes for presumed normal tension glaucoma. An epiretinal membrane was documented pre treatment in the right eye.

Results 14 months after treatment the patient re-presented with symptoms of distorted vision to the right eye. Fundoscopy showed right eye macular thickening and OCT scan confirmed CMO with a fine epiretinal membrane. The CMO was attributed to bimatoprost which was stopped. 10 months after stopping bimatoprost, OCT showed a flat retina.

Conclusion Bimatoprost, like other topical prostaglandin therapies, can induce CMO. This disturbance is more common in pseudophakics, aphakics and uveitic patients and after rupture of the posterior capsule; all conditions where the blood ocular barrier has been more compromised than in phakic eyes. Similarly an epiretinal membrane may alter the blood retinal barrier and predispose to CMO. To our knowledge, this is the first case of CMO with bimatoprost in a phakic eye and is a caution for its use in patients with ocular co-morbidity such as ERM.

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Cyclosporine A-loaded and limbal stem cell-seeded nanofibers for the local suppression of inflammatory and transplantation reactions

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Purpose Purpose. To prepare nanofibers containing the immunosuppressive drug cyclosporine A (CsA) and to assess the potential of these nanofibers to inhibit allotransplantation and inflammatory reactions in vitro and in vivo.

Methods Methods. Nanofibers containing 10 weight percent of CsA were prepared from biocompatible polymer poly(L-lactid) by electrospinning procedure. The kinetics of drug release was characterized in aqueous solutions in vitro and in vivo. The growth of mouse limbal stem cells (LSC) on CsA-loaded nanofibers was evaluated. The ability of CsA-loaded nanofibers to inhibit allotransplantion reactions in vitro and inflammatory reactions in vivo was characterized.

Results Results. The incorporation of CsA into PLA polymer did not influence the pharmacological activity of CsA nor affected the diameter, shape or architecture of nanofibers. The addition of CsA-containing nanofibers into mixed lymphocyte culture significantly inhibited in a dose-dependent manner cell proliferation and production of proinflammatory cytokines IL-2, IL-17 and IFN- Mouse LSC grew on CsA-loaded nanofibers comparably as on CsA-free nanofibers. The covering of inflammatory sites with CsA-loaded nanofibers significantly attenuated the local inflammatory reaction.

Conclusion Conclusion. The CsA-loaded and LSC-seeded electrospun nanofibers can be used as scaffolds for LSC transfer and simultaneously as drug carriers for the local suppression of transplantation and inflammatory reactions.

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Axitinib modulates hypoxia-induced blood–retina barrier permeability and expression of growth factors

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Purpose Hypoxia-induced breakdown of the inner and outer blood–retina barrier and increased expression of growth factor are closely associated with the development and progression of diabetic macular edema. This study was performed to investigate the effects of the multikinase inhibitor axitinib on hypoxia-induced increased tissue permeability, vascular endothelial growth factor A (VEGF), and platelet-derived growth factor (PDGF) expression of human retinal pigment epithelial (RPE) cells and human umbilical vein endothelial cells (HUVECs). In addition, the effects of axitinib on the expression of VEGF receptors 1/2 (VEGFR-1/2) and PDGF receptor beta (PDGFR-β) were explored.

Methods Primary human RPE cells and HUVECs were treated with axitinib (0.5 µg/mL). Viability of cells and expression of VEGFR-1/2 and PDGFR-β, and their mRNAs, were investigated by reverse transcription-polymerase chain reaction (RT-PCR) and immunohistochemistry. Cells were exposed to hypoxia. Viability, tissue permeability, expression, and secretion of VEGF and PDGF were determined by RT-PCR and enzyme-linked immunosorbent assays.

Results Treatment with axitinib reduced expression of VEGFR-1/2 and PDGFR-β. Hypoxia decreased cell viability and increased tissue permeability, expression, and secretion of VEGF and PDGF. Axitinib significantly reduced hypoxia-induced overexpression and secretion of the growth factors and tissue permeability.

Conclusion Our in vitro results suggest that axitinib may have promising properties as a potential treatment for diabetic macular edema.

