October 7-10

www.ever.be

EVER 2015 NICE

Abstract book

European Association for Vision and Eye Research


EVER
European Association for Vision and Eye Research

TABLE OF CONTENTS

EVER PAST PRESIDENT LECTURE

Retinal Vein Occlusions : From pathophysiological mechanism to clinical therapeutical issues

Constantin POURNARAS
Ophthalmology Center La Colline, Geneva, Memorial Rothschild, Clinical Research Group, CH

Summary

Central or branch retinal vein occlusion constitute the second most common sight threatening retinal vascular disease in developed countries. Retinal arteriolar sclerosis, systemic hémodynamic disturbunces, thrombophilic conditions, rheological disturbunces and local ocular pathologies are frequently associated to the occlusive event.Therefore, basic and translational research was focused on both the pathogenic mechanisms and the various treatment modalities. The reduction of arteriolar blood flow and the veins vasodilation are the major hemodynamic changes on the vasculature in the by RVO affected vessels. Arteriolar vasoconstriction and consecutive reduction of arteriolar blood flow leads to tissue hy-poxia, Na+/ K+ -ATPase pump dysfunction, formation of intracellular retinal edema, and neuronal cell destruction by necrosis and apoptosis. The formation of extracellular retinal edema and hemorrhages are caused by changes in the inner blood-retina barrier (BRB), as demonstrated by the observed disturbances of the intracelleular jonctions proteins between the adjacent endothelial cells. Visual acuity is decreased due to the development of macular edema, capillary non-perfusion, and vitreous hemorrhage secondary to retinal neovascularization. The interplay between the vasoac-tive systems involving the endothelial growth factor (VEGF), the prostaglandis (PGs) and the inflam-matory factors, have an important impact on the progression of retinal microangiopathies. Alltought numerous clinical therapeutical approaches focused on the specific pathogenic me-canismes resulted to a limited efficacy, retinal photocoagulation and the intravitreal treatments offer new insights for the managmenet of RVO, leading to the limitation of the visual loss.

Rare retinoblastoma: a goldmine for discovery of fundamental principles of biology and healthcare

Brenda GALLIE
Canada

Summary

Study of retinoblastoma, a rare eye cancer in children, revealed the essential genetic basis of cancer and delivered personalized medicine for families. Where awareness and resources are available, 98% of children survive retinoblastoma. Next big impact will be the unique opportunity to conduct clinical trials of molecular retinoblastoma prevention trials. However, globally 70% of children with retinoblastoma still die. To address this disparity, One Retinoblastoma World, using a "constellation model" of collaboration, has emerged with multiple innovative partnerships. Ongoing studies map (www.1rbw.org) centres and link to a global learning health system, directly providing evidence from the bedside to optimize care of each newly diagnosed child. Retinoblastoma will become a "Zero Death" cancer.

KEYNOTE LECTURE

Translational applications in corneal and ocular surface diseases

Reza DANA
Harvard Medical School, Schepens Eye Research Institute- Massachusetts Eye & Ear Infirmary, Boston MA, United States

Summary

The field of Cornea and Ocular Surface has made significant advances in the recent past. Compared to our colleagues in Retina and Glaucoma where the principal leaps forward have been in pharmaco-therapy, in Cornea our primary advances have been in the realm of microsurgery and new technologies (e.g., DSEK/DMEK, femtosecond). Nevertheless, significant work has also been done in understanding the pathophysiology of common corneal and ocular surface disorders, with translational applications in our clinics. This talk will provide a short summary of some of the translational research performed by our team in understanding the pathogenic mechanisms and novel treatment options for corneal neovascularization, graft-versus-host disease (GVHD), and dry eye syndrome

Multidisciplinary treatments for malignant eyelid tumors: surgical and non-surgical options, sentinel lymph node biopsy, and surveillance

Bita ESMAELI
Houston, Texas, United States

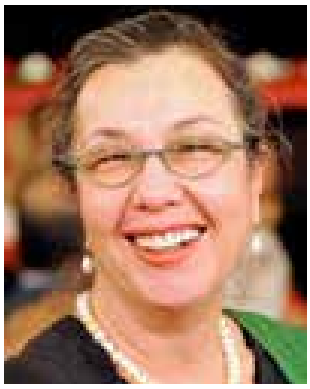
Summary
Malignant tumors of the eyelid are varied in their presentation and stage. Surgical treatments and reconstructive outcomes for each stage and histology will be reviewed. Adjuvant local treatments such as radiation therapy as well as non-surgical medical treatments will also be discussed. Indications and clinical cases where sentinel lymph node biopsy may be beneficial and other recent advances in the field will be reviewed.

European Ophthalmology Heritage - a celebration:
Homage at Professor Ignacio Barraquer
Melanoma of the ciliary body. Iridocyclectomy (1968)

Joaquin BARRAQUER
Barcelona, Spain

Summary

Melanoma of the ciliary body. Iridocyclectomy (1968) Introduction: View of the operating facilities of the "Centro de Oftalmología Barraquer" conceived (1950) and incorporated (1958) by Ignacio Barraquer (1884-1965) and his sons José Ignacio (1916-1998) and Joaquín Barraquer (1927); specifically designed for teamwork and teaching. Dome-shaped plastic separation allowing observers to watch ocular surgery at minimal distance of the operating field without disturbuing the surgical team and maintaining asepsis and climatization. Presentation: Application of Flieringa ring. Different steps of irido-cyclectomy for extirpation of melanoma, removal of the crystalline lens with suction cup (phakoeresis). Closure of the wound with multiple sutures. Closing view: Hommage to Professor Ignacio Barraquer to commemorate the 50th anniversary of his death (1965)



Visual impairment in opera characters

Aydin PINAR
Turkey

Summary

Opera brings the work of singers and musicians together in a theatrical pageant of musical colour and dramatic art. The librettists who devise the stories in works of opera have variously used characters with eye diseases or blindness as major or minor characters in the plots of these stories. This talk will present an array of those operatic characters, along with the possible cause or diagnosis of their eye problems, and will explore the roles which they play in the operas in which they appear, along with their dramatic significance in the flow and resolution of the plot.

Acta Ophthalmologica

Regulating the body clock – The unrecognised role of the eye

Russell FOSTER
United Kingdom

Summary

Little more than a decade ago discussion that the eye might contain another photoreceptor, different from the rods and cones, generated either polite amusement or a hostile rebuttal. The dogma was that all light detection took place by these photoreceptors whilst the other cells of the retina act only to process visual signals. However, several lines of research led to the discovery that the vertebrate eye, including humans, contains another class of photoreceptor based upon a small number of photosensitive retinal ganglion cells (pRGCs). These specialised neurons detect environmental irradiance and regulate a wide range of physiology and behaviour including the regulation of 24h body clocks, sleep, alertness, mood and even pupil size. Furthermore, the pRGCs have been shown to utilize a novel light signalling pathway based upon the photopigment melanopsin. Collectively these findings have transformed our understanding of how the eye detects light and are redefining our assessment, treatment and care of individuals with eye disease. The discovery and current understanding of this "third" class of ocular photoreceptor will be reviewed in this presentation.

Ophthalmic Research
Journal for Research in Experimental and Clinical Ophthalmology

Degenerative myopia and its treatment

Peter WIEDEMANN
Germany

Summary
High myopes are handicapped by visual impairment and degenerative complications eventually leading to blindness. Myopic refraction can be corrected by refractive lens exchange. Retinal detachment may be the consequence and a possible prevention by vitrectomy will be discussed. However, the fundamental problems of degenerative myopia, the features of myopic fundus disease and the posterior staphyloma cannot be treated. Scleral cross linking possibly stiffens the sclera. By this means we could stop eye growth and possibly reduce myopic complications. Experiments to stop eye growth by scleral crosslinking will be presented.

WEDNESDAY OCTOBER 7, 2015

• 1111

Diabetic retinopathy - pathophysiology

MARQUES-NEVES C

Faculty of Medicine of Lisbon University, Ophthalmology, Lisbon, Portugal

Diabetic retinopathy (DR) is a common complication of diabetes and is a leading cause of visual impairment and blindness in many countries. This visual impairment results from long-term accumulated damage to the small blood vessels in the retina. It takes several years before any clinical symptoms of retinopathy appear in diabetic patients. The definition of diabetic retinopathy is based on observation of vascular changes. The first recognizable vascular abnormalities are microaneurysms and small hemorrhages, followed by signs of vascular leakage, such as hard exudates and larger hemorrhages, vascular dropout, and neovascularizations. A number of hyperglycemia-induced metabolic stresses have been implicated in the pathophysiology of DR. The microvasculature of the retina responds to hyperglycemia through a number of biochemical changes, including the activation of protein kinase C, increased advanced glycation end-products formation, polyol pathway and oxidative stress. However, it has been long known that the neuroretina is affected at an early stage by diabetes-induced metabolic changes. DR is now recognized as a neurovascular complication or sensory neuropathy resulting from disruption of the neurovascular unit.

• 1112

Neurodegeneration and vascular impairment in the eye of diabetic patients

SIMO R , Hernández C

Vall d'Hebron Research Institute and CIBERDEM, Diabetes and Metabolism Research Unit, Barcelona, Spain

Diabetic retinopathy (DR), one of the leading causes of preventable blindness, has been considered a microcirculatory disease of the retina. However, there is emerging evidence to suggest that retinal neurodegeneration is an early event in the pathogenesis of DR, which participates in the development of microvascular abnormalities. Therefore, the study of the underlying mechanisms leading to neurodegeneration and the identification of the mediators in the crosstalk between neurodegeneration and microangiopathy will be essential for the development of new therapeutic strategies.
In my lecture, an updated discussion of the mechanisms involved in neurodegeneration, as well as the link between neurodegeneration and microangiopathy, will be presented. Finally, the therapeutic implications and new perspectives based on identifying those patients with retinal neurodegeneration will be given.

• 1113

The changes of the retinal layers in diabetic patients without retinopathy

FERREIRA J (1), Costa L (1), Proença R (1), Vicente A (1), Cunha J P (1), Abegão Pinto L (2)

(1) *Centro Hospitalar de Lisboa Central, Ophthalmology, Lisbon, Portugal*
(2) *Faculdade de Medicina - Universidade de Lisboa, Pharmacology & Ophthalmology, Lisbon, Portugal*

Diabetic retinopathy is considered to be a neurovascular disease. But in fact, retinal neurodegeneration is present before any microcirculatory abnormalities can be detected in ophthalmoscopic examination. We know this from functional studies documenting electroretinogram abnormalities, loss of dark adaptation, contrast sensitivity and color vision and abnormal microperimetry occur before any vascular abnormality is detected. Novel imaging devices have allowed this pre-vascular damage to be quantified in a non-invasive and reproducible way using spectral domain optical coherence tomography (SD-OCT) that allows in vivo retinal layer thickness measurement. The extent to which this new technology can be used in the clinical setting for early screening in diabetic retinopathy will be the focus of this lecture. The review of the state of the art in this exciting new field of study may prove valuable in the management of this condition.

• 1114

The changes of the retinal layers in diabetic patiens with retinopathy

VUJOSEVIC S (1), Bini S (1), Berton M (1), Midena G (2), Martini F (1), Midena E (3)

(1) *Ophthalmology, Neuroscience- University of Padova, Padova, Italy*
(2) *Campus Biomedico, Medicine, Roma, Italy*
(3) *Ophthalmology, Neuroscience- University of Padova- Fondazione G.B.Bietti IRCCS, Padova- Roma, Italy*

Purpose: Retinal neurodegeneration and inflammation are considered early events in diabetic retinopathy(DR). Herein are described changes, in retinal glial and neuronal cells, with spectral domain(SD-OCT) in patients with non proliferative DR.**Methods:**130 subjects were evaluated:88 diabetics with DR and 42 normals.All subjects underwent full ophthalmologic examination and SD-OCT. After automatic retinal segmentation in 5 layers, the thickness of each layer was calculated and compared. Intraretinal hyperreflective spots(HRS) were evaluated on linear scans. **Results:**A significant increase in inner nuclear (INL) and outer plexiform($p < 0.01$) and decrease in retinal nerve fiber layer (RNFL) thickness ($p< 0.01$) was found in DR eyes (without DME) vs controls.HRS number was significantly higher in diabetics with DR with or without DME vs controls,($p < 0.05$). HRS number increased with progressing DR.**Conclusion:**Selective thinning of inner retina in the macula, suggesting an early neuronal loss(accompanied by Muller cells activation with increased INL thickness) in DR is reported. HRS increase and migration to outer retina, may represent a surrogate of microglial activation.SD-OCT may be useful in detecting intraretinal changes in DR.

• 1121

Virtual review- in glaucoma and beyond

CRAWLEY L
London, United Kingdom

Virtual review clinics are becoming more common as a method of delivering consultant led care for patients with chronic conditions on a background of inexorable rise in service provision pressure. In this session we will look at glaucoma and other medical specialities using virtual clinics and explore the benefits and challenges of this new way of working.

• 1122

Managing a 100 patient glaucoma clinic

AHMED F
Imperial college- London, Imperial College Ophthalmic Research Group, London, United Kingdom

Due to an aging population the number of patients seen in glaucoma clinics is dramatically increasing year on year, causing great strains on glaucoma services. New methods in efficiently managing increased numbers of patients with the same number of clinicians and time will be discussed. We also look into the future and see how patients maybe managed from their homes.

Commercial interest

• 1123

Early adopters- ahead of the curve and lessons learned

LONGSTAFF S
Sheffield, United Kingdom,

Abstract not provided

• 1124

New software for an old problem

DIAMOND J
Bristol Eye Hospital, Glaucoma Department, Bristol, United Kingdom

There are huge benefits to be won by switching from old fashioned medical notes to paperless medical records: as a consequence, use of electronic patient records (EPRs) for glaucoma management has become more widespread in recent years. There are a number of different EPR systems in use in the glaucoma clinic, each of which has strengths and weaknesses. Before selecting a system, clinicians need to consider how and where the system will be used, paying particular attention to venue (hospital or community), primary user (ophthalmologist, optometrist, nurse or technician), compatibility with other equipment (visual fields and disc imaging), ability to archive older medical records and accessibility for virtual review. It is also of great importance to consider speed of data entry: most EPR systems are slower to use than old-fashioned paper notes and if that differential is significant, the economics of switching to an EPR will be poor and uptake will suffer as a consequence. In his presentation Jeremy Diamond will consider these issues in more detail, providing helpful insights to those who wish to switch from paper to paperless working.

Commercial interest

• 1131
Pathophysiology of uveitis

DICK A
University of Bristol, Bristol, United Kingdom

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

• 1132
Classification of uveitis

ANDROUDI S
Thessaloniki, Greece

The uveitis is a condition that involves inflammation of the uveal tract (ie, iris, ciliary body, choroid) or adjacent ocular structures (eg, retina, optic nerve, vitreous, sclera). In most cases, the etiology remains elusive and is often of an autoimmune nature. 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. Uveitis may be classified in a number of ways, according to several systems and multiple descriptors. 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).

• 1133
Signs and symptoms of uveitis

NERI P (1), Arapi I (2), Pirani V (1), Gresti G (1)
(1) Università Politecnica delle Marche, The Eye Clinic, Ancona, Italy
(2) Mother Theresa University Hospital- University of Medicine, The Eye Clinic, Tirana, Albania

Inflammation of uveal tract can be divided into: anterior, intermediate, posterior, and panuveitis. Uveitis can be a sight-threatening disease. The commonest ocular symptoms are: blurred vision, ocular pain, photophobia and floaters, depending on the type of uveitis. The onset of uveitis can be either acute or insidious, involving one or both eyes. Posterior uveitis is usually associated with vitritis. Anterior chamber cells and flare should be graded according to standardized uveitis nomenclature (SUN) working group. Binocular indirect ophthalmoscopy (BIO) score is used to grade vitreous involvement. Vitreous changes may comprehend: vitreous hemorrhage, vitreous strands, and vitreous traction. A further classification of posterior uveitis depends on the primary site of inflammation, which can identify: retinitis, choroiditis, retinochoroiditis, and chorioretinitis. Posterior pole uveal involvement can be: focal, multifocal, and placoid. Retinal vasculitis can be associated with several sub-types of posterior uveitis. Uveitis can present several complications such as, anterior and posterior synechiae, which can lead to uveitic glaucoma, cystoid macular oedema, retinal and choroidal neovascularizations, and retinal ischemia.