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Gangliosides of the retina

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Purpose Gangliosides are glycosphingolipids particularly abundant in the brain and nervous system, including the retina. A large variety of gangliosides have been described and the profile is specific to the organ or cell type. It has been shown that ganglioside composition of the retina changes during development. Also, it is known that mouse models accumulating specific gangliosides exhibit retinal abnormalities associated with impaired vision. However, the precise role of gangliosides in this organ and its pathologies is still poorly understood. We aimed to determine ganglioside profile of the retina and different retinal cell types.

Methods Three techniques of ganglioside extraction and purification based on solvent phase partition and solid phase extraction were compared and applied to retina samples. Gangliosides were then analyzed by high performance thin layer chromatography and colorimetric revelation, and identified by comigration with standards.

Results Rat whole retina mainly contained complex polysialogangliosides. GD3 appeared to be the major one, followed by GD1b, GT1b and GD1a. In contrast, retinal pigment epithelium cells (ARPE) and Müller cells exhibited a simpler ganglioside profile with a great majority of monosialoganglioside GM3. Small amounts of GM1 and GD3 were also detected, as well as GD1a specifically in Müller cells. Moreover, Müller cells contained larger amounts of gangliosides than ARPE cells.

Conclusion We showed here the specific ganglioside profile of the rat retina and two specialized retinal cell types: ARPE and Müller cells. It will be interesting to identify specific modifications of ganglioside profile associated with pathological conditions in these cells, which are affected during the development of age-related macular degeneration and glaucoma, respectively.

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Pasireotide (SOM230) protects the retina from ischemia induced retinopathies

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Purpose The aim of the present study was to investigate the neuroprotective properties of SOM230, a new metabolically stable analogue of somatostatin, with a 12h plasma half-life and high affinity for the sst1,2,3,5 receptor subtypes.

Methods Female Sprague-Dawley rats (250-300g) were employed in an ex vivo model of retinal chemical ischemia and an in vivo model of retinal AMPA excitotoxicity. Immunohistochemistry, TUNEL staining, FACS and western blot analysis were employed to examine retinal cell loss and neuroprotection.

Results Chemical ischemia led to the loss of ChAT, bNOS, and PKC immunoreactivity which was reversed by SOM230 in a concentration dependent manner (10-4-10-7 M). Partial protection was observed even at the low concentration of 10-7M. CYN-154806 (10-5M; sst2 antagonist) reversed SOM230 (10-5M) neuroprotective actions. Similarly, SOM230 (10-5, 10-6, 10-7 M) was neuroprotective (dose-dependent) in vivo, as was shown by bNOS immunoreactivity studies. An approximate 80% neuroprotection was observed with the dose of 10-7M. These data were substantiated by TUNEL staining and FACS analysis. The anti-apoptotic Bcl2 protein was found to be involved in the neuroprotection.

Conclusion SOM230 appears very efficacious in its anti-apoptotic neuroprotective properties, in both models of retinal ischemia, affording neuroprotection at the concentration or dose of 100nM. These data suggest that sst2/5 analogs with similar pharmacokinetic properties may play an important role alone or in a multi drug treatment in ensuring the most efficacious retinal therapy. [This study was funded by the Graduate Program of Neuroscience to K.T, and the C. Spyraki award to D.K.]

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Investigation of the liquid in- and outflow parameters of the human eye using a modified strategy of the mechanical loading test

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Purpose To obtain an additional information about the status of the inflow and outflow systems of the eye from ophthalmologic procedures based on static loading, with further application to diagnostics.

Methods The standard method, based on static load application, for the estimation of parameters characterizing the aqueous humor dynamics was supplemented with an unloading test. After a four-minute stationary mechanical loading by a Schiøtz tonometer, the load was removed and IOP was measured in a discrete regime for up to 20 min using the same tonometer. Clinical measurements were carried out on glaucoma (13) and non-glaucoma (4) patients. The data obtained were processed using our mathematical model that represents the eyeball as an elastic water-filled shell whose inner volume is regulated by dynamic balance between the liquid inflow and outflow and is assumed to be a function of IOP and the elastic and geometric characteristics of the system.

Results The most important result is a strong difference between two characteristic times: the time that characterizes the rate of pressure fall under load and the time that characterizes the rate of pressure recovery after removing the load. The characteristic time is directly related with the outflow facility. The difference varies in different groups of patients. The results can be understood within the assumption of nonlinear IOP dependence of the outflow facility coefficient.

Conclusion The modified mechanical loading test is a useful tool for investigating the biomechanical behavior of glaucoma and non-glaucoma eyes. Our preliminary results give grounds to expect that the effect revealed may be applied to diagnostics.

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Optic nerve head blood flow response to increase of arterial blood pressure in humans

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Purpose Autoregulation in ocular tissues allows a constant blood flow despite variations in ocular perfusion pressure and may be impaired in ocular diseases. The purpose of this study was to investigate the effect of increased blood pressure (BP) and ocular perfusion pressure (OPP) during isometric exercise on the optic nerve head blood flow (FONH).

Methods In 21 healthy subjects, aged 18 to 40 years, BP was measured using a pneumatic transcutaneous sensor Nexfin™ and blood flow was measured using LDF. OPP was defined as (0.74 × mean BP) – intraocular pressure. Handgripping consisted of static contraction of the finger flexors at 30% of maximum contraction force using a hand dynamometer during two minutes.

Results Data was analyzed in 15 healthy subjects, exhibiting a homogeneous response of BP to handgrip (linear regression of BP versus time, R> 0.8). A large increase in OPP during exercise up to 50% was not associated with a proportional increase in FONH, vascular resistance increased about 30%. The blood flow-pressure relationship showed blood flow significantly increased by approximately 30%, mainly due to the rise of velocity.

Conclusion This new data strongly supports the notion of autoregulation in ocular blood flow, protecting the eye from over-perfusion. However the increase in OPP is not completely counterbalance despite the regular increase of vascular resistance. This blood flow regulation is possibly due to a vasoconstriction, taking place outside of the sampled volume, probably in the arterioles proximal to the capillary bed of the neuroretinal rim. In the future, real time measurements of vascular resistance during handgripping could be investigated in glaucoma patients.

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A novel device for the measurement of intraocular pressure, ocular rigidity and pulsatile blood flow.

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Purpose Several instruments and methods are applied for the non invasive measurement of intraocular pressure, ocular rigidity and pulsatily blood flow. Most of this instruments and methods are based on the deformation force-area principle. The purpose of this study was to present a novel device for the measurement of intraocular pressure, ocular rigidity and pulsatily blood flow.

Methods The device consists of an opto-mechanical head comprising a deformation sensor and a force sensor, a camera and a microstepping motor. The deformation sensor is an optoelectronic device consisting of two beamsplitters a plano-convex lens, an illuminating fiber and a receiving fiber. Eighty three eyes were enrolled in a preliminary study, the intraocular pressure was measured with the novel device followed by a Goldman applanation tonometer measurement.

Results The average IOP measured by the device was 17 (std 5.38) mmHg and the average rigidity coefficient was 0.01013 (std 0.039)μl-1, the IOP measured by the GAT was 13.9 (std 3.23) mmHg. The statistical analysis indicated a significant statistical difference (p=9*10-8) between the two devices.

Conclusion Significant errors of the measurement are related to the centration of the optical head and the hand driven indentation. To overcome these limitations the device was upgraded with the addition of a coaxial camera for centration control and a microstepping motor for the applanation movement. An investigation of the accuracy and repeatability of the system with these new additions is underway.

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Effects of benzalkonium chloride on antigen presenting cells in vitro

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Purpose To characterize the phenotype, function and cytokine production of antigen presenting cells (APC) when exposed to the most common preservatives in eye drops, benzalkonium chloride (BAK).