• 1134
Laboratory work-up and specialized investigations

PLEYER U
Charite, Campus Virchow, Augenklinik, Berlin, Germany

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

• 1135

Imaging in uveitis : techniques and indications

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

This tutorial will address the main complementary imaging techniques used in the field of (posterior) uveitis. In case imaging work-up is decided, fluorescein angiography (FA) is performed routinely since a few decades. FA gives information on the superficial structures and lesions of the fundus including pathology of the retina, retinal vessels, optic disc, and subretinal fluid collection, as well as the RPE for which it is the examination method of choice, and the choriocapillaris in the first seconds of angiography. Most of the time it only confirms and gives the precise extension of lesions already identified by the clinical examination. The choroid is however involved at least as often as the retina and often all or part of choroidal lesions are occult and not detected by the clinical exam or FA. Only indocyanine green angiography (ICGA) gives visual access to choroidal inflammatory pathology where it can distinguish stromal choroidits (birdshot, VKH) from choriocapillaritis (MEWDS, APMPPE, etc). So if angiography is deemed necessary during initial appraisal of a case dual FA/ICGA should be performed as choroiditis can not be excluded à priori. Other methods addressed will be OCT, UBM, FAF as well as anterior segment OCT.

• 1136

Therapeutic management of uveitis

DICK A
University of Bristol, Bristol, United Kingdom

This talk will overview the contemporary therapeutic approaches to treatment of noninfectious 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. Evidence of efficacy 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 will be provided.

• 1141

DALK Techniques from manual to femtolaser

NUBILE M, Salgari N, De Nicola C, Mastropasqua L
Ophthalmology Clinic, Centre of Excellence in Ophthalmology, National High-Tech Eye Center (CNAT)

The continuous evolution of corneal transplantation has recently demonstrated that the surgical approach based on selective lamellar keratoplasty represents the gold-standard for the treatment of corneal disease. The replacement of the diseased corneal layers with deep anterior lamellar (DALK) or endothelial keratoplasty clearly gives advantages to patients in terms of safety and outcomes. The introduction of femtosecond laser technology (FSL) into the clinical practice, after the wide use for refractive surgical corneal procedures, allowed a significant refinement in terms of precision and customization of both penetrating and lamellar keratoplasty (ALK and DALK). The main advantages of using FSLs are represented by the possibility of performing complex-shaped trephination in both donor and recipient tissues (for example top-hat or zig-zag cut profiles) and the great precision of lamellar dissection. The concept of reducing or avoiding sutures (femtosecond laser suture-less ALK) is still debated. However to date cut quality and interface smoothness represents critical points to be improved.

• 1142

Big Bubble DALK: The ladder to success, step by step

KATAMISH T
Cairo University, Cairo, Egypt

Deep anterior lamellar keratoplasty (DALK) has too many techniques to achieve, one of them and most reproducible is the big bubble technique. The steep learning curve known to this operation some times considered a barrier for many surgeons to try and master. However in my presentation I will try to go through the operation step by step giving my own personal tips and tricks for executing the perfect big bubble DALK. Special emphasis will be put on the following important steps: (1) Trephine adjustment and partial thickness trephination of the recipient cornea. (2) Technique of air injection and big bubble formation, which is considered the key step of this technique. (3) Safe opening of big bubble roof. (4) Cruciate incision and cutting of the reaming stroma after lamellar dissection of superficial corneal layers. (5) Descemet's membrane staining and stripping from donor cornea. Moreover, I will put a focus on the new anatomical pre- Descemet's layer (Dua's layer), describing and demonstrating by many video clips the different types (type 1, type 2 and mixed type) of big bubbles based on this new anatomical layer. The aim of my presentation is to allow the participants to perform big bubble DALK in a safe and reproducible way with very high percentage of success in obtaining the big bubble.

• 1143

DALK: Intraoperative pitfalls and how to manage them

DUA H S
Queens Medical Centre- Derby Road, Eye Ear Nose Throat Centre, Nottingham, United Kingdom

Deep anterior lamellar keratoplasty (DALK) has two major advantages over conventional keratoplasty - it completely eliminates failure due to rejection and leaves behind a stronger eye. The steep learning curve associated with the technique deters or frustrates surgeons. This part of the course will highlight the intra-operative pitfalls and how to avoid, anticipate and avoid them using the Big Bubble (BB) technique.

Key steps that will be dealt with are (a) Centration and Trephination. (b) Air injection and identification of the different types of BB (Types 1, 2 and mixed). (c) Lamellar dissection of the anterior stroma and puncturing the bubble without damaging the posterior lamella (Dua's layer + Descemets membrane (DM) or DM alone) (d) Excising the deep residual stroma and extending the dissection if an adequate size bubble is not achieved. (e) Confirmation of type of BB after removing all anterior stroma. (f) Precautions to take to avoid tear or burst (g) How to deal with a tear and aqueous leak (h) What to do if a BB is not achieved. (i) What to do if unsure whether a BB is present or not. (j) Peeling donor DM and suturing the donor graft. All tips will be demonstrated with videos of actual surgical events.

Commercial interest

• 1144

DALK: Post operative management

SAID D
Research institute of Ophthalmology, Ophalmology department, Maadi-Cairo, Egypt

Success of DALK, like that of any other operation depends on good surgical technique, appropriate post-operative examination, treatment, early detection of any problems and adequate management thereof.
In the immediate post operative period eye pressure check is important especially if air is left in the anterior chamber. High pressure can cause Urrets-Zavalia syndrome if not treated.
Topical steroids, antibiotics ,mydriatic and hypotensive medication if needed, are the mainstay postoperatively. Steroids can be tapered and discontinued earlier than for PK as there is no risk of endothelial rejection.
In the early postoperative days, special attention should be paid to the sutures, epithelial defects, signs of inflammation and infection. A loose suture needs to be removed and replaced as soon as possible as it carried a high risk of infection and vascularization. The latter can be a precursor of stromal rejection. Epithelial rejection does occur and behaves exactly like in PK with an advancing epithelial line that stains with fluorescein.
Astigmatism is a major problem, strategies for management include, selective suture removal, glasses, contact lenses, arcuate incisions, laser refractive surgery and toric intraocular implants.

• 1145

Discussion, Questions and Answers

DUA H S
Queens Medical Centre- Derby Road, Eye Ear Nose Throat Centre, Nottingham, United Kingdom

In this part of the course there will be an open discussion in which members of the audience will be encouraged to participate, to share their experience and anecdotes.
All the faculty of the course will be present to take questions and discuss or describe in further detail points they have made in their presentations.
The audience may be asked questions to assess if they had understood key aspects of the course.

Course participants will be requested to complete feedback forms.

Commercial interest

• 1151

Differential diagnosis of papilloedema

KAWASAKI A
Hopital Ophtalmique Jules Gonin, Lausanne, Switzerland

Optic disc swelling is a non-specific manifestation of injury to the intraorbital portion of the optic nerve, the nerve head (or disc). By convention, the term "papilledema" refers to optic disc edema that is due to increased intracranial pressure. Increased intracranial pressure typically causes bilateral swelling of the optic discs, although asymmetry in the degree of disc edema is not uncommon. Truly unilateral papilledema is rare . In most cases of papilledema (increased intracranial pressure) , visual function is relatively preserved. This lecture will present the differential diagnosis of patients who present with bilateral disc edema of unknown etiology and discuss how to distinguish those who have true papilledema of increased intracranial pressure.

Commercial interest

• 1152

Work up of the patient with suspected pseudotumor cerebri syndrome

SZATMARY G
Hattiesburg, United States

While various etiologies of secondary pseudotumor cerebri syndrome (PTCS) have been recognized (eg. venogenic,endocrine) the pathogenesis of primary PTCS remains unknown. The diagnostic criteria of PTCS has been revised (Modified Dandy criteria) in 2013 mainly owing to the increasingly recognized imaging features of the disease. This lecture will present the different etiologies of increased intracranial pressure. We will discuss the diagnostic workup of typical vs. atypical patients suspected of having PTCS. We will highlight red flags that should alert the clinician to pseudotumor cerebri mimics that carry serious neuro-ophthalmological consequences and require high index of clinical suspicion. Finally, the take home massages and some of the difficult diagnostic dilemmas will be demonstrated through illustrative case presentations.

• 1153

Follow-up and decision making on treatment choices of the patient with established pseudotumor cerebri syndrome

PARSA C
Quinze-Vingts National Eye Hospital / UPMC-Sorbonne Universités, Ophthalmology, Paris, France

Once a diagnosis of pseudotumor cerebri is established, the critical task becomes to protect the optic disc from excessive swelling potentially causing auto-infarction. Assessing tolerable versus threshold levels for such swelling, and selecting a treatment plan based on the degree of disc swelling and findings from perimetry will be reviewed. Technical and procedural steps will be exposed to reduce the chances of auto-infarction when large degrees of swelling are present using the principles of blood perfusion and regulation to the optic nerve head. Initiation of medical versus surgical treatment will be discussed. Precautions regarding intracranial pressure lowering techniques using lumbar puncture & drainage, optic nerve sheath fenestration, or shunt placement will be examined based on principles of blood perfusion as well as perineural sheath anatomy. Chronic long-term effects of disc swelling will also be addressed.

• 1211

Pathophysiology of macular hole formation

STAPPLER T
Royal Liverpool University Hospital, St Paul's Eye Unit, Liverpool, United Kingdom

Purpose Our understanding of the pathophysiology of macular hole development has evolved in line with a novel classification system. As novel pharmacological treatments have been introduced previously unseen interactions with the pathophysiology have been observed.
Methods Histopathological correlation studies as well as the effects of novel pharmacological agents on the pathogenesis of macular holes will be presented, including rare cases of macular hole formation.
Results Perifoveal PVD with vitreomacular adhesion and vitreoschisis allow cortical vitreous to remain on the retinal surface and become a scaffold for cell proliferation and form epiretinal membranes. These alter the cleavage plane for the surgeon. Pharmacological vitreolysis leads to novel and challenging clinical scenarios. The Liverpool experience will be shared.
Conclusions Histopathological correlation studies demonstrate a large proportion of additional epiretinal membrane components on peeled internal limiting membranes. In pharmacological vitreolysis novel strategies in the management of macular holes will be presented.

• 1212

Macular hole peeling

FERRARA V
Borgomanero, Italy

Abstract not provided

• 1213

Posturing or not

SIMCOCKX P
Exeter, UK

Abstract not provided

• 1214

Myopic macular holes

MURA M
Academic Medical Center, Ophthalmology, Amsterdam, The Netherlands

Myopic traction maculopathy is common in highly myopic patients and characterized by different stages: macular schisis (MS),macular detachment (MD) without macular hole (MH), and MD with MH. MH-related retinal detachment is an uncommon complication associated with posterior staphyloma. Surgical management is based on transvitreal approach and posterior scleral procedure. Since the introduction of pars plana vitrectomy (PPV),retinal detachments with MH in highly myopic eyes were mostly treated with the transvitreal surgery. However,vitrectomy alone does not address the major risk factor of the macular schisis, which is the posterior staphyloma.To give a new shape and support to the posterior scleral wall by means of macular buckling has the advantage of releasing both the traction caused by the posterior staphyloma and the anteroposterior traction caused by the vitreous cortex.A more recent T-shaped scleral buckle has been proposed by Devin et al. We performed this macular buckling combined or not with PPV as a primary surgery or with a previous failed surgical approach in patients affected by MH with MD and MH with or without MS.
In our opinion a combined surgical approach could be the most effective way to treat this disease.

• 1215

Partial thickness Macular holes and pharmaceutical treatment of FTMH

POURNARAS J A C

Jules Gonin Eye Hospital, Ophthalmology, Lausanne, Switzerland

The pathophysiology of full thickness macular hole and lamellar macular hole are different and will be discussed. Oct characteristics will be repeated according to new classification. Taking in account the natural history, indication of treatment will be detailled according to each stage of those diseases. Recently, ocriplasmin has been introduced as an alternative treatment to vitrectomy. Favorable Prognostic factors have been recognized as age inferior to 65 years old, full thickness macular hole < 400 microns, the absence of epiretinal membrane, vitreous adhesion < 1500 microns and phakic status. While management of full thickness macular hole shows good visual prognosis for the patients, the visual result of lamelar macular hole is not so obvious.

• 1221

Mistakes in the diagnosis of children intraocular tumors

CASSOUX N
Institut Curie, Ophtalmology Oncology, Paris, France

Abstract not provided

• 1222

Suspicious choroidal naevi: when to observe when to treat

KIVELÄ T
Department of Ophthalmology, Helsinki University Central Hospital, Helsinki, Finland

Recognition and characterization of choroidal naevi is based on fundus examination with the slit lamp and indirect ophthalmoscope, which ideally is supplemented with optical coherence tomography (presence of subretinal fluid, thickness and internal structure of lesions less than 1 mm in thickness), fundus autofluorescence (presence if recent or prior subretinal fluid, orange pigment) and ultrasonography (thickness and acoustic profile of lesions thicker than 1 mm). In spite of the advent of imaging, the challenge lies in telling small melanomas from naevi. The mnemonic 'To Find Small Ocular Melanomas' reminds us to look for tumour Thickness more than 2 mm, subretinal Fluid, visual Symptoms, Orange pigment and tumour Margin touching the optic disc. Each of these indicators approximately doubles the likelihood of growth and malignancy, although none of them alone is specific – up to ten percent of non-growing naevi have orange pigment and subretinal fluid, for example, whereas some small melanomas initially show none of the five features. Surveillance for growth, a biopsy, or both, may thus be needed to make the treatment decision. This talk will introduce these principles using clinical examples.

• 1223

Difficulties in the diagnosis of achromic and hemorragic lesions

DESJARDINS L
Institut Curie, Paris, France

Achromic choroidal lesions can be an achromic melanoma, a choroidal hemangioma or a metastasis.It is rarer to have scleritis ar the origin of an achromic chorodal mass but this can be seen in sarcoidosis rarely.
Achromic choroidal melanomas are not rare. They are often mushroom shape and have a typical ultrasonographic aspect.In the presence of an achromic melanoma, it is always important to rule out the possibility of a metastasis by doing a chest and abdominal CT. Metastasis are easy to diagnose when they occur in a patient with known metastatic disease, when they are multiple or bilateral. They are trickier when they are unique with no known previous cancer. This is quite frequent in lung cancer where the choroidal mass is often the first manifestation Choroidal hemangioma have a typical orange color and can be easily diagnosed by indocyanin green angiography (early hyper and wash out on the late phase).
Hemorragic mass are frequent in older patient, especially in case of diabetes and high blood pressure. If there is a doubt MRI with gadolinium injections or dopler ultrasonography can easily differentiate a hematoma from, a choroidal tumor.

• 1224

Problems in the diagnosis of intraocular lymphoma

CASSOUX N
Institut Curie, Ophtalmology Oncology, Paris, France

Abstract not provided

• 1225

Indications and interpretations of various imaging techniques

ZOGRAFOS L.
Cabinet Privé du Prof. L. ZOGRAFOS, Jules-Gonin Eye Hospital, Lausanne, Switzerland

A large variety of imaging techniques are presently used in ocular oncology in order to document intraocular, epibulbar and iris tumors. The imaging of choroidal and retinal tumors is obtained either by digital or by scanning laser fundus cameras. Panoramic fundus pictures are obtained both with transpupillary and transscleral illumination. Imaging of epibulbar and iris tumors is obtained with split lamp photographies and gonio photographies. Standard fluoresceine angiography and ICG as well as panoramic angiography (102° - 150°) in ocular oncology are used according to the location and the extend of the tumors and the serous retinal detachment. Retinal thickness, retinal structure and the interface between retina and pigmented epithelium are studied by OCT. More recently, OCT en Face and Angio-OCT provide useful informations on the extend of the retinal detachment and the retinal vascular changes of the macular area. The more appropriate technique has to be always used in order to obtain the best quality of imaging and avoid diagnostic errors.

• 1231

B27-associated uveitis, Fuchs uveitis

WILLERMAIN F (1,2)
(1) CHU Saint-Pierre, Ophthalmology, Brussels, Belgium
(2) Brugmann, Ophthalmology, Brussels, Belgium

B27-associated uveitis is a very frequent form of non infectious intraocular inflammation which account for approximately 50 % of acute anterior uveitis. Its main clinical features, natural history and association with seronegative arthritis are well known. Fuchs uveitis is another frequent cause of anterior and intermediate uveitis. Its natural history is well characterised as well as its association with intraocular production of anti-rubella antibodies. Both diseases are thus often considered as easy diagnosis. However, several aspects of those diseases remain challenging and debated. In this interactive course, based on clinical cases, we will insist on those difficult aspects as well as on the more recent issues discussed in the literature.