Methods APC were obtained from a human leukemia cell line THP-1. APC were exposed to 4 concentrations of BAK (10-5%, 5.10-5%, 10-4% and 5.10-4%) and PBS during 24 hours. Cellular toxicity was evaluated with an annexin V-PE/7-AAD double-staining flow cytometry analysis. Phenotype modification was evaluated by flow cytometry through a panel of cluster of differentiation: CD11b, CD11c, CD33, CD45, CD54 and CD86. Phagocytosis function was analyzed using carboxylate-modified fluorescent microspheres and quantified by flow cytometry. The cytokine production of APC exposed to BAK was measured in supernatants by a human cytokine array.

Results BAK had almost no cellular toxicity at concentrations below 5.10-5%. A dose-dependent cellular toxicity of BAK was observed from 5.10-5% to 5.10-4%. At low concentrations, BAK modified the phenotype of APC with an increased expression of CD11b, CD11c, CD54 and CD86, and a decrease of CD33 and CD45. APC phagocytosis function was also increased when exposed to low concentration of BAK. Cytokines in supernatants of APC exposed to 10-5% BAK during 24 hours revealed decreased levels of IL-1β and CXCL10, and increased levels of CD40L, CXCL11, G-CSF, S-TREM-1, IL-17E, IL-6, IL-23, IL-27 and IFN-γ.

Conclusion The interaction between APC and epithelial conjunctival cells are involved in iatrogenic ocular surface diseases. Low concentrations of BAK could have a stimulating effect on APC, modifying phenotype, function and cytokine production.

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Effect of lacritin, a novel glycoprotein, on ocular surface and tear film integrity

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Purpose Dry eye is extremely common and debilitating. Treatment options are palliative at best and do not address the underlying pathology. Lacritin, a newly discovered glycoprotein, is secreted naturally in human tears by the lacrimal gland. Human recombinant lacritin stimulated tear secretion in normal rabbits and is well tolerated, leading us to hypothesize that topical application of lacritin will not adversely affect ocular surface and tear film integrity.

Methods We compared full length lacritin construct with cyclosporin (Restasis®), in terms of tear break up time (TBUT) and goblet cell density using impression cytology. Lacritin (10, 50 μg/ml), or cyclosporin (0.05%), were administered bilaterally to New Zealand white rabbits three times daily for 14d (n=4/group).

Results TBUT after lacritin (10 or 50 μg/ml) treatment was 12±2sec, which was similar to vehicle alone, but significantly decreased after cyclosporine treatment for 14d (6±3sec, p<0.001). Preliminary results indicate that goblet cell density decreased by 7±8% after cyclosporine but was not decreased after lacritin. No local irritant effects were noted by slit lamp examination after lacritin treatment, but redness and mild congestion were present in the cyclosporin group.

Conclusion Thus, treatment with lacritin was better tolerated than cyclosporin. This data suggests that lacritin does not adversely ocular surface and tear film integrity when compared to cyclosporine. Evaluation with inflammatory markers, such as CD-11c, is currently ongoing. Glycoproteins, such as, lacritin, represent a new, unique therapeutic approach that may more closely address the pathology of dry eye.

Commercial interest

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ElVisWeb: an interactive web-application for the visualization of ERG recordings based on the Electrophysiology of Vision Markup Language

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Purpose Recently, we proposed a standard for the exchange of electrophysiological recordings of vision, called Electrophysiology of Vision Markup Language (ElVisML). Here we present a Web 2.0 application, ElVisWeb, for visualizing data encoded in ElVisML. It intends to facilitate the exchange of recordings on mailing lists like CEVNet in a standardized way and to allow for sharing of data along with published articles.

Methods Main goals of ElVisWeb were easy usage and deployment. It is developed completely in JavaScript and as web application it does not require any installation on the client. It uses the single-page-interface paradigm (SPI): An ElVisML-file can be pasted into a text-field and a graphical representation of it is compiled. ElVisWeb can be deployed on any web-server or executed locally. For convenience, there is an upload functionality, which requires PHP on the server, however. ElVisWeb leverages open source JavaScript libraries for XML-processing (http://dev.abiss.gr/sarissa) and charts generation (http://www.jqplot.com).

Results A Web 2.0 application for visualization of electrophysiological recordings of vision, ElVisWeb, was successfully implemented. It is designed for easy usage and deployment. Recordings encoded in ElVisML can be visualized with no additional software installation.

Conclusion ElVisML is a standardized way for exchanging electrophysiological data. ElVisWeb is a first step towards an open ecosystem around ElVisML. It provides chart generation for recordings and may be used in mailing lists like CEVNet or for sharing data along with published articles. It is also ready to be used on mobile devices.

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Asymmetric color perception in the shopping aisle: some implications for merchandising

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Purpose To investigate the perception of colored items in the aisle of a virtual store and establish whether it may be affected by their position on shelves.

Methods 50 apparently healthy, right-handed university students, recruited on a voluntary basis, were included in this study. Inclusion criteria included: 1) visual acuity ≥ 20/20 in each eye; 2) normal color vision; 3) right-handedness, assessed by the Edinburgh inventory; 4) no history of ophthalmic and/or neurological disorders. Each subject was asked to look at 3 series of 18 images each on a plasma screen; the images showed a virtual modern store aisle, as it would be seen by a customer standing at one end in a central position and looking straight ahead. On both sides, the virtual aisle had 5 shelves, each containing 39 items of the same size and shape. In each image, apart from one single colored item, all other items were gray. In each series, the colored item was always of the same color, namely blue, red or green. All colors were monochromatic and had the same level of saturation. To avoid perceptive bias, all the images shown were perfectly symmetrical to the vertical axis. For each image, subjects were asked to locate as quickly as possible the colored item. Correctness and response time of answers were recorded. Statistical analysis was performed by ANOVA.

Results Statistical analysis showed that the coloured items were perceived significantly more accurately and rapidly when they were located on the left.

Conclusion Results support the idea of an asymmetric perception of colored items in the shopping aisle, suggesting that item location on store shelves may have important implications for merchandising.

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Glare visual performance in young subjects under night driving conditions

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Purpose Under night driving conditions visual performance is compromised and become worse with disability glare, age and certain ocular pathologies. The aim of this study was to analyze mesopic visual function of young subjects.

Methods The sample included 37 right eyes of healthy young adults (22.2 ± 1.8 years). The selected criteria were: Best-corrected VA of at least 0.04 logMAR, and refraction ≤ ± 3.75. Under mesopic (0.1 to 0.2 cd/m2) luminance conditions and with the best-optical correction in the right eye, the logMAR VA was measured using high-contrast (HC-96%) and low-contrast (LC-10%) logMAR Bailey-Lovie letter charts, and the mesopic contrast sensitivity (CS) without / with glare was assessed with Mesotest II. The intraocular straylight was measured with the C-Quant.

Results Under mesopic conditions, the HC and LC logMAR VA was 0.28 ± 0.1 and 0.70 ± 0.1 respectively, showing a significant correlation between them (Pearson's correlation = 0.75; p< 0.00); The mesopic log CS without glare was 0.19 ± 0.1 and with glare was 0.11 ± 0.1. Disability glare induced a 42% decrease in mesopic log CS (p < 0.00). LC logMAR VA was significant correlated with mesopic log CS without and with glare (Pearson's correlation = 0.4, p< 0.02, and 0.42, p< 0.02 respectively). The intraocular straylight Log (s) was 0.87 ± 0.1, but did not show any significant association with logMAR VA nor the log CS without and with glare under mesopic luminance conditions.

Conclusion The results indicated that mesopic assessment of the low contrast logMAR VA and log CS without and with glare might potentially predict the glare visual performance under night driving conditions.

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Electrophysiological assessment of fundus albipunctatus

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Purpose Fundus Albipunctatus is a congenital, stationary retinal disease with rod system degeneration. The disorder is caused by mutation in the RDH5 gene. It is characterized by impaired night vision and numerous small white-yellow retinal lesions. Flash ERG reveals severe rod function impairment after usual period of dark-adaptation, which normalize after prolonged dark adaptation.

Methods A case of a 12-year-old female presented with symptoms of poor night vision. The patient underwent the visual acuity, colour vision tests (D15), fundus photography, fluorescein angiography, automated static perimetry. The standard dark adapted electroretinogram (30min) and a prolonged dark adaptated ERG (120 min), photopic ERG and multifocal electroretinogram (mfERG) were performed.