• 1232

Infectious uveitis

PLEYER U
Charite, Campus Virchow, Augenklinik, Berlin, Germany

The differential diagnosis of infectious uveitis is broad and an essential step in any initial work-up. Underlying organisms include all types of infectious agents. The more common infectious causes of uveitis include viruses, T. gondii, T. pallidum, Mycobacterium tuberculosis that will be covered in this course. Based on clinical features further diagnostic tools will be discussed and critically reviewed. In particular newer evolving techniques in the investigations will be included, e.g. intraocular fluid evaluation for polymerase chain testing for the genome and antibody synthesis against the causative organisms.

• 1233

Behçet's disease, VKH, sarcoidosis

KHAIRALLAH M (1), Kahloun R (2), Ksiaa I (2)
(1) Fattouma Bourguiba University Hospital, Ophthalmology, Monastir, Tunisia
(2) Fattouma Bourguiba University Hospital- Faculty of Medicine- University of Monastir, Ophthalmology, Monastir, Tunisia

Ocular involvement associated with Behçet disease is characterized by a relapsing remitting panuveitis with diffuse vitritis, retinal infiltrates, and occlusive vasculitis. Proper management relies on the early use of immunosuppressive drugs in combination with corticosteroids and administration of biologic agent in resistant and severe posterior segment involvement. VKH disease is a bilateral panuveitis that may be associated with extraocular manifestations. Exudative retinal detachment, associated with typical imaging findings, is the most specific feature to acute VKH disease. Sunset glow fundus is typical to chronic VKH disease. Complications are more likely to occur in the chronic recurrent phase. The mainstay of treatment for acute VKH disease relies on systemic corticosteroid therapy for at least 6 months. Immunosuppressive therapy is mainly used in chronic recurrent disease. Main ocular features of sarcoidosis include bilateral granulomatous anterior uveitis, vitritis with snowballs, multifocal chorioretinitis, and segmental periphlebitis. Diagnosis may be challenging in the absence of apparent systemic involvement. Treatment of ocular sarcoidosis relies on corticosteroids and immunosuppressive agents, in severe cases.

• 1234

Inflammatory choroiditis

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

White dot syndromes (WDS)is a term introduced around 1995 to describe posterior uveitis syndromes that were poorly understood such as MEWDS, APMPPE, multifocal choroiditis (MFC), serpiginous choroiditis (SC), birdshot retinochoroiditis (BRC) and many others depending on the extension with which the term is used. Unfortunatelly the term is of no utility as it is purely based on the the white dots most posterior uveitis exhibit and as it emcompasses entities that look alike but have nothing in common as far as mechanism is concerned. Thanks to indocyanine green angiography (ICGA) it became possible to get away from this pot-pourri terminology and allowed to sort out choroiditis entities according to the pathophysiological mechanism subdividing choroiditis into diseases of the choriocapillaris (primary choriocapillaritis) including MEWDS, APMPPE, MFC, SC and atypical and overlapping entities on one side and stromal choroiditis on the other side including Vogt-Koxanangi-Harada disease (VKH), BRC, sarcoid and tubercular choroiditis. The appraisal of these diseases and the rationale of their new classification will be explained and examples will be given to illustrate this new comprehensive approach that should make WDS obsolete.

• 1235

Retinal vasculitis

BODAGHI B
Hopital Pitie-Salpetrière, Ophtalmologie, Paris, France

Retinal vasculitis is a sight-threatening inflammatory or infectious condition, requiring an accurate clinical examination followed by an extensive but oriented work-up and an efficient therapy. The place of retinal vasculitis in the IUSG or SUN classifications remain indistinct as it may be associated to an intermediate, posterior or panuveitis. It is important to determine the level of vitreous haze and the type of involved vessel. Complications such as macular edema, retinal ischemia and neovessels must be excluded promptly. The main associated conditions are sarcoidosis, Behçet's disease, birdshot choroidopathy, SLE, IRVAN, Susac syndrome, tuberculosis, syphilis, toxoplasmosis, acute retinal necrosis and CMV retinitis. Imaging techniques such as fluorescein and ICG angiography together with OCT are irreplaceable to determine the basic characteristics of the disease and potential complications. Treatment must be adapted to the severity of the disease and relies on systemic or local corticosteroids associated with conventional immunosuppressors or biologic agents. In patients with an associated infection, specific antibiotics or antivirals are necessary. Laser photocoagulation and vitrectomy may be selectively performed.

• 1241

Introduction of conofocal examination

WYLEGALA E
Ophthalmology Clinic, Railway Hospital, Katowice, Poland

Abstract not provided

• 1242

Conofocal features of healthy cornea

DOBROWOLSKI D
Ophthalmology, District Railway Hospital, Katowice, Poland

Abstract not provided

• 1243

Infectious and non infectious keratitis

SMEDOWSKI A (1,2,3)
(1) Medical University of Silesia, Ophthalmology, Katowice, Poland
(2) Medical University of Silesia, Physiology, Katowice, Poland
(3) University of Eastern Finland, Ophthalmology, Kuopio, Finland

Abstract not provided

• 1244

Corneal dystrophies

NOWINSKA A
Ophthalmology, District Railway Hospital, Katowice, Poland

Abstract not provided

• 1245

Corneal degeneration

WOWRA B
Katowice, Poland,

Abstract not provided

• 1246

Case examples summarizing knowledge of course

WYLEGALA E
Ophthalmology Clinic, Railway Hospital, Katowice, Poland

Abstract not provided

• 1251
Cases

HAMEL C
U1051, INSERM, Institut des Neurosciences de Montpellier

Case reports will be presented

• 1252
Cases

BLACK G C (1), Hall G (2), Ramsden S (2)
(1) *St. Mary's Hospital- Children's University Hospitals NHS Trust, Manchester, United Kingdom*
(2) *Central Manchester University Hospitals NHS Foundation Trust, Centre for Genomic Medicine, Manchester, United Kingdom*

Within the context of the Ophthalmic Genetic Clinic, the diagnosis of Inherited Eye Diseases (IED) requires an integrated approach. This can not only determine clinical management and treatment, but also direct genetic counselling, which is valuable both for the patient and relevant to their wider family. Such an approach requires an accurate history (including a detailed three generation family history), as well as detailed clinical examination, imaging and investigation. Increasingly, such an process requires the integration of genomic testing via Next Generation Sequencing with can include multigene panels, clinical exomes or even whole genome sequencing.

The presentation will include a range of examples to span the breadth of IED including developmental disorders (such as microphthalmia/anophthalmia and congenital cataract), anterior segment disorders as well as inherited retinal disorders (both childhood and adult onset). This will illustrate the power of a multidisciplinary and integrated apporach to the diagnosis of IED.

• 1253
Cases

AUDO I
Department of Genetics, Institut de la Vision, UMRS_968

Case reports will be presented

• 1254
Cases

HOLDER G
Electrophysiology, Moorfields Eye Hospital, London, United Kingdom

Case reports will be presented

• 1255

Cases

LEROY B P (1,2,3,4)
(1) Department of Ophthalmology, Ghent University Hospital, Ghent, Belgium
(2) Center for Medical Genetics, Ghent University Hospital, Ghent, Belgium
(3) Division of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia
(4) Center for Cellular & Molecular Therapeutics, Children's Hospital of Philadelphia, Philadelphia

Case reports will be presented

• 1321

Establishing new OCT parameters: Is race-specific phenotyping necessary?

CHAUHAN B
Ophthalmology and Visual Sciences, Dalhousie University, Halifax, Canada

Establishing phenotypes of the normal optic nerve head via normative databases is vitally important for clinicians. Attributing likelihoods for glaucoma based on single OCT examinations helps clinicians triage and assign resources for further or more intensive testing. It is recognized that significant race-specific differences in optic nerve head parameters exist, however, it their utility has not improved diagnostics. One reason could be that these databases have thus far used only conventional parameters that do not exploit measurements now possible to characterize neuroretinal rim parameters that are anatomically and geometrically accurate, or the deep optic nerve head. This presentation will review the literature on race-specific databases, postulate reasons for their inability to yield better diagnostics and present new alternative race-specific OCT data that may enhance clinical glaucoma practice.

• 1322

OCT in assessing glaucoma progression

GARWAY-HEATH D
Moorfields Eye Hospital, Glaucoma, London, United Kingdom

OCT imaging enables the measurement of various structures in the optic nerve head (ONH) and retina which may be progressively damaged in glaucoma. Examples include the neural rim and lamina cribrosa at the ONH and the retinal nerve fibre layer (RNFL) in the peripapillary region of the retina and ganglion cell layer (and associated structures) in the macula. Most of these can be measured with high precision (low variability), which makes them good candidates for identifying progression and quantifying rates of progression. The presentation will provide a critical review of the literature for the application of OCT imaging to measure progression in glaucoma, considering the various potential anatomical targets. The application of OCT imaging in clinical practice will be discussed, including pitfalls in relation to image quality and artifacts. The presentation will also discuss the clinical relevance of OCT-measured change in relation to vision function and how imaging outcomes should be interpreted.

• 1323

OCT in animal models

NORMANDO E M (1,2)
(1) *Western Eye Hospital- Imperial College Healthcare NHS Trust, Imperial College Ophthalmology Research Group ICORG CTU, London, United Kingdom*
(2) *UCL Institute of Ophthalmology, Glaucoma & Retinal Neurodegeneration Research Group, London, United Kingdom*

Due to their accessibility, animal models are playing a major role in understanding some of the underlying causes of glaucoma. Optical Coherence Tomography (OCT) has been used extensively in these animal models giving us the advantage of longitudinal ***in-vivo*** assessments of the natural history of this disease. Outer retina involvement has recently been demonstrated ***in-vivo*** in experimental glaucoma. OCT segmentation software are now available as an aid for understanding the involvement of retinal layers other than the RNFL. Retinal blood flow is also currently under investigation in experimental glaucoma using ultra high resolution OCT. Furthermore, investigations of the irido-corneal angle configuration and its structural modifications in response to anti glaucoma drugs have also been conducted in experimental models using anterior segment OCT. The talk will discuss the utility of OCT in animal models in Glaucoma.

• 1331

Understanding the molecular genetic causes of inherited corneal disorders

DAVIDSON A
UCL, Institute of Ophthalmology, London, United Kingdom

Inherited corneal diseases comprise a group of clinically and genetically heterogeneous disorders that can lead to bilateral severely impaired vision and/or blindness. Advances in next generation sequencing (NGS) technologies have revolutionised clinical genetics over the past five years. The application of NGS, in combination with genome wide association studies, to the field of inherited corneal disorders has provided significant insights into the genetics of corneal diseases and their underlying aetiology. An overview of our current understanding of the genetics of monogenic corneal dystrophies, as well as the contribution of genetic factors to complex conditions such as keratoconus and Fuchs endothelial corneal dystrophy (FECD), will be provided. Examples from our laboratory exploiting NGS platforms, in combination with careful phenotyping of patient sub-groups, to identify novel genetic causes and mechanisms of inherited corneal disorders such as; posterior polymorphous corneal dystrophy, epithelial recurrent erosion dystrophy, and X-linked megalocornea, will be highlighted. Furthermore the impact of these findings on clinical care and their potential to provide translational outcomes will be discussed.

• 1332

The impact of genetics on the clinical management of patients with monogenic corneal diseases

TUFT S J (1), Evans C (2), Davidson A (2), Hardcastle A (2)
(1) Moorfields Eye Hospital, London, United Kingdom
(2) UCL Institute of Ophthalmology, London, United Kingdom

Over the last decade there has been a major reassessment of the classification of inherited corneal disease. In this presentation I discuss our program to genotype all patients attending our tertiary referral center who have suspected monogenic corneal disease. This has enabled us to distinguish the phenotypes of several closely related dystrophies as well as identify a small number of patients who have previously been misclassified. Some patients with important systemic associations have been identified and referred for further investigation and management. Finally, patients without changes in the genes commonly associated with corneal dystrophy have been selected for further evaluation. The impact of this for clinical care will be discussed.

• 1333

Monogenic corneal disorders in children

KHAN A (1,2)
(1) King Khaled Eye Specialist Hospital, Division of Pediatric Ophthalmology, Riyadh, Saudi Arabia
(2) King Faisal Specialist Hospital and Research Center, Department of Developmental Genetics, Riyadh, Saudi Arabia

Pediatric monogenic corneal disorders tend to be under-recognized or misdiagnosed. However, careful phenotyping distinguishes several such conditions and can sometimes predict the underlying gene mutations. After this presentation, the attendee will be familiar with phenotype-genotype correlations for selected monogenic corneal disorders in children.

• 1334

The Czech Republic experience in a corneal clinic

LISKOVA P
Charles University, Prague, Czech Republic

The spectrum of monogenic corneal disorders identified in the Czech Republic is diverse. We have observed some of the rare disorders, such as cornea plana, megalocornea, Harboyan syndrome and brittle cornea syndrome, in Czech patients. We have also observed a founder effect for posterior polymorphous corneal dystrophy, which appears to have the highest worldwide prevalence in the Czech Republic. Molecular genetic confirmatory testing can be performed in settings with limited laboratory diagnostic services either on a research basis or via research collaborations. Experience from the Czech Republic suggests that monogenic corneal disorders, particularly those that are non-syndromic, are under-diagnosed.

• 1341

Comparative Study of Tacrolimus and Bevacizumab on Corneal Neovascularization in Rabbits

KIM S E (1), Park J H (1), Chung S K (2)
(1) Seoul St. Mary's hospital- College of Medicine- The Catholic University of Korea, ophthalomology and visual science, Seoul, South-Korea
(2) St. Paul's hospital- College of Medicine- The Catholic University of Korea, ophthalomology and visual science, Seoul, South-Korea

Purpose To compare the anti-angiogenic effects of tacrolimus and bevacizumab on corneal neovascularization in rabbits.
Methods Neovascularization was induced in 32 eyes of 16 rabbits by placing suture in the corneal stroma. Seven days after suture placement, all rabbits were divided into four groups and were treated subconjunctivally with bevacizumab 0.05mL (5mg/0.05mL; AVA_sub), Tacrolimus 0.05mL (0.25mg/0.05mL; TAC_sub), balanced salt solution (0.05mL was subconjunctivally injected in one eye of each rabbit and applied by eye drops in the other eye, control group), and Tacrolimus eye drops (5mg/5mL applied four times daily; TAC_drop). Digital photographs were obtained and the surface area of corneal neovascularization was measured 7 days after subconjunctival injections. Corneal specimens were analyzed histopathologically and were used to measure the concentration of VEGF, TNF-α, IFN-γ, IL-1ß, and MCP-1 mRNA by RT-PCR.
Results In digital photographs, the neovascularized area was decreased in all treatment groups (AVA_sub 0.58, TAC_sub 0.60, TAC_drop 0.68) compared with the control group (BSS 0.81). The histological examination showed markedly regressed new vessels in treatment groups, and the immunohistochemical staining revealed weakly stained with anti-VEGF and anti-F4/80 antibodies in the treatment groups. In semi-quantitative RT-PCR, the concentration of VEGF (AVA _sub 0.24, TAC_drop 0.18), TNF-α (AVA_sub 0.19, TAC_sub 0.24, TAC_drop 0.15), and IL-1ß (AVA_sub 0.19, TAC_sub 0.33, TAC_drop 0.18) mRNA were significantly lower in the treatment groups than in the control group (VEGF 0.47, TNF-α 0.44, IL-1ß 0.87) ($P < 0.05$).
Conclusions Topical and subconjunctival tacrolimus application may be useful in reducing corneal neovascularization and have comparable effects to subconjunctival bevacizumab injection.

• 1342

HLA-A*02:06 and PTGER3 polymorphism exerts additive effects in cold medicine-related Stevens-Johnson syndrome with severe ocular complications in Japanese and Korean populations

UETA M (1), Tokunaga K (2), Sotozono C (3), Sawai H (2), Yoon K C (4), Kim M K (5), Seo K Y (6), Joo C K (7), Kinoshita S (1)
(1) Kyoto Prefectural University of Medicine, Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto, Japan
(2) Graduate School of Medicine- University of Tokyo, Department of Human Genetics, Tokyo, Japan
(3) Kyoto Prefectural University of Medicine, Department of Ophthalmology, Kyoto, Japan
(4) Chonnam National University, Department of Ophthalmology, Gwangju, South-Korea
(5) Seoul National University College of Medicine, Department of Ophthalmology, Seoul, South-Korea
(6) Severance Hospital- Institute of Vision Research- Yonsei University College of Medicine, Department of Ophthalmology, Seoul, South-Korea
(7) Seoul St. Mary's Hospital- College of Medicine- The Catholic University of Korea, Department of Ophthalmology and Visual Science, Seoul, South-Korea

Purpose We reported that *PTGER3* SNPs were associated with Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) with severe ocular complications (SOC). We also reported that about 80% of our SJS/TEN patients had taken cold medicines within several days before disease onset and designated them cold medicine related-SJS/TEN (CM-SJS/TEN) patients, and that HLA-A*02:06 was significantly associated with CM-SJS/TEN in Japanese and Korean populations . Moreover, we documented that ***HLA-A*02:06*** with ***TLR3*** polymorphisms exerted more than additive effects in SJS/TEN with SOC. In the current study we focused on CM-SJS/TEN with SOC and analyzed an interactive effect between ***PTGER3*** SNPs and ***HLA-A*02:06*** in Japanese and Korean populations.
Methods Samples from 132 Japanese patients with CM-SJS/TEN with SOC were collected and 221 healthy Japanese volunteers were also recruited as controls. Samples from 30 Korean patients with CM-SJS/TEN with SOC were collected and 120 healthy Korean volunteers were also recruited as controls. Genotyping of PTGER3 gene SNPs was performed using the TaqMan SNP genotyping assay or the DigiTag2 assay. HLA-A genotyping was performed using using commercial bead-based typing kits, WAK Flow.
Results In Japanese population, we found an interaction with additive effects between ***HLA-A*02:06*** and the high-risk genotypes ***PTGER3*** rs1327464 GA or AA (OR = 10.8, p = 2.56 x 10-7). Moreover, we also found an additive effect between ***HLA-A*02:06*** and the high-risk genotypes ***PTGER3*** rs1327464 GA or AA (OR = 14.2, p = 5.58 x 10-6).
Conclusions These finding might show that the combination of these two polymorphisms could give improvements for a genetic testing as compared to using only one susceptibility gene.

• 1343

Expression of Tissue inhibitor of metalloproteinase in ocular Stevens-Johnson Syndrome: An Immunohistochemical Study

VENUGOPAL R (1), Sen S (2), Kashyap S (2), Sharma A (3), Agarwal T (1), Sharma N (1)
(1) Dr.R.P.Centre for Ophthalmic Sciences- All India Institute of Medical Sciences, Ophthalmology, New Delhi, India
(2) Dr.R.P.Centre for Ophthalmic Sciences- All India Institute of Medical Sciences, Ocular Pathology, New Delhi, India
(3) Dr.R.P.Centre for Ophthalmic Sciences- All India Institute of Medical Sciences, Ocular Microbiology, New Delhi, India

Purpose Tissue inhibitor of metalloproteinase-1 (TIMP-1) forms complexes with Matrix Metalloproteinases to inhibit tissue degradation and extracellular matrix(ECM) accumulation. Involvement of TIMP-1 in Stevens -Johnson syndrome(SJS) ocular pannus formation remains unexplored. Therefore, this study aims to evaluate the expression of TIMP-1 in SJS ocular sequelae patients.
Methods Pannus tissues of 18 SJS patients excised during ocular surface reconstruction surgeries were collected. Clinical and histopathological parameters were examined. Immunohistochemistry (IHC) was performed on all cases for TIMP-1 and evaluated on the basis of epithelial/stromal staining intensity. Expression of TIMP-1 was statistically correlated with the histopathological and clinical parameters.
Results Mean age was 25.6 ±13.10 years. There was a male preponderance. Antipyretics (38%) were the most common cause of ocular SJS. Mean duration from onset of systemic episode to first presentation was 8.3 ± 6.2 years. Mean BCVA was 2.72 logMAR ± 0.47, mean Schirmer's value was 0.27 ± 1 mm. Epithelial hyperplasia was found histologically in 88.8% and stromal vascularization in 55%. Stromal fibrosis was indentified in 22%. TIMP-1 expression was found in pannus epithelium in 13 cases and in stroma in 15 cases. Epithelial TIMP-1 expression was statistically significant with epithelial hyperplasia, epithelial keratinization, squamous metaplasia, inflammation and stromal fibrosis ($p<0.05$). Stromal TIMP-1 positivity correlated significantly with epithelial keratinization ($p=0.0134$).
Conclusions TIMP-1 protein expression correlated with the histopathological factors in ocular manifestations of SJS. This indicates TIMP-1's contribution in pannus formation which involves ECM modifications. This may help TIMP-1 to be considered as a possible therapeutic target in SJS.

• 1344

In-vitro anti angiogenic effects of cryo-preserved amniotic membrane

FARAJ L (1), Stewart E (1), Albert R (2), Allen C (1), Petrovski G (2), Dua H (1), Amoaku W (1)
(1) University of Nottingham, Ophthalmology, Nottingham, United Kingdom
(2) University of Szeged, Ophthalmology, Szeged, Hungary

Purpose Amniotic membrane (AM) has long been used as a biological substrate in Ophthalmology. It has a valuable role in ocular surface burns, ulcers, and nonhealing epithelial defects. AM is non-immunogenic and has anti-inflammatory and anti-fibrotic properties. AM is also supports epithelial cells proliferation and migration.These effects are mediated through a host of growth factors and cytokines. Despite its clinically accepted role in reducing corneal vascularisation when applied on the eye, there have been contradicting reports on its in-vitro anti angiogenic effect. The purpose of this study was to establish the effect of clinically prepared AM on angiogenesis and to identify the factors responsible for this role.
Methods The effect of clinically prepared cryo-preserved AM on human umbilical cord endothelial cells (HUVEC) proliferation was quantified using. The amniotic membrane effect on angiogenesis was quantified on matrigel. Responsible anti-angiogenic factors were identified using searchlight protein analysis and immun-blocking experiments.
Results AM had a profound and significant direct effect on angiogenesis. A gradient effect was observed where HUVEC closer to the AM failed completely to migrate and form any tubules. HUVEC also failed to survive directly on the AM. proliferation was reduced significantly when exposed to AM conditioned medium. Analysis of the soluble factors released by the AM included high levels of anti-angiogenic factors,Thrombospondin and tissue inhibitors of metalloproteinase 1 and 2.
Conclusions The AM in-vitro has significant anti-angiogenic properties. This effect is attributable to an array of soluble anti angiogenic factors. This can opens a new field of using AM conditioned solutions for ocular surface vascularisation if the physical presence of the AM over prolonged period of time is not desired.

• 1345

Intratarsal injection of kenacort in the treatment of severe cases of VKC

LAZREG S
Cabinet Lazreg, Cabinet d'ophtalmologie, Dar el Beida, Algeria

Purpose To treat refractory cases of Vkc with intratarsal injections of trialcinolone .
Methods We treated Severe cases of Vkc that have already experienced different anti allergic treatments and topical steroids with frequent relapses and dependancies to steroids with intratarsal injection of 40 mg of dexametasone , the follow up visits were performed at D0, D 3, D7 and D30 (slit lamp examination, corneal staining, ocular pressure)
Results 87 severe cases of Vkc 63 males , mean age 10,4+/- 3,5years , 90% bilateral , and 100% of corneal involvement . 70% mixed forms and 15% of tarsal forms, the mean follow up was 20+/-7 months . at D3 we had a decrease of all ocular signs(photophobia, redness and pruritis) at D7 decrease of corneal staining and trantas nods, and at d30 , total remission of the Vkc, the mean duration of the efficacy of the treatment was 10.4+/- 2.6 months , no adverse event was observed .
Conclusions Intratarsal injection of steroids is very effective in severe and resistant cases of Vkc , especially in our countries where this disease is very severe , frequent and when topical cyclosporine is not available .

• 1346

3D model of pterygium and corneal limbus: Investigating histopathology and stem cell distribution.

BLOM N (1), Andreasen A (2), Heegaard S (3), Hjortdal J (1), Nielsen K (1)
(1) *Aarhus University Hospital, Department of Opthalmology, Aarhus C, Denmark*
(2) *Aarhus University, Department of Biomedicine Anatomy, Aarhus, Denmark*
(3) *Glostrup Hospital- University of Copenhagen, Department of Ophthalmology, Copenhagen, Denmark*

Purpose This study aims to create a complete histological 3D computer model of pterygium in situ, mapping the anatomy of the disease tissue, its relation to the corneal limbus and the distribution of limbal stem cells.
Methods One human eye affected with pterygium was obtained from a cornea donor post mortem. The anterior part of the eye was cut into 900 consecutive horizontal sections. Every other section was stained with HE to be digitized, aligned and 3D reconstructed using interactive 3D visualization software. Immunohistochemistry targeting CK19, MMP-1, p63 and VEGF was performed on the remaining sections alternating across the structure so as to create evenly distributed overlaying models.
Results Using the sections a high-resolution model of the pterygium and limbus was created, and in aligning the immunostained sections to the model, a spatial map of the staining was created.Analyzsing the model we found a mostly normal temporal limbus with intact architecture, however nasally the limbus was found to be buried under the pterygial mass and only partly intact, showing a number of pathological changes.
Conclusions The limbal degeneration underneath the pterygium appears to be a precondition for or a consequence of the pterygial growth.

• 1347

Analysis of molecular mechanisms that predispose patients to develop post-PRK haze

RAJIV KUMAR N , Ghosh A , Shetty R , Pahuja N
NARAYANA NETHRALAYA FOUNDATION, GROW RESEARCH LABORATORY, BANGALORE, India

Purpose Factors that predispose certain patients to develop post-surgical haze remain unknown. We analyzed gene expression in corneal epithelium collected from patients prior to haze development following PRK. We further developed an in-vitro model to study haze using TGFβ that mimics pre-disposed and post haze conditions
Methods Corneal epithelium was collected intraoperatively from patients undergoing PRK. 4 eyes that developed haze postoperatively and 10 eyes of age matched controls without haze were analysed. Microarray analysis was followed by bioinformatics and validation. ***In vitro*** studies were performed on HCE cells on differential doses of TGFβ with or without wound for inflammatory markers, structural & pro-fibrotic genes and regulators of signaling cascades
Results Microarray analysis revealed 1100 up regulated and 1700 down regulated genes in haze patients. ECM- Receptor interactions were elevated in patients prior to haze induction while Wnt signaling genes and CXC motif chemokines were reduced. Structural genes (Col I, Col IV, MMP2 & 14, TIMP1) were reduced in haze patients which correlated with ***in-vitro*** model. Inflammatory factors TNFα, IL-11 were elevated, but IL6 and IL1 did not show appreciable changes. Regulators of signaling cascades EGFR and Wnt3a were reduced in haze patients & ***in vitro***. We propose a signal transduction network including few novel genes like PREX1, PXDN, SOX17, WNT3A, CXCL10 etc which can be factors that predispose patients to haze
Conclusions Our study shows that molecular factors poise the cornea in some patients to developing corneal haze after surgery

• 1348

Corneal lenticules as an ex-vivo model to study keratocyte biology

SHROFF R (1), Shetty R (2), Kumar D (3), Kumar S (3), Pahuja N (1), GHOSH A (3)
(1) *NARAYANA NETHRALAYA, CATARACT - REFRACTIVE AND CORNEA, BANGALORE, India*
(2) *NARAYANA NETHRALAYA, CORNEA AND REFRACTIVE SERVICES, BANGALORE, India*
(3) *NARAYANA NETHRALAYA, GROW LAB, BANGALORE, India*

Purpose Keratocytes show differential gene expression in culture media; and are extensively used to study wound healing, corneal disease biology and response to topical drugs. However, mono-layer culture cannot replicate the 3-dimensional biological environment of corneal stroma. Hence, we propose to establish corneal lenticule as an ***ex-vivo*** model to study keratocyte biology for corneal diseases, drug response studies and in wound healing experiments.
Methods SMILE surgery was performed using the VisuMax femtosecond laser system (Carl Zeiss Meditec AG, Jena, Germany). After the refractive lenticule of intra-stromal corneal tissue was created using the femtosecond cutting procedure, it was dissected and separated through the side-cut opening and removed manually. SMILE lenticules from patients were obtained in MK media and were transferred to DMEM F12 with 10% FBS and 1% PSA. The media was replenished every 24h and lenticules were harvested at 0h, 24h, 48h, 78h and 96h. Gene Expression analysis was performed for pro-fibrotic genes (fibronectin, -sma, vimentin, TGF-β and TGF-βR2), pro-inflammatory (IL-6 and TNF-) and structural genes (Col1-A1, Col4-A1and Col5-A1).
Results Our results demonstrate that lenticules remain metabolically active in culture media for long periods of time as evident from the varying expression of different pro-fibrotic, pro-inflammatory and structural genes after 0h, 24h, 48h, 78h and 96h of culture. Furthermore, linear regression analyses show that clinical parameters like lenticule thickness do not affect the expression profile of the various genes by the keratocytes contained in the lenticule.
Conclusions In conclusion, lenticule can be used as an ex-vivo model to study keratocyte biology in various corneal diseases and for drug testing.

• 1351

Reviewer - friend or foe?

PLEYER U
Charite, Campus Virchow, Augenklinik, Berlin, Germany

Abstract not provided

• 1352

What do we need...

DUA H S
Queens Medical Centre- Derby Road, Eye Ear Nose Throat Centre, Nottingham, United Kingdom

Abstract not provided

• 1353

How to keep your research published

KIVELÄ T
Department of Ophthalmology, Helsinki University Central Hospital, Helsinki, Finland

A key criterion for publishing a paper is novelty. This extends from original data to the introduction and discussion of the results. No part of the manuscript can be cut and pasted, or cursorily adjusted, from published literature - not even from the author's previously published papers. Violation of this rule, if detected after publication, often results in retraction of the paper, something which can now happen even years after its publication. One must also be certain to submit only unaltered images and data. The advent of post-publication peer review almost ensures that if images have been tampered with, this will be detected, again resulting in retraction. A third way of having one's paper retracted is to include authors who did not know about or did not approve the submission. These and certain other ways of getting a paper pulled out of the medical literature will be highlighted by recent examples, and the audience will be introduced to useful tools and web sites related to post-publication review. It is best to know about them before they strike you.

• 1354

Ingredients of a good paper...

STEFANSSON E
University of Iceland, Reykjavik, Iceland

Abstract not provided

• 1361

History of IOLs - did it start in Poland?

GRZYBOWSKI A
Poznan, City Hospital, Poznan, Poland

It was reported that 1. the idea of IOL implantation originated from Italian itinerant oculist Tadini, 2. the first attempt of IOL implantation was conducted by Italian ophthalmologist Joannis Virgilius Casaamata (1741-1807) in 1795 in Dresden. The majority of these facts, however, is based on secondary sources and need verification. The study is based on analysis of original materials related to Tadini, Casanova and Casaamata and some contemporary descriptions related to this issue, including original doctoral dissertations. The study enabled to collect some information about life and work of Tadini and Casaamata. The original description of Tadini's concept of intraocular lens implantation was delivered in Casanova's Memoirs. It is clear that Tadini has never attempted this procedure. The interesting description of the first, although unsuccessful, attempt by Casaamata comes from the dissertation of Swiss surgeon Rudolph Schiferli (1775-1837) in 1797 entitled „On Cataract" (Theoretisch-praktische Abhandlung über den grauen Starr). In conclusion, the first concept of intraocular lens implantation was created by Tadini, and the first attempt of this procedure by Casaamata.

• 1362

Visual quality assessment and imaging techniques used to study biomaterials

SPALTON D
St Thomas' Hospital, London, United Kingdom

Cataract surgery has evolved from a sight saving procedure to one which improves the quality of vision. Quality of vision can be thought of as the physical resolving power of the eye, what the patient sees together with associated dysphotopsia, quality of the IOL relies on quality of manufacture and quality of the optics influenced by quality of surgery. Environmental scanning electron microscopy has proved extremely useful in assessing the profile of an IOL, intra lenticule glistenings can be imaged and semi quantified and atomic force microscopy examines surface smoothness and a wide range of other techniques are require to assess other biomaterial properties. Optics can be characterised by measuring modulation transfer function, Strehl ratio and wavefront, and vision by acuity and contrast sensitivity, measurement of forward scatter of light remains difficult and controversial. Patient reported outcomes are being increasingly used to differentiate clinical from subclinical improvement.

• 1363

Does IOL choice impact on Driving Performance?

BEIKO G
St. Catharines, Canada

Purpose: Does the IOL implanted at cataract surgery affects the driving habits and crash risk of patients.
Methods: Retrospective analysis of patients who met the visual requirements for a drivers license and had bilateral implantation of the same lens. The patients had at least 2 years of follow-up. Two groups of patients were identified; each with one of two types of acrylic IOLs. Both groups were given the Driving Habits Questionnaire, by a single investigator.
Results: 90 patients participated; 51 had acrylic IOL type A and 39 had acrylic IOL type B. The demographics were similar for age, sex, diabetes, glaucoma and IOL power implanted. Group A was more likely to have road traffic accidents (P=0.066) and less likely to drive at the same speed or faster than general flow of traffic (P= 0.094). Group A to be less likely to have travelled beyond their immediate neighbourhood, to be less likely to rate their quality of driving at average or above and to be more likely to have difficulty driving at night; but this did not reach significance.
Conclusions: At two years postoperatively, the choice of IOL implanted at the time of cataract surgery may have an impact on driving habit and crash risk.

Commercial interest

• 1364

Opacification of intraocular lens

MATSUSHIMA H
Dokkyo Medical University, Ophthalmology, Tochigi, Japan

Soft hydrophobic acrylic intraocular lenses (IOLs) are increasingly being used because they can be implanted through small incisions, provide good postoperative vision. However, long-term postoperative follow-up has identified various problems, including calcification, glistening and whitening.
Calcium deposit on surface of IOLs are sometimes reported about hydrophilic acrylic materials. Calcification reduces the transmission of light and renders the fundus virtually invisible and decrease visual function easily.
Glistening has been attributed to water retention in voids of hydrophobic acrylic materials and nonuniformity of polymer network structures. Whitening refers to the clinical appearance from sub surface nano glistenings (SSNG) of reflected white light due to light scattering as light encounters nano sized fluid filled vacuoles that occur at the anterior and posterior IOL surface. With a hydrophobic IOL, the fundus remains visible despite opacification and less effect of visual function. As a result, removal and replacement of IOLs is indicated in only a few cases. However, sever glistening and whitening increased glare and decreased contrast sensitivity.

• 1365

Current problems with IOLs.

ALIFFARTH G
Ruprecht Karls Universität, Ruprecht Karls Universität, Heidelberg, Germany

Abstract not provided

• 1371

Physiology of retinal oxygenation

STEFANSSON E
University of Iceland, Reykjavik, Iceland

The retina receives O2 from retinal and choroidal circulations. Both vascular beds can now be imaged with noninvasive spectrophotometric oximetry in human subjects. This allows study of normal O2 metabolism and physiology and clinical research in retinal disease. Normal physiology: Technical and biological variability in retinal O2 saturation is low compared to most clinical parameters. Test-retest studies show standard deviations of about 1% and in a healthy population the standard deviation is only 5-11% of the mean, low compared for example to IOP measurements. Retinal O2 saturation is relatively stable with age and shows only a minor reduction over decades of life. Retinal oximetry reliably detects retinal O2 saturation consumption due to changes in illumination. Retinal and choroidal oximetry data agree well with invasive studies in animals and human subjects. Ischemic retinopathies: Abnormal O2 saturation has been documented in diabetic retinopathy, retinal vein and artery occlusions and neovascular AMD. This agrees well with invasive PO2 studies and presence of Hypoxia-Inducible-Factor in these diseases. Atrophic retinopathies: Retinal atrophy in glaucoma and retinitis pigmentosa reduces O2 consumption and this is detected by retinal oximetry. Retinal oximetry may be a good method to quantify progressive retinal atrophy.

• 1372

Blood flow and oxygenation in atrophic diseases

TODOROVA M
University Eye Hospital Basel, Department of Ophthalmology, Basel, Switzerland

There is increasing evidence that alterations in retinal-choroidal blood flow play a role in the pathogenesis of atrophic diseases. Studying the oxygen saturation of retinal vessels on patients affected by glaucoma and inherited diseases of the retina, suggest the oxygen metabolism to be altered. To which extend the role of the oxygen saturation contributes to the blood flow fluctuations and thus, to the progression of atrophic disease will be discussed in this presentation.

• 1373

Relation of oxygen saturation to stage of diabetic retinopathy

SIN M , Chrapek O , Sinova I , Stanakova L , Rehak J
University Hospital and Faculty of Medicine and Dentistry- Palacky University, Department of Ophthalmology, Olomouc, Czech Republic

Aim: To assess whether oxygen saturation of the retinal vessels is related to degree of diabetic retinopathy.
Methods: A prospective study included 114 eyes of 76 patients with diagnosed diabetes and 57 eyes of 29 non diabetic patiens. The diabetic patients were divided into groups according to severity of the retinopathy.
Results: In healthy controls mean arterial saturation was 96.5±2.6%, mean vein saturation was 62.3±7.4% and A-V difference was 34.3±7.2%. In diabetic patients with no retinopathy mean arterial saturation was 96.5±3.2%, mean vein saturation was 66.3±6.3% and A-V difference was 30.2±4.9%. In patients with mild diabetic retinopathy mean arterial saturation was 96.7±4.6%, mean vein saturation was 67.9±7.2% and and A-V difference was 28.8±8.2%. In patients with moderate nonproliferative retinopathy mean arterial saturation was 97.8±4.6%. mean vein saturation was 69.9±6.7% and A-V difference 27.9%±5.8%. In patients with severe non-proliferative and proliferative retinopathy mean arterial saturation was 100.5±5.6%, mean vein saturation was 74±7.2% and A-V difference was 26.5±7.8%.
Conclusion: We confirmed an increase in oxygen saturation in both retinal artery and vein in relation to degree of diabetic retinopathy.

• 1374

Choroidal blood flow and thickness measurements

SCHMIDL D
Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria

Most of the ocular blood supply goes into the choroidal circulation. Intensive research has been directed towards choroidal structure and function in health and disease. Indeed, choroidal blood flow and its regulation has been found to be altered in several ocular diseases, such as age-related macular degeneration. Several techniques for the assessment of choroidal blood flow have been developed including laser Doppler flowmetry, laser speckle flowgraphy, laser interferometric measurement of fundus pulsation amplitude or pneumotonometric measurement of pulsatile ocular blood flow. All these techniques have significant limitations and currently no gold standard method for the assessment of choroidal blood flow exists. With the introduction of enhanced depth imaging optical coherence tomography (OCT) systems, it is now possible to image choroidal thickness in vivo. Alterations in choroidal thickness have been observed in several ocular diseases. The correlation between functional and structural choroidal parameters is, however, weak. Further research is required to better understand the results obtained in patients with ocular pathologies and to investigate whether choroidal thickness is a good biomarker for choroidal disease. European

THURSDAY OCTOBER 8, 2015

• 2111

Fundus autofluorescence and Photobleaching : Definitions

MATHIS T *(1), De Bats F (2), Cahuzac A (3), Wolff B (3), Scemama Timsit C (3), Uzzan J (4), Kodjikian L (1), Mauget-Faÿsse M (3)*
(1) Hôpital Croix-Rousse, Ophthalmology, Lyon, France
(2) Pôle vision- clinique du Val d'ouest, Ophthalmology, Lyon, France
(3) Fondation Ophtalmologique Rothschild, Ophthalmology, Paris, France
(4) Clinique Mathilde, Ophthalmology, Rouen, France

Fundus autofluorescence (AF) imaging is a non-invasivemethod for detection of fundus fluorophores. The 488nm blue (short wavelength: SW) or the 787nm near-infrared (NIR) wavelenght are usually used to induce AF of fluorophores located in the retinal pigment epithelium (RPE). In case of excitation with SW light, the resulting AF comes predominantly from A2E located in the lipofuscin granules of the RPE. On the other hand, excitation with NIR light seems to highlight the melanin. Regardless of the type of fluorophore in the RPE, the exciting light has to pass first through the retina and especially through the photoreceptor layer. The photopigment absorbs a part of the light, which will not be transmitted to the RPE. Therefore, RPE fluorophores will be less AF. In the same time, photo-isomerization of the 11-cis-retinal to 11-trans-retinal by the photon absorbance will be the beginning of the visual signal. Thereby, retinal photopigment loose its absorption property and the light will be easily distributed to the RPE fluorophores. This photoreceptor bleaching phenomenon could be used to better understand the origin of the hyper-AF pattern: hyper-AF of the RPE or lack of absorbance of signal due to photopigment loss.

• 2112

Fundus autofluorescence imaging in White Dot Syndromes

DE BATS F *(1), Wolff B (2), Mathis T (1), Scemama Timsit C (2), Cahuzac A (2), Uzzan J (3), Mauget-Faÿsse M (2)*
(1) croix rousse hospital, ophthalmology, lyon, France
(2) foundation rothschild, ophthalmology, paris, France
(3) clinique mathilde, ophthalmology, rouen, France

The term 'white dot syndromes' (WDS) refers to several inflammatory diseases of the retina and choroid caused by immune dysregulation. Retinal and choroidal changes observed with multimodal imaging are transient and may disappear quickly in some cases. Multimodal imaging with color fundus photography, fluorescein, indocyanine green angiographies, spectral Domain Optical Coherence Tomography help in identifying the diagnosis. They also help assess the level of inflammatory activity and detect complications. Fundus autofluorescence (AF) imaging is an ***in vivo*** imaging method that allows a metabolic mapping of natural or pathological fundus fluorophores. Blue fundus AF imaging is obtained with a confocal laser scanning ophthalmoscope using an excitation short wavelength (SW) at 488 nanometers. In this work, SW-AF imaging was obtained using a HRA Heidelberg instrument. SW-AF imaging is an important, non invasive and complementary technique that helps early diagnosis and follow-up of WDS. The characteristics of the SW-AF abnormalities are often pathognomonic of each inflammatory disease. Further prospective studies including more patients will be necessary to confirm these results.

• 2113

Fundus autofluorescence imaging in Toxic Retinopathies and in Gravitational descending atrophic retinal pigmented epithelial tracks

CAHUZAC A *(1), Wolff B (2), Lehmann M (3), Scemama C (2), Mauget-Faÿsse M (2)*
(1) Fondation Ophtalmologique Rothschild, Service Pr Sahel, paris, France
(2) Fondation Ophtalmologique Rothschild, Service Pr Sahel, Paris, France
(3) Hotel Dieu, Ophtalmologie, Paris, France

Fundus autofluorescence (FAF) was studied in toxic retinopathy due to synthetic antimalarial drugs (SAM). It was not a screening tool, however it was useful for non-invasive follow up once retinal toxicity is established.
FAF was also studied in Central serous chorioretinopathy (CSC) and diffuse retinal pigment epitheliopathy (DRPE) where it showed abnormalities at both acute and late stage as well as gravitational descending atrophic retinal pigment epithelial tracks, with different caracteristics depending on the acute or chronic stage of the disease.
FAF was also studied in choroidal hemangioma where it showed various pattern of atrophic retinal pigment epithelial tracks, in chronic retinal detachment (RD) and in post-traumatic retinal lesions.
Fundus autofluorescence is a major non-invasive tool to monitor damaged retinal epithelium areas in various pathologies such as toxic retinopathy, CSC, DRPE, chroidal hemangioma and chronic retinal detachment.

• 2114

Fundus autofluorescence imaging in Ocular Oncology

SCEMAMA TIMSIT C *(1), Mauget-Faÿsse M (2), Wolff B (3)*
(1) Fondation ophtalmologique Adolphe de Rotschild, service du Pr Sahel, PARIS 19 eme, France
(2) Fondation Rothschild, service du Pr Sahel, Paris, France
(3) Strasbourg, rétine, strasbourg, France

PURPOSE : To evaluate fundus autofluorescence aspect in retinal and choroidal tumor, paraneoplastic syndrome and intraocular lymphoma.
METHODS : All the study patients underwent a complete ophthalmologic examination including biomicroscopic, fundus examination, color photography, fundus autofluorescence, fluorescein angiography, indocyanin green angiography and SD-OCT.
RESULTS : A total of 14 patients with choroidal or retinal tumor or paraneoplastic syndrome were analysed. 3 cases diagnosed with choroidal melanoma, 1 case of melanocytoma, 2 cases of choroidal nevi, 2 cases of choroidal metastasis, 2 cases of choroidal hemangioma, 1 case of choroidal osteoma, 1 case of intraocular lymphoma, 2 cases of paraneoplastic syndrome (1 BDUMP and 1 AEPPVM) were analysed. The color fundus photographs, angiography and B-scan findings were compared with FAF imaging. In most of cases FAF imaging is perfectly corellated with, color fundus photographs, angiography, and OCT findings (orange pigment, drusens, calcifications, pseudovitelliform deposits, atrophy...)
CONCLUSION : FAF imaging allows a very interesting analysed in ocular oncology without used of dye, a good correlation was found with color fundus photographs, angiography and OCT findings

• 2115

Fundus autofluorescence imaging in AMD and in Retinal Dystrophies and Perspectives

UZZAN J
Rouen, France,

Abstract not provided

• 2121

The EGS Guidelines: from diagnosis to medical management

TRAVERSO C
Savona, Italy,

Abstract not provided

• 2122

The EGS Guidelines: a surgical approach to glaucoma

HOMMER A
Private Office, Vienna, Austria

Also the first step in treating glaucoma is medical therapy in most cases there are patients where lasertrabeculoplasty is the appropriate initial treatment. In addition there are patients, where the target pressure could not be reached and/or the disease is progressing despite maximum medical therapy. In consequence of the risk for the visual function incisional surgery is the next therapeutic step. In the presentation EGS recommendations and flow charts for the different glaucoma surgeries will be presented and discussed.

Commercial interest

• 2123

The link with the EBO: the glaucoma subspecialty diploma

SUNARIC MEGEVAND G
Memorial Rothschild Foundation, Centre Ophtalmologique de Florissant, Geneva, Switzerland

The EBO has gained worldwide respect for its efforts on harmonizing education and training in general ophthalmology within Europe. The comprehensive EBO Diploma examination, awards successful candidates the title of the Fellow of the European Board of Ophthalmology (FEBO), and is the most evident result of such efforts. More recently the EBO has established a Subspecialty European Board of Ophthalmology Diploma Examination (FEBOS) with the goal to increase standards of knowledge and care in various subspecialties. The first of these subspecialty examinations to be introduced is in the field of glaucoma and is developed in close collaboration with the European Glaucoma Society (EGS). The FEBOS-Glaucoma examination and diploma represent a logical continuation of the efforts in providing sustainable education and glaucoma care within Europe led by the EGS.
The goals, the organisation and requirements to sit the subspecialty exam as well as the first experience with the FEBO-Glaucoma exam and Diploma will be presented.

• 2124

Discovering the treasures of the EGS website: from educational opportunities to newsletter

STALMANS I
UZ St. Rafael, Leuven, Belgium

The European Glaucoma Society stands for Innovation, Education and Communication. The EGS website www.eugs.org content reflects these goals. The fourth edition of the EGS Guidelines is now downloadable free of charge. The Tip of the Month and Journal club contain clinical tips and tricks and relevant highlights from the literature which are monthly updated. The congress calendar gives information on upcoming meetings. And the EGS also promotes education by supporting travel grants and fellowship programs. These are only a few examples to illustratie that the website is a rich source of useful clinical and practical information. During this lecture, a virtual tour through the website will be provided.

• 2125

Future and perspectives

TUULONEN A
Tampere, Finland

The primary mission of the European Glaucoma Society (EGS) is to promote well being of glaucoma patients, i.e. to develop and

constantly improve sustainable glaucoma care in Europe by identifying and applying the best methods on a country wise basis to

deliver good quality care at a sustainable cost.

1. Current Map: Where are we now?
   What are the most important challenges in every-day practice

2. Where Do We Want to Go: Outcome and Quality of Care with Relation to Patients' Well Being
   What are the outcomes we should identify and agree
   How to formally assess the quality of outcomes

3. Road map for improved care: How are we going to get there?
   Good practices and policies
   Practical tools to improve care

4. The role of the EGS Committees as 'Enablers' – How to Pave the Way to Better Care?
   Innovation, Education, Communication
   Implementation
5. Next steps
   How to develop, lead and measure a sustainable glaucoma unit
   How to measure well-being of glaucoma patients

• 2131

New development in clinical ultrasound

SCHMETTERER L
Medical University of Vienna, Clinical Pharmacology, Vienna, Austria

Since more than 40 years ultrasound is used as a clinical tool in diagnostics. In the early years mainly used in cardiology it has now become standard in many fields including ophthalmology. In the eye the technique has been used to visualize all tissues and to quantify blood velocities in retrobulbar vessels. In the recent years the technique saw many innovations that have so far only partially transferred to the eye: Four-dimensional scanners yield three-dimensional volumetric images. In addition, new approaches came up allowing for quantitative measurement of tissue biomechanical properties. Transversal resolution has been improved using high-frequency imaging. Finally therapeutic applications include drug delivery that may also be applicable to the eye.

• 2132

Ultrasound biomicroscopy in diagnosis of anterior segment pathology

RAMAZANOVA K , Kiseleva T , Lugovkina K
Moscow Helmholtz Research Institute of Eye Diseases, Ophthalmic Ultrasound Department, Moscow, Russia

PURPOSE: To demonstrate the role of ultrasound biomicroscopy (UBM) for the diagnosis of anterior segment pathology.
METHODS: UBM was performed in 7 patients with corneal opacity (6 eyes) and with anterior chamber (AC) opacity (1 eye).
RESULTS: In first case with total hyphema UBM demonstrated thickening of the iris. Second case with post-contusional corneal edema and hyphema demonstrated signs of iridodialysis and cyclodialysis. Third patient with central corneal scar had a signs of intraocular epithelial proliferation. With UBM the epibulbar cyst extension into anterior chamber was confirmed in fourth clinical case. In patient with fungal corneal ulcer (fifth case) UBM demonstrated central corneal defect and anterior chamber opacities.Lipodermoid was found in sixth clinical case. UBM helped to confirm that the sclera was not involved. In seventh case with corneal nebula after ocular burns UBM demonstrated iridocorneal adhesion and retrocorneal fibrous membrane. UBM results in all clinical cases determined tactics of treatment.
CONCLUSIONS: UBM is a safe and effective diagnostic tool in the management of eyes with disorders of the anterior segment especially when visualisation is limited and multiple traumatic injures are involved.

• 2133

Ultrasonography in the management of orbital diseases

GUTHOFF R F
Institut für Biomedizinische Technik, Rostock, Germany

Based on a 30 year experience in ophthalmic ultrasound a flowchart is presented dealing with orbital anatomical structures, their recognition and their possible pathological changes mainly based on B-scan technology.
The following entities are of importance:

1. pseudo exophthalmus
2. myogenic exophthalmus
3. vascular-exophthalmus
4. infiltrating legions
5. expanding legions
6. optic nerve legions
7. legions from surrounding structures (bones, sinusis).

This system helps to decide which diagnostic or therapeutic steps should follow in order to support a decision orientated straight forward patient management.

• 2134

Ultrasound methods in the assessment of ocular blood flow

KISSELEVA T *(1), Ramazanova K (1), Gavrilenko A (2), Kuklin A (2), Adzhemyan N (1), Chudin A (1)*
(1) the Helmholtz Research Institute of Eye Diseases, Ultrasound Department, Moscow, Russia
(2) Russian Research Center of Surgery, Department of Vascular Surgery, Moscow, Russia

Purpose: to investigate ocular blood flow in vascular diseases (VD) with use of ultrasonic Doppler Methods **Methods**: 610 patients suffered from ischemic optic neuropathy (ION)-180;the retinal vein occlusion (RVO) -110; diabetic retinopathy (DR)-80;age-related macular degeneration(AMD)- 240 patients were observed. Color Doppler Imaging(CDI) and Power Doppler (PD), 3D-mode were used to estimate blood-flow of the ophthalmic artery (OA), the central retinal artery (CRA), the posterior cilliary arteries (PCA).The Doppler spectrum of blood flow and its main indices including the peak systolic velocity (PSV),end-diastolic velocity (EDV) and resistance index (RI) were measured. **Results**: Signs of disordered blood flow in the CRA were detected in RVO:diastolic flow was absent or markedly reduced, decreased PSV and an increase RI in comparison with the norm. CDI showed reduced flow velocities in PCA in patients with ION. The decrease of flow velocities in the OA, the CRA and the PCA in patients with dry AMD and significant increase of RI in the PCA in wet AMD were registered. Decreased PSV and EDV in the CRA and the PCA were determined in patients with DR. **Conclusion:** CDI, PD and 3D-mode are valuable methods for the clinical management of VD.

• 2141

Monocarboxylate transporters and their functions in the retina

OSBORNE N
Oxford University, Oxford, United Kingdom

Monocarboxylate transporters (MCTs) have important functions in healthy tissues, being involved in the transmembrane transport of lactate and other monocarboxylic acids. MCTs are a family of transporters which is presently composed by 14 members, but only MCT1 to 4 have been biochemically characterized. MCTs are located in the cornea, iris and ciliary body as well as the retina and pigment epithelium (RPE)/choroid. MCT1 is localized particularly to the apical and MCT3 to the basal membrane of the RPE. MCT1 is located to photoreceptor inner segments, Müller cells, retinal capillaries, and the two plexiform layers. In contrast MCT2 labelling is concentrated in the inner and outer plexiform layers with MCT4 being associated only in the inner nuclear retina and the plexiform layers.
In an attempt to understand the role of pyruvate/lactate transport in the retina the influence of a specific MCT inhibitor (4-cyano-4-hydroxycinnamate or 4-CIN) was tested on ischemia/reperfusion in the rat. No evidence was found to support the view that blockade of lactate/pyruvate entry into mitochondria for oxidative metabolism has an influence on the outcome of retinal ischemia/ reperfusion.

• 2142

Doppler Optical Coherence Tomography - A New Method For The Assessment Of Neurovascular Coupling In The Retina

WERKMEISTER R , Aschinger G , Schmetterer L
Medical University of Vienna, Center for Medical Physics and Biomedical Engineering, Vienna, Austria

In recent years, we have shown that a dual-beam bidirectional Doppler OCT system allows to measure total blood flow in the ocular fundus and can also be used to detect changes in this flow values due to various stimuli.
Neurovascular coupling (NC) refers to a phenomenon where local blood flow is elevated with increased neuronal activity. NC may be essential to deliver increased amounts of oxygen, glucose and other nutrients to neurons when they are active. As such a breakdown in NC may contribute to cell death in neurodegenerative diseases.
OCT - due to its high resolution - is superior to other methods used to measure physiological parameters in the human body. In a recent study, we measured total retinal blood flow in the human eye and assessed flow changes due to a stimulus with diffuse luminance flicker. We measured an increase of about 40%, which is assumed to occur as a consequence of an increased firing rate of retinal ganglion cells.
Our results show that dual-beam bidirectional DOCT may serve as a powerful tool to study changes in ocular blood flow due to changes in neuronal activity and, thus may contribute to the investigation of neurodegenerative diseases and the development of neuroprotective strategies.

• 2143

Neuro-vascular coupling – molecular mechansims and potential clinical applications

GARHOFER G
Medical University of Vienna, Vienna, Austria

The coupling between neural activity, metabolism and blood flow is an essential physiological mechanism to assure constant supply of the tissue with oxygen and nutrients. Further, it has been shown that several ocular diseases, such as glaucoma or diabetic retinopathy are accompanied by a breakdown of this physiological mechanism. Despite many efforts, the signaling pathways that trigger the hyperemic response of the vasculature are still incompletely understood, which makes the significance of changes in the response during disease difficult to interpret. Recent experimental data from animal studies challenges the current view that NO is the key mediator of flicker induced vasodilatation and indicates a more complex interaction between neurons, blood vessels, vasodilating and vasoconstricting factors at the level of the retina.
This talk aims to summarize our current understanding of the mechanisms underlying neuro-vascular coupling in the human retina. Further, the role of neuro-vascular coupling and its potential application in the diagnosis and follow up in neuro-degenerative diseases such as glaucoma will be discussed.

• 2144

Candidate Retinal Biomarkers in CNS Neurodegenerative Disease

HUDSON C
School of Optometry, University of Waterloo, Waterloo, Canada

To institute early prevention of the common CNS neurodegenerative diseases, including Alzheimer's Disease (AD), Parkinson's Disease (PD),Lewy Body Disease and Vascular Cognitive Disorders, cost-effective, non-invasive early diagnostic biomarkers are essential. Early detection of these diseases is critical given the growing evidence that new therapies will only be effective in pre-symptomatic or prodromal stages of the degenerative process. Retinal imaging by spectral domain optical coherence tomography is currently used to evaluate morphological neurodegenerative changes caused by ophthalmic disease. Evidence suggests that this technique may also provide a biomarker in AD and PD, revealing changes in the retinal nerve fibre layer that correlate with cortical thinning and possibly prior to emergence of clinical symptoms. This presentation will up-date the evidence supporting the use of non-invasive retinal imaging as a pre-symptomatic prognostic biomarker of CNS neurodegenerative disease.

• 2151

Behçet's uveitis in Japan: evaluation of the long-term efficacy and safety of infliximab treatment

TAKEUCHI M
National Defense Medical College, Saitama, Japan

Retrospective 13 multicenter observational study. were performed using a questionnaire of 164 Behçet's patients treated with infliximab for more than 1 year were studied in Japan. The mean age at initiation of infliximab treatment was 42 years, and the mean treatment duration was 33 months. The frequency of ocular attacks significantly decreased significantly after infliximab treatment,, and best collected visual acuityand was improved in approximately 55% of the eyes after treatment in all groups. However, The mean uveitis relapsed in 59% of all patients after infliximab treatment, and approximately 80% of relapses occurred within a year after the initiation of infliximab treatment. Ninety % of them were controlled by increasing doses of topical corticosteroids and shortening the interval of infliximab infusion. Adverse effects were observed in 35%. Infliximab treatment was continued in 85% of the patients, but 15% of the patients discontinued infliximab treatment because of adverse effects or insufficient efficacy. Infliximab was effective and safereduced the frequency of ocular attacks and improved visual acuity in patients with Behçet-related uveitis, and was generally well tolerated with few serious adverse events.

• 2152

Behçet's uveitis in Turkey, why is it still number one?

TUGAL-TUTKUN I
Istanbul University Istanbul Faculty of Medicine, Istanbul, Turkey

Pathogenetic mechanisms underlying Behçet's disease include complex interactions between genetic factors, environmental factors, and immunological aberrations. The strong association of Behçet's disease with the HLA-B51 antigen has been known for more than 3 decades. Recent genome-wide association studies have also shown several shared genetic factors throughout the old Silk Route. In contrast to the recent trend for lower disease prevalence and milder disease forms in Japan, Behçet's disease still accounts for around 25% of uveitis cases in Turkey. This suggests the strong role of environmental factors in disease onset and phenotype. Infections are suspected in the initial triggering of the disease as well as in relapses of its manifestations. It is thought that an aberrant immune response may be generated to different microorganisms recognized by pattern receptors in genetically susceptible individuals. An impaired microbial clearance and exuberant innate and adaptive immune responses to microbial products may have a major contribution to the pathogenesis. Better socioeconomic status with improved living conditions and personal hygiene in the Turkish population will hopefully lead to a lower disease prevalence and severity.

• 2153

Choroidal thickness in acute and convalescent VKH disease

TAKASE H
Department of Ophthalmology & Visual Science, Tokyo Medical and Dental University (TMDU), Tokyo, Japan

Vogt-Koyanagi-Harada (VKH) disease is a systemic autoimmune disorder against melanocytes, and is one of the leading causes of uveitis in many countries including Japan. The distribution of the melanocytes in the systemic organ such as eyes, internal ears, meninges, or skin, leads to the various symptoms or signs of VKH disease. Because melanocytes are abundantly present in the choroid, the primary site of the intraocular inflammation of VKH disease is the choroid. Therefore, to monitor the disease activity of VKH disease, indocyanine green angiography (ICGA) had long been the most useful tool. Recently, advances in optical coherence tomography (OCT) made it possible to visualize the cross section of the choroid in addition to the retina, and the findings in choroidal OCT are found to complement those in ICGA. In this presentation, the features of the choroidal changes by ICGA and OCT in VKH disease are discussed.

• 2154

Stromal choroiditis in East (VKH) and West (birdshot)

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

Background and aim: Both Vogt-Koyanagi-Harada (VKH) disease and birdshot retinochoroiditis (BRC) are primary stromal choroiditis entities, meaning that the initial inflammatory process necessarily starts in the choroidal stroma. The aim here was to point out similarities and differences between these two stromal choroiditis entities and to show that early treatment is able to modify the phenotypes of both conditions. Patients and methods: Two groups of patients respectively of VKH and BRC cases were analyzed and followed clinically and angiographically using dual fluorescein (FA) and indocyanine green (ICGA) angiography.Results: 13 of 28 BRC patients and 11 of 24 VKH patients had enough follow-up data to be included in the study. Early diagnosis and treatment in both VKH (9/11) and BRC (6/13), allowed to avoid sunset glow fundus in the former and BRC fundus lesions in the latter. The main similarities and differenced will be pointed out. Conclusion: VKH and BRC differ substantially from each other. However choroidal stromal inflammation is characterized by a similar process and responds equally to therapy.

• 2155

Relationship of ocular disease activities before and after starting infliximab using Behçet's disease ocular attack score 24

KABURAKI T (1), Okinaga K (1), Takamoto M (1), Ohtomo K (1), Yoshida A (2), Kawashima H (2), Komae K (1), Fujino Y (3)
(1) Department of Ophthalmology, The University of Tokyo Hospital, Tokyo, Japan
(2) Department of Ophthalmology, Jichi Medical University, Tochigi, Japan
(3) Department of Ophthalmology, Japan Community Health care Organisation, Tokyo Shinjku Medical Center

Purpose: To investigate the relationship of ocular disease activities before and after starting infliximab using Behçet's disease ocular attack score 24 (BOS24). Patients and Methods: We studied 69 eyes of 35 patients with ocular Behçet's disease (BD) who had started infliximab therapy. Total BOS24 scores during 1-year period (BOS24-1Y) before and after starting infliximab therapy were calculated and its correlation was examined. Patients were divided into three group according to the BOS24-1Y before starting infliximab; H group (BOS24-1Y of 40 points or more, n=14), M group (20 to 39 points, n=12) and L group (19 points or less, n=9). Ocular disease activities after starting infliximab were compared among three groups. Results: Significant correlation was observed between BOS24-1Y scores before and after starting infliximab (P<0.0001). BOS24-1Y after starting infliximab in H, M and L group were 20.9±28.3, 7.3±15.2, 0.6±1.9 points, respectively (p<0.05). After starting infliximab, ocular attacks were disappeared in 8 cases (89%) in L group, whereas severe ocular attacks still occurred in 7 cases (50%) in H group. Conclusions: BOS24-1Y before starting infliximab could be a predictor for disease activity after starting infliximab.

• 2156

The CD4/CD8 ratio in vitreous fluids is of high diagnostic value in sarcoisosis

MARUYHAMA K
Tohoku Univeristy Graduate School of Medicine, Ophthalmology, Sendai, Japan

Sarcoidosis is an idiopathic inflammatory disorder involving multiple organs, and ocular manifestation is one of the common features. A well-known immunological feature in sarcoidosis is an increased CD4+ helper T cell type 1 lymphocyte subset in BALF. In this study, we investigated the vitreous lymphocyte subsets of sarcoidosis to elucidate the immunological features of this disorder in the eye. Our study enrolled 86 sarcoidosis patients. Diagnoses included 53 eyes with definitive sarcoidosis (D-S) of 41 patients, 60 eyes with suspected sarcoidosis (S-S) of 45 patients. Vitreous samples from the uveitis patients were analyzed with flow cytometry. Our result presented that the CD4/CD8 ratio was high in the D-S/S-S in the vitreous samples. Moreover, a high CD4+ population indicated sarcoidosis uveitis. Therefore, diagnostic vitrectomy using flow cytometric analysis may be a useful adjunct for the diagnosis of sarcoidosis, particularly in complex cases.

• 2157

Viral retinopathies: a spectrum of disease from East to West

BODAGHI B
Hopital Pitie-Salpetrière, Ophtalmologie, Paris, France

Viral retinopathies remain an absolute emergency among all other infectious entities. They may occur in immunocompromised or immunocompetent patients at any age. Most of the cases are associated with herpes viruses and happen to be necrotizing. Acute retinal necrosis has been initially described in Japan with important clinical characteristics. Molecular tools are of utmost importance in order to confirm the viral type. VZV seems more aggressive than HSV1 or 2. CMV retinitis occurs more frequently in immunocompromised patients. More recently, the nonnecrotizing type of viral retinopathy has been reported, masquerading as different autoimmune entities. Furthermore, other types of nonherpetic viral retinitis may be encountered in different geographical areas. Treatment is always challenging. Despite a few reports on the use of oral antivirals, most of the patients require intravenous therapy and intravitreal injections. Treatment is always long in order to prevent a relapse, especially in the second eye. Laser photocoagulation has not demonstrated its efficacy but may be proposed in selected cases. Primary vitrectomy should not be proposed in all patients as it may increase the risk of retinal detachment. Visual prognosis is guarded

• 2161

Myopia-associated changes of the optic disc

OHNO-MATSUI K
Ophthalmology and Visual Science, Tokyo Medical and Dental University, Yushima

Abstract not provided

• 2162

Optic nerve hypoplasia: Evaluation and genetic considerations

YU-WAI-MAN P (1,2)
(1) *Institute of Genetic Medicine Newcastle University, Wellcome Trust Centre for Mitochondrial Research, Newcastle upon Tyne, United Kingdom*
(2) *Moorfields Eye Hospital, Neuro-Ophthalmology and Genetics, London, United Kingdom*

The minimum prevalence of optic nerve hypoplasia has been estimated at 1 in 10,000 and unlike other causes of childhood blindness, the incidence of this congenital disorder is still increasing in the developed world. From a practical point of view, children with optic nerve hypoplasia need to be properly evaluated given the strong association with a number of developmental brain abnormalities and potentially life-threatening neuroendocrine dysfunction. This presentation will also review the complex aetiology and emerging genetic basis for this important cause of visual impairment in young children.

• 2163

Optic disc tumors

BOSCHI A
Cliniques Universitaires St. Luc, Ophtalmologie, Bruxelles, Belgium

The optic disc can be involved by a variety of primary and secondary tumors. Primary tumors include capillary and cavernous hemangiomas, astrocytomas, and melanocytomas. Secondary optic disc tumors like leukemia, metastatic carcinoma, and from adjacent structures (choroidal melanoma, retinoblastoma, meningioma) may also invade the nerve head. Clinical features are varied, differential diagnosis and actualised management will be discussed.

• 2164

Using OCT to evaluate the funny looking disc

BORRUAT F X
Hopital Ophtalmique Jules Gonin, Neuro-Ophthalmology, Lausanne, Switzerland

Optic nerve appearance (optic disc swelling, atrophy, excavation) can be sometimes challenging, even to the experienced ophthalmologist. Namely, it may be difficult to distinguish early papilledema from pseudopapilledema. OCT can reveal abnormalities which can frequently help to establish the correct diagnosis and organize the proper investigations, if necessary. At the end of the session, the participants should be able to identify the OCT features suggestive of either true papilledema or pseudopapilledema/ optic disc drusen.

• 2171

Human pluripotent stem cells as a source of corneal epithelium

SKOTTMAN H
University of Tampere, BioMediTech, Tampere, Finland

In healthy cornea, epithelium is renewed by limbal stem cells (LSCs) and LSCs transplantation has been used to treat limbal stem cell deficiency (LSCD). However, this is only possible if enough healthy limbal tissue is available. Thus, novel cell sources are needed. Human pluripotent stem cells (hPSC) including embryonic stem cells (hESC) and induced pluripotent stem cells (hiPSCs) provide unique opportunities for differentiation of limbal and corneal epithelial cells.
We have previously developed an efficient method for differentiating hPSC towards corneal epithelial progenitor cells capable of terminal differentiation towards mature corneal epithelial-like cells. With the protocol protein expression of the corneal epithelial progenitor marker ΔNp63 was greatly enhanced, with up to 95% of cells being ΔNp63-positive. Finally, after a total of six weeks in differentiation culture, the two markers specific to differentiated corneal epithelium, cytokeratins 3 and 12, were expressed in an average of 35% and 71% of cells, respectively. In recent studies we have continued the molecular and functional characterization of these cells providing more support that those could potentially be used for treating LSCD in the future.

• 2172

Genetic modification possibilities in treating corneal diseases

MOORE T (1), Courtney D (1), Atkinson S (1), Maurizi E (1), Allen E (2), McLean I (2), Leslie Pedrioli D (2), Moore J (1), Nesbit A (1)
(1) University of Ulster, Biomedical Sciences Research Institute, Coleraine, United Kingdom
(2) University of Dundee, Division of Molecular Medicine, Dundee, United Kingdom

Treatment of genetic eye disease poses significant medical and surgical challenges. Two gene based therapies were assessed using an in-vivo firefly luciferase bioluminescence mouse model to target corneal epithelium. Short interfering RNA (siRNA) targeting selectively only the mutant allele was assessed for efficacy, through its ability to downregulate corneal epithelial luminescence ***in vivo*** using live animal imaging. This innovative animal model provides clear advantages enabling assessment of topical, subconjunctival and intrastromal delivery. Potent and sustained ***in vivo*** gene silencing >50% for up to 7 days was observed after intrastromal injection of siRNA and various topical formulations are further being assessed. siRNA therapy provides transient effect, however, Type II Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/CRISPR-associated nuclease 9 (Cas9) holds great promise to provide 'one off' permanent gene editing. Gene-specific cleavage of the mutant allele was detected through this method. DNA repair resulted in frameshift mutations predicted to result in mutant allele knockout. This offers exciting potential for translation into clinical treatment of corneal genetic diseases.

• 2173

Novel techniques in corneal regeneration and bioscaffold engineering

LAGALI N (1), Rafat M (2,3), Xeroudaki M (1), Koulikovska M (1), Fagerholm P (1)
(1) Linköping University, Department of Ophthalmology, Linköping, Sweden
(2) Linköping University, Department of Biomedical Engineering, Linköping, Sweden
(3) LinkoCare Life Sciences AB, LinkoCare, Linköping, Sweden

Restoration of corneal transparency and a functioning epithelium and stroma may involve multiple procedures that are limited by availability of donor tissue and an inability of host tissue to self-regenerate. We present a tissue-engineered collagen-based hydrogel bioscaffolds for regenerating a transparent stroma and providing the additional possibility of carrying and delivering corneal stem cells to the stroma or epithelium. We present in vitro results of bioscaffold compatibility with epithelial and stem cells, and techniques for the optimal implantation of scaffolds using femtosecond laser surgery. Using models of in vivo bioscaffold implantation in the rabbit, we evaluate transparency, stability, and controlled degradation characteristics of the scaffolds. Tissue engineering provides the opportunity to tune the size, thickness, transparency, homogeneity and degradation rate for specific applications. For example, the bioscaffold may be used to substantially thicken the stroma or allow non-invasive in vivo tracking of its controlled degradation as it releases therapeutic cells. In vitro and in vivo results with bioscaffolds are presented that provide the basis for further preclinical and clinical development.

Commercial interest

• 2174

Clinical results and in vitro characterization of cornea limbal epithelial stem cells cultured in autologous serum

MOE M
Oslo University Hospital, Department of Ophthalmology, OSLO, Norway

Slow-cycling limbal epithelial stem cells (LESCs) are responsible for continuously renewing the entire corneal epithelium. Ocular burns, infectious and inflammatory diseases can all cause chronic scaring, decreased vision and severe pain due to limbal stem cell deficiency (LSCD) in the cornea. Center for Eye Research / Department of Ophthalmology, Oslo University Hospital is offering transplantation of autologous ***ex vivo*** expanded human corneal epithelial tissue to patients with LSCD. However, even though many of these patients gain significant life quality by means of increased vision and reduced pain by this treatment, in our recent published retrospective case series evaluating our surgical technique, only 56 % of the patients had a persisting improvement in subjective symptoms/objective findings. Further clinical experience will reveal in which clinical situations this treatment modality is most likely to succeed – and fail. In parallel, we aim to develop a novel, improved protocol for enrichment of viable LESCs for clinical transplantation to further improve success rate of the treatment. Clinical results as well as results of translational research for improving graft quality will be presented.

• 2175

Long-term cultivation of corneal stem cells - possible applications from benchside to bedside

PETROVSKI G

Department of Ophthalmology, University of Szeged, Szeged, Hungary

Long-term cultures of corneal stem cells can be developed for future tissue engineering and clinical applications. Cornea limbal and stromal tissue explants can be cultivated and expanded for longer periods of time (months) under special conditions and without the use of scaffolds. Viable 3D cell outgrowth from the explants can be achieved within 4 weeks time. The outgrowing limbal epithelial stem cells (LESCs) revealed a unique fingerprint of markers specific for stemness, proliferation, limbal epithelial cells and differentiated cornea epithelial cells. Morphological and immunostaining analysis concluded that long-term culturing can form stratified 3D tissue layers with a clear extracellular matrix deposition and organization of collagen, which was similar to that formed by corneal stromal stem cells (CSSCs). Overall, modelling 3D long-term structures of corneal stem cells can be used for generating highly pluripotent, long-standing 3D cultures from limbal and stromal stem cells, which can be used for further research purposes and clinical transplantation.

• 2211

Intravitreal Aflibercept (IVT-AFL) for Diabetic Macular Edema (DME): 3 Year Data from VIVID-DME and VISTA-DME

STAURENGHI G (1), Metzig C (2)
(1) University Eye Clinic, Department of Biomedical and Clinical Science "Luigi Sacco", Milan, Italy
(2) Bayer Healthcare, Global Medical Affairs, Berlin, Germany

Purpose To evaluate long-term outcomes with IVT-AFL injection in the treatment of DME.
Methods 406 patients (VIVID-DME) and 466 patients (VISTA-DME) were randomized to IVT-AFL 2mg every 4 weeks + sham laser (2q4), IVT-AFL 2mg every 8 weeks (after 5 initial monthly doses) + sham laser (2q8), or laser + sham injections. From week (W)100 to W148, laser patients could receive IVT-AFL if retreatment criteria were met. Primary efficacy endpoint was the mean change from baseline (BL) in best corrected visual acuity (BCVA) at W52. Outcomes at W100 and W148 are described.
Results At W100, mean BCVA gains from BL in the IVT-AFL 2q4, 2q8 and laser groups were +11.4, +9.4 and +0.7 letters (VIVID-DME; P<0.0001), and +11.5, +11.1 and +0.9 letters (VISTA-DME; P<0.0001). In VISTA-DME, improvements in BCVA were maintained to W148 in the IVT-AFL 2q4 (+10.4 letters) and 2q8 (+10.5 letters) groups. Cataract was the most frequent ocular serious AE in both studies through 100 weeks (VIVID-DME: 2.2%; VISTA-DME: 1.3%); incidence of Antiplatelet Trialists' Collaboration-defined arterial thromboembolic events with IVT-AFL was similar across the studies (VIVID-DME: 4.8%; VISTA-DME: 7.8%). Safety outcomes at W148 in VISTA-DME were consistent with W100 data with no new safety signals observed. The third year of VIVID-DME is ongoing.
Conclusions In both studies, IVT-AFL demonstrated superior outcomes compared with laser through W100, with similar efficacy in the 2q4 and 2q8 groups. In VISTA-DME, BCVA gains from BL with both IVT-AFL regimens were sustained through W148. Through 100 weeks the incidence of AEs was consistent with the known safety profile of IVT-AFL.

Commercial interest

• 2212

Impact of Intravitreal Aflibercept (IVT-AFL) on Diabetic Retinopathy in the VIVID-DME and VISTA-DME Studies

LARSEN L M (1), Metzig C (2)
(1) Glostrup Hospital, Department of Ophthalmology, Glostrup, Denmark
(2) Bayer Healthcare, Global Medical Affairs, Berlin, Germany

Purpose Post-hoc analysis to assess changes in the diabetic retinopathy severity scale (DRSS) score and the development of proliferative diabetic retinopathy (PDR) in VIVID-DME and VISTA-DME.
Methods Patients (pts) were randomized to IVT-AFL 2mg every 4 weeks + sham laser (2q4), IVT-AFL 2mg every 8 weeks (after 5 initial monthly doses) + sham laser (2q8), or laser + sham injections. Primary efficacy endpoint was mean change from baseline (BL) in visual acuity at week (W)52; the proportion of pts with a ≥2-step improvement from BL on the DRSS was a secondary endpoint at W100. Pts were considered to have developed PDR if BL DRSS score was <61 and there was ≥1 post-baseline DRSS score ≥61. Results are presented for pooled IVT-AFL 2q4 and 2q8 treatment arms.
Results The proportion of pts receiving IVT-AFL vs. laser with a ≥2-step improvement in DRSS at W100 was 31.0% vs. 8.2% (VIVID-DME) and 37.0% vs. 15.6% (VISTA-DME). The proportion of pts receiving IVT-AFL vs. laser who developed PDR through W100 was 1.8% vs. 5.3% (VIVID-DME) and 2.6% vs. 12.3% (VISTA-DME); when data were integrated across the two trials, the respective proportions were 2.4% vs. 9.4% (nominal P≤0.0001). The most common ocular serious AE in IVT-AFL-treated pts was cataract (VIVID-DME, 2.2%, VISTA-DME, 1.3%).
Conclusions A greater proportion of pts treated with IVT-AFL experienced ≥2−step improvements in DRSS scores at W100 compared with laser-treated pts. A smaller proportion of IVT-AFL-treated pts in both studies developed PDR compared with laser. These findings demonstrate the beneficial impact of IVT-AFL not only on DME, but also on the underlying diabetic retinopathy.

Commercial interest

• 2213

Evaluation of the Variation in Thickness of the Different Retinal Layers in Diabetic Patients with OCT

VICENTE A (1), Cardigos J (1), Lívio C (1), Proença R (1), Santos A (1), Cunha J P (1), Abegão Pinto L (2), Ferreira J (1)
(1) Centro Hospitalar Lisboa Central, Ophthalmology, Lisbon, Portugal
(2) Faculdade de Medicina- Universidade de Lisboa, Pharmacology & Ophthalmology, Lisbon, Portugal

Purpose To present a comparison of the thickness variation of the different retinal layers in diabetic patients without diabetic retinopathy.
Methods A prospective observational study was performed. 175 eyes of 175 patients: 125 diabetic patients without diabetic retinopathy and 50 subjects without diabetes (age and gender matched) from the ophthalmology outpatient clinic were included. Optical Coherence Tomography (OCT SPECTRALIS®) was performed with high-resolution macular scans. Automated retinal layer segmentation was performed using validated software and layers thicknesses were determined. The coefficient of variation of the different layers was calculated. A p value <0.05 was considered statistically significant.
Results Diabetic patients were in average 66.9±9.3 years old. There weren't significant differences in the coefficients of variation between diabetic and non-diabetic patients: total retinal thickness (9.3% vs. 9.3%; p=0.39), RNFL (41.09% vs. 42.25%; p=0.33), GCL (30.39% vs. 31.13%; p=0.20), IPL (23.62% vs. 24.13; p=0.40), ILN (21.26% vs. 19.86; p=0.44).
Conclusions Previous studies have demonstrated that choroidal thickness coefficient of variation is lower in diabetic patients. Nevertheless, in retinal layers no difference was found in diabetic patients without macular edema. There is a combination of choroid with diminished thickness coefficient of variation and retinal layers with normal thickness coefficient of variation. This suggests that vascular choroidal pathology precedes retinal layers dysfunction. Exudation and lipid accumulation associated with microvascular retinal dysfunction and changes in axonal homeostasis only appear at a second step. This study emphasizes the importance of the retinal layer thickness measurement with OCT in the evaluation of diabetic patients.

• 2214

Choroidal Thickness in Diabetic Patients without Diabetic Retinopathy

FERREIRA J (1), Vicente A (1), Proença R (1), Dias-Santos A (1), Santos B (2), Cunha J P (1), Abegão Pinto L (3)
(1) Centro Hospitalar Lisboa Central, Ophthalmology, Lisbon, Portugal
(2) Associação Médica Olhar bem, Statistics, Lisbon, Portugal
(3) Faculdade Medicina Universidade Lisboa, Pharmacology & Ophthalmology, Lisbon, Portugal

Purpose To evaluate choroidal thickness (CT) in diabetic patients without diabetic retinopathy (DR) using enhanced depth imaging spectral-domain optical coherence tomography (EDI SD-OCT). To correlate CT with disease duration, systemic blood pressure (BP), glycemia, intraocular pressure (IOP) and ocular pulse amplitude (OPA).
Methods Prospective, observational case-control study. A complete ophthalmological examination was performed (visual acuity, refraction, Goldmann applanation and dynamic contour tonometries, fundoscopy and axial length). CT was assessed by a non-invasive procedure using an EDI-OCT (Spectralis Heidelberg) at 13 locations (subfoveal and 3 measurements 500µm apart in all 4 directions - nasal, temporal, superior and inferior).
Results 180 patients were recruited: 130 diabetic patients with no DR and 50 healthy controls; one eye per patient included in the study. CT at 1500µm above the fovea was significantly thicker in the diabetic group (239.9±56µm vs 268.2±67.7µm, p=0.001). None of the other topographic region comparisons were statistically different (p>0.05). In diabetic patients CT was not correlated with disease duration, BP, glycemia or IOP. CT was positively correlated with OPA in 12 points in diabetic patients (r between 0.19 and 0.27, p<0.05) but not in the control group. CT variation coefficients in the diabetic group were statistically lower than in the control group (p<0.01).
Conclusions The thickening of the choroid at 1500µm superior of the fovea in diabetic patients without DR may correspond to the diabetic choroidopathy in mid-periphery presented before DR. Moreover, this tissue may be functionally different, as the pattern of correlations seems to differ between groups. Further studies are needed to explore these differences and the potential of the CT in the clinical setting.

• 2215

Choroidal Thickness and Systemic Examination in Diabetic Patients without Diabetic Retinopathy

CARDIGOS J (1), Vicente A (1), Costa L (1), Crisóstomo S (1), Marques N (1), Cunha J P (1), Pinto L A (2), Ferreira J (1)
(1) Centro Hospitalar de Lisboa Central, Ophthalmology, Lisbon, Portugal
(2) Faculdade de Medicina da Universidade de Lisboa, Pharmacology and Ophthalmology, Lisbon, Portugal

Purpose The choroidal circulation receives nearly 95% of ocular blood flow and it is essential for a normal retinal structure and function. Recently, several clinical studies showed a variation in choroidal thickness (CT) even before the presence of diabetic retinopathy (DR), which the meaning remains uncertain and questionable. Our objective was to analyze and correlate the CT with the disease duration, systemic blood pressure (SBP) and analytic evaluation.
Methods Prospective, observational case-control study. A complete ophthalmological examination was performed, including dynamic contour tonometry and axial length. CT was assessed by a non-invasive procedure using an OCT (Spectralis Heidelberg Engineering) with an enhanced depth mode (EDI) at 13 different locations (subfoveal and 3 measurements 500 µm apart in all 4 directions - nasal, temporal, superior and inferior). The SBP was measured and an analytical evaluation was performed, including glycemia, glycosylated hemoglobin - HbA1c, lipid parameters, renal function, ionogram and microalbuminuria. Correlation between variables was explored using Spearman correlations.
Results The study included 65 diabetic patients without DR (36 females; mean age 67.23 ± 9.08 years), with an average disease duration of 90.42 ± 81.82 months. The CT didn´t showed a correlation with disease duration, SBP, glycemia, HbA1c, renal function, lipid parameters, homocysteinemia, natremia or microalbuminuria. However, the CT was positively correlated with potassium and chlorine serum levels in 5 points, with statistic significance (r between 0.26 and 0.31, $p < 0.05$).
Conclusions CT may be positively influenced by serum levels of potassium-chlorine in diabetic patients but not in healthy controls. These abnormal CT relationships can be detected even with no visible DR. Further studies are needed to explore these differences.

• 2216

Automatic method to distinguish manifestation areas of early diabetic retinopathy from image artefacts by using L*u*v* colour space

SUZUKI N (1), Yamane K (2)
(1) National Institute of Technology- Numazu College, Department of Mechanical Engineering, Numazu, Japan
(2) Hiroshima University, Ophthalmology and Visual Science, Hiroshima, Japan

Purpose The RGB colour space was converted into seven different colour spaces: XYZ, CMY, HSL, HSV, HSI, L*a*b* and L*u*v*. The L*u*v* colour space presented optimal results, with the highest sensitivity and best reproducibility. We employed three-dimensional analysis of L*u*v* colour spaces to detect early diabetic retinopathy.
Methods Six patients with small haemorrhages, hard exudates and photocoagulation marks were evaluated using fundus photography, which revealed image artefacts in the fundi of some patients. We constructed an experimental device similar to the optical system of a fundus camera, and created artificial eyes of the fundus, which were painted with four different colours. The image artefacts were photographed under each artificial eye using the experimental device. We analysed all images using Scilab 5.4.0 and SIVP 0.5.3 software. The software interpreted the values of the L*u*v* colour space as a three-dimensional graph, which was modified using a Gaussian filter.
Results We calculated the difference between the manifestation and perimanifestation areas and image artefact and periartefact areas using the L*u*v* values. The L*u*v* values' ratios of the image artefact to manifestation areas in the human eye were as follows: haemorrhage (6.2, 11.4, 7.4); hard exudate (3.2, 7.7, 2.5) and photocoagulation mark (8.1, 3.9, 6.2).
Conclusions L*u*v* colour space is an effective mean of differentiating between small haemorrhages, hard exudates and photocoagulation marks from image artefacts.

• 2217

Dexamethasone Reverses the Effects of High Glucose on Human Retinal Endothelial Cells In Vitro

STEWART E , Saker S , Amoaku W
University of Nottingham, Academic Ophthalmology, Nottingham, United Kingdom

Purpose Diabetic retinopathy is the leading cause of preventable blindness in the working population and its prevalence continues to increase as the worldwide prevalence of diabetes grows. The main cause of visual loss in diabetic eye disease is diabetic macular oedema caused by an increase in microvascular endothelial permeability. Endothelial cell permeability is influenced by multiple factors which have not been fully elucidated, particularly in human models. Inflammation has been reported in the pathogenesis of diabetic retinopathy and the potential use of anti-inflammatory agents such as the glucocorticoid dexamethasone is being extensively studied.
Methods The effect of high glucose (25 mM) and dexamethasone on retinal endothelial cell proliferation and permeability were assessed using Cell-8 proliferation reagent and passage of Evan's blue albumin, respectively. qPCR was used to quantify gene expression of selected tight junction molecules (Occludin, Claudin-5, JAM-A and JAM-C) and adheren junction (VE-Cadherin) molecules with high glucose and dexamethasone.
Results High glucose decreased endothelial cell proliferation and this effect was reversed by dexamethasone. High glucose conditions significantly increased endothelial cell permeability and this effect was decreased with dexamethasone treatment for 24 and 72 hours. In retinal endothelial cell exposed to high glucose claudin-5, occludin and JAM-A gene expression were reduced and that of JAM-C increased when evaluated with qPCR; dexamethasone was effective in partially reversing these changes.
Conclusions Dexamethasone reverses high glucose induced alterations in retinal endothelial cell behaviour.

Commercial interest

• 2218

Myofibroblasts in proliferative diabetic retinopathy can originate from infiltrating fibrocytes and through endothelial-to-mesenchymal transition (EndoMT)

ABU EL ASRAR A (1), De Hertogh G (2), Van den Eynde K (2), Alam K (3), Van Raemdonck K (4), Opdenakker G (4), Van Damme J (4), Geboes K (2), Struyf S (4)
(1) King Abdulaziz University Hospital, Ophthalmology, Riyadh, Saudi Arabia
(2) University of Leuven, Laboratory of Histochemistry and Cytochemistry, Leuven, Belgium
(3) King Saud University, Ophthalmology, Riyadh, Saudi Arabia
(4) University of Leuven, Rega Institute for Medical Research- Dept. of Microbiology and Immunology, Leuven, Belgium

Purpose The fibrovascular epiretinal membranes from patients with proliferative diabetic retinopathy (PDR) are characterized by the accumulation of a large number of myofibroblasts. We explored the hypothesis that proliferating endothelial cells via endothelial-to-mesenchymal transition (EndoMT) and/or bone marrow-derived circulating fibrocytes contribute to the myofibroblast population present in PDR membranes.
Methods Epiretinal membranes from 14 patients with PDR were studied by immunohistochemistry. In addition, we investigated the phenotypic changes that take place in human retinal microvascular endothelial cells following exposure to transforming growth factor-β1 (TGF-β1), connective tissue growth factor (CTGF) and the proinflammatory cytokines interleukin-1β (IL-1β) and tumor necrosis factor-a (TNF-a).
Results All membranes contained neovessels expressing the endothelial cell marker CD31. CD31+ endothelial cells co-expressed the fibroblast/myofibroblast markers fibroblast-specific protein-1 (FSP-1) and a-SMA, indicative for the occurrence of endoMT. In the stroma, cells expressing FSP-1, a-SMA, the leukocyte common antigen CD45, and the myelomonocytic marker CD11b were detected. Double labeling showed co-localization of CD45 with FSP-1 and a-SMA and co-localization of CD11b with a-SMA and matrix metalloproteinase-9, demonstrating the presence of infiltrating fibrocytes. Retinal microvascular endothelial cells changed morphology upon cytokine exposure, lost the expression of endothelial cell markers (endothelial nitric oxide synthase and vascular endothelial-cadherin) and started to express mesenchymal markers (calponin, snail, transgelin and FSP-1).
Conclusions These results suggest that endothelial cells as well as circulating fibrocytes may differentiate into myofibroblasts in the diabetic eye and contribute to pathologic fibrosis in PDR.

• 2221

Risk management: how does patient management in ophthalmology compare with those of other medical disciplines?

KOTECHA A
UCL Institute of Ophthalmology, BRC for Ophthalmology, London, United Kingdom

Risk management in medicine involves identifying, evaluating and monitoring actual and potential areas of risk of harm to patients. The ophthalmologist's main concern in the care of the glaucoma patient is the risk of their patient progressing to irreversible sight loss. As such, glaucoma patients receive lifelong care once diagnosed, and undergo a multitude of tests over their lifetime. This talk will explore how the care of the glaucoma patient compares with the care of patients from other disciplines and will attempt to address whether glaucoma ophthalmologists are more 'risk averse' in the management of their patients.

• 2222

Are we over prescribing in Glaucoma?

TUULONEN A
Tampere, Finland

The current cultural and legal environments exert tremendous pressure to do more. To choose to do nothing seems to be more open to criticism, rather than to take action, despite the risk that action might later prove to be harmful. It is well-known for decades that high resource allocation does not necessarily lead to measurable benefits to the patients.

Prescribing diagnostic tests and treatments are indicated when they provide benefits and outcomes that are important to patients, i.e. when interventions improve patients' well-being in every-day life. More frequent testing leads to more diagnoses with newly detected cases being in general milder and non-optimal specificities of diagnostic tests falsely classifying non-glaucoma cases having glaucoma. Thus, outcomes will seem to improve, which stimulates to do even more.

When we have evidence of treatment effectiveness, does it automatically imply that treatment should be administered to ***every*** patient? When e.g. the total costs of glaucoma medications increase five-fold in 5 years, and one country treats 30% more patients with glaucoma compared to its neighbor, which patients are under- or over-treated? Very different conclusions may result from the same evidence.

• 2223

Detecting and managing blindness risk in glaucoma

MCNAUGHT A
Cheltenham General Hospital, Gloucestershire Eye Unit, Cheltenham, United Kingdom

Glaucoma patients are sometimes described as a homogeneous disease group, with the implication that the 'a priori' lifetime risk of visual impairment is similar for all patients, or that predicting the eventual risk of visual impairment is problematic. This is an oversimplification of the true situation. The risk of eventual visual impairment can be substantially different between individual patients, with these differences being evident at the first visit to the glaucoma clinic: a diagnosis of secondary glaucoma e.g. PXF, or angle closure glaucoma, is a an important adverse risk factor, as is the initial severity of visual field loss, height of presenting IOP, and, perhaps most important of all, the age of the patient at presentation. The risk of eventual significant visual loss for patients presenting as OHT is low, though, research work, notably the OHTS study, has highlighted risk factors evident at diagnosis which aid more accurate estimation of the visual prognosis. The prognostic importance of the initial findings at diagnosis, and a review of the literature is presented: including new insights from a recent UK audit of a countywide clinical population detailing the annualised relative risk of individual glaucoma patients requiring glaucoma surgery, segregated by presenting diagnosis.

• 2224

Risk of visual impairment from glaucoma

CRABB D
City University London, Optometry and Visual Science, London, United Kingdom

Monitoring diagnosed glaucoma patients represents a significant burden on clinical services, with an estimated one million visits annually in the UK alone. Visual field (VF) tests are routinely used for detecting worsening of vision. We modelled VF loss during patient's predicted lifetime by examining more than 400,000 VFs from four regionally different glaucoma clinics/services in England. Levels of VF loss were summarised using the Mean Deviation (MD) index from each test. MD at diagnosis and MD loss during predicted remaining lifetime, using a linear rate of MD deterioration (dB/year) and residual life expectancy tables, were calculated and plotted on motion graphs**.** Most patients followed in clinics have stable disease. Five percent (95% confidence interval: 4 to 6%) of patients were predicted to be at risk of statutory blindness in their lifetime [1]. Likelihood of a patient suffering serious visual impairment in their lifetime is linked to level of VF loss at presentation. These findings, from retrospective analysis of 'big data' residing in clinics, could help inform planning of follow-up in glaucoma and also illuminate the importance of detecting the disease before it becomes advanced. ([1] Saunders et al 2014. ***IOVS***)

• 2225

Automated 'big-data' analysis to risk stratify your patients

JOHNSTON R
Gloucestershire, United Kingdom

Abstract not provided

• 2231

The Four Seasons of Dry Eye Disease Seasonal Variations in Presenting Symptoms and Signs of Dry Eye Disease in Norway

EIDET J R , Ræder S , Chen X , Badian R , Utheim Ø , Utheim T P
Oslo University Hospital, Center for Clinical Research, OSLO, Norway

Purpose To investigate the seasonal variations of presenting symptoms and signs of dry eye disease (DED) in Norway
Methods 930 DED patients examined between August 2012 and May 2015 at the Norwegian Dry Eye Disease Clinic in Oslo, Norway, were consecutively included. All patients underwent a comprehensive ophthalmological examination. Presenting symptoms and signs were related to the season according to when each patient had been examined. Weather report data from the exact day of examination in Oslo, including mean temperature, relative humidity, hours of sunshine, and mean wind, from the Norwegian Meteorological Institute, were also compared with the presenting symptoms and signs.
Results Mean seasonal temperatures for Oslo during spring, summer, fall and winter were 7°C, 16°C, 7°C, and -2°C, respectively. Compared to the rest of the year, tear film break-up time (TFBUT) was highest during summer (P<0.001), ocular protection index (OPI) lowest during winter (P=0.013), Schirmer I lowest during summer (P=0.004), tear meniscus height was highest during winter (P=0.004), meibum quality least pathological during winter (P=0.001), the percentage of patients being diagnosed with meibomian gland dysfunction lowest during winter (P<0.001), and intraocular pressure highest during winter (P=0.001). Weather report data correlated the strongest with meibum quality and intraocular pressure, which both were associated with mean temperature (r=0.24; P<0.001 and r=-0.21; P<0.001). Self-reported symptom load and dry eye severity level (DESL) did not differ between seasons.
Conclusions Parameters for assessing DED show seasonal variations, which are important to consider when examining patients with DED. Moreover, contrary to common belief, our results suggest that meibomian gland function appears to improve during winter and with low temperatures.

• 2232

Altered micro-RNA21 expression correlates with enhanced peripheral IL-23p19 levels patients with primary Sjögren's syndrome

NI GABHANN J (1), Pilson Q (1), Jefferies C (1), Murphy C (2)
(1) *Royal College of Surgeons in Ireland, Molecular and Cellular Therapeutics, Dublin, Ireland*
(2) *Royal College of Surgeons in Ireland, Department of Ophthalmology- Royal Victoria Eye and Ear Hospital, Dublin, Ireland*

Purpose *Sjögren's syndrome* (SS) is a systemic autoimmune disorder characterized by inflammation that affects mucous membranes particularly those of the exocrine glands, causing dry eyes and dry mouth. Previous investigations have suggested that dysregulated systemic inflammation contributes to the development and pathogenesis of SS. This study aimed to investigate potential mechanisms responsible for over production of pathogenic cytokines in SS patients.
Methods Peripheral blood mononuclear cells and serum were prepared from whole blood taken from both healthy controls and pSS patients. Gene induction and micro-RNA expression were analysed by real-time PCR. Cytokine levels were determined by ELISA.
Results We observed significantly enhanced expression of the pro-inflammatory micro-RNA, miR-155 ($p \leq 0.05$) and significantly reduced levels of the IL-10 promoting miR, miRNA-21 ($p \leq 0.05$) compared to healthy controls. In keeping with this altered pattern of miR expression we observed significantly increased serum levels of pro-inflammatory cytokines (IL-6, IL-8 and TNF-a) as well as the Th17 promoting cytokine, IL-23p19 ($p \leq 0.05$). Altered expression of previously identified targets of miR-155 (SHIP-1, SOCS1 – potent anti-inflammatory regulators) and miR-21 (IL12p35 and PDCD4, positive regulators of inflammation) was also observed. Significantly a moderate negative correlation ($r = -0.657$, $p \leq 0.05$) was observed between reduced miR-21 expression and increased peripheral IL-23p19 levels in pSS patients, suggesting a link between altered miR expression and disease pathogenesis.
Conclusions Our data suggest that abnormal expression or regulation of miRs and consequently miR regulated genes in innate immunity may contribute to the initiation and progression of SS via overproduction of pathogenic cytokines.

• 2233

Standardising the Schirmer Test by Enclosing the Strip in a Waterproof Sheath.

WILLSHIRE C (1), Buckley R (1), Bron A J (1,2)
(1) *Anglia Ruskin University, Vision and Eye Research Unit, Cambridge, United