Results Visual acuity of both eyes was not decreased. In the peripheral visual field a concentric restriction was found. Scotopic ERG rod responses (0.009 and 0.017 cd x s / m2) were significantly reduced and a standard ERG response was borderline. Photopic ERG was normal. In the mfERG P1 densities were slightly reduced in the eccentric rings (R4-R5).

Conclusion The comparison of standard adapted scotopic ERG (30 min) and prolonged dark adapted Scotopic ERG (120 min) is the most useful clinical test in diagnosis and differentation of Fundus Albipunctatus. The mfERG can be helpful in detecting patients suffering from Fundus Albipunctatus with progressive cone dystrophy.

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Colour vision in adult amblyopia

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Purpose Amblyopia is a disorder of visual processing. There is evidence that the parvocellular pathway, which prefers chromatic stimuli, is selectively damaged in amblyopia. Consistent with this hypothesis, previous studies have demonstrated that patients with amblyopia show poorer performance on colour vision tests.

Methods Ten adult amblyopic subjects (3 strabismic, 5 anisometropic and 3 mixed) were tested using the Farnsworth Munsell 100 Hue (FM100Hue)colour vision test. In separate testing sessions, positive spherical lenses were used to induce blur in the fellow eye (FFE)to match the near acuity of the amblyopic eye (AME). The test (all boxes)was performed under five conditions(randomised): AME,FFE,binocularly (BIN),FFE with blur and BIN with the FFE blurred. Age matched controls were included to assess the effect of defocus in normal subjects, with blur placed in front of the non-dominant eye to induce mild, moderate or severe blur.

Results Amblyopic participants performed well in the FM100Hue test, with scores falling within normal age means in 9/11 subjects (in the AME). Strabismic amblyopes had a more pronounced deficit in error scores. Across all amblyopic subjects, performance was significantly beter under BIN conditions (p=0.023). Induced blur in controls only affected error scores under the severe blur condition, and had litle effect in amblyopic participants.

Conclusion This study has shown that amblyopes perform well in this commonly performed colour vision test, and demonstrated improved test performance under binocular conditions. The low spatial frequency of the stimuli may allow for extensive pooling of chromatic information therefore allowing performance of this test to be robust to a parvocellular dysfunction.

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Prevalence of uncorrected refractive errors among schoolchildren in northeast of Iran

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Purpose To determine the prevalence of uncorrected refractive errors (UCREs) among schoolchildren In northeast of Iran.

Methods In a cross sectional study using random cluster sampling, 2020 schoolchildren 6 to 1 years of age were selected. The participants totaled 1551 (response rate=76.7%), 643 boys and 908 girls of elementary and junior high school students from the schools of northeast of Iran. Refractive errors were measured under cycloplegia. Myopia was defined as a spherical equivalent (SE) of - 0.5 dioptre (D) or worse, hyperopia as a SE of +2.0 D. or more, and astigmatism as cylinder equal to or worse than -0.75 D. UCRE was defined as a minimum of 2 lines improvement of visual acuity in the better seeing eye.

Results The prevalence of UCRE was 6.2% (95% confidence interval [CI]: 5-7.4%). UCRE was more in boys than girls (P= 0.068). UCRE was not related to age and parent's education. Myopia and astigmatism were the most common UCREs respectively. Present and corrected visual acuity was not different in 83.3% of the students. Visual acuity of 3 or more and 4 and more lines increased in 2.5% and 0.8% of the subjects after correcting refractive errors respectively. In 21.1%, 9.5% and 3.2% of the students with old correction, visual acuity of 2 or more, 3 more, 4 or more lines increased after new correction respectively .

Conclusion The results of this study indicated that the prevalence of UCREs in schoolchildren of Iran northeast were similar to the most places of the world . Vision screening and correction refractive errors can prevented from visual impairment in schoolchildren.

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How does Bangerter filter affect the normal visual perception?

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Purpose The Bangerter filter (BF) has become an alternate form of amblyopia patching treatment due to its high social-psychological compliance and effective therapeutic outcomes. This study aims to investigate the effects of different BF densities on the normal visual system in order to quantify filter densities based on vision perception variables.

Methods Thirty-two binocularly normal subjects participated in this study. Visual acuity (VA), vernier acuity (VNA) and contrast sensitivity (CS) under spatial frequencies (SF) of 0.5, 1, 2, 5, 10 cyl/deg were measured while the dominant eye was patched with randomly selected BF of densities: 0.8, 0.6, 0.4, 0.2.

Results Mean VA and VNA values under the four BF densities were a) 0.29, 0.30, 0.35, 0.54 logMAR and b) 3.24, 4.81, 5.29, 8.19 min of arc respectively. There was a significant difference ($p<0.05$) in VA change between BF 0.2 and rest of the density groups. BF 0.8 and 0.2 groups showed a significant VNA change compared to BF 0.6 and 0.4 ($p<0.05$). There were no significant effects noted in CS at SF of 0.5, 1 and 2 cyl/deg across low to high BF groups ($p>0.05$). BF 0.2 was the only density that had a significant influence on middle and high SF (5 and 10 cyl/deg) ($p<0.05$).

Conclusion BF does not alter vision perception abilities in a predictable manner suggested by the manufacturer. Only the high BF density has shown a significant change. Careful attention must be paid on the inconsistencies in low and middle BF densities for the patching treatment.

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Halo size in healthy subjects

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Purpose The measurement of the halo size has been proposed as an objective method to characterize the quality of vision in refractive surgery patients who complain of night vision problems. Our purpose was to know the size of halo in the visual field of healthy subjects using a commercial campimeter and to analyze the effect of age.

Methods Measurements were obtained in the better eye of 90 healthy subjects (mean age 46.5±19.4). Halo was measured using the MON CV-3 campimeter that is equipped with high luminance light sources (200,000 cd/m2) which generated the halo source. The test was performed using optotypes of low luminance (1 cd/m2 and 5 cd/m2) presented over a dark background at a distance of 2.5 m. Optotypes were viewed under a visual angle of 15 arc minutes. Three measurements were taken starting from the side opposite to the light source. The outer limit of the halo was recorded and the visual angle subtended by the radius of the halo was then calculated in arc minutes. Furthermore, the pupil size was evaluated under mesopic conditions with the Colvard pupillometer.

Results Mean halo size was 111.7 ± 41.4 arc min using optotypes of 1 cd/m2 and 44.5 ± 30.3 arc min with 5 cd/m2. A significant positive correlation was found between halo and age at both luminance levels: 1 cd/m2 ($r = 0.56$; $p = 0.00001$) and 5cd/m2 ($r = 0.57$; $p = 0.00001$). With age there was a significant increase of halo size of 10 arc min per decade at both luminance levels. The halo size did not depend on the pupil diameter.

Conclusion In healthy eyes, halo size in the visual field increased significantly across the lifespan. Measuring the size of the halo using a campimeter is a useful tool for assessing visual impairment caused by glare.

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A new method for assessing central and peripheral visual acuity

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Purpose This research aims to assess central and peripheral visual acuity in human.

Methods We assume that visual acuity will decrease in peripheral vision because the density of human photoreceptor cone cells diminishes exponentially. We designed a program to measure visual acuity in two different models (minimum discernible, minimum separable) According to the distance between subject's eye and screen, this program has 3 cases (basic, release, accumulate model), which are classified by position of nodal points. In addition, there is a selection of four different line patterns to define visual field. After all these options are selected, the program displays various-sized circles (discernible model) and Landolt rings (separable model) on the locations of screen corresponding to the visual angle.

Results Distribution of visual acuity according to the visual angle could be acquired by proposed method. Central visual acuity was nearly 20/20 and the peripheral visual acuity was diminished according to the increment of visual angle in normal volunteers.

Conclusion Distribution of the visual acuity according to the visual angle corresponded to the density of the photoreceptor cone cells, not to the density of the rod cells. Developed program and system might be useful for other researches concerning visual acuity.

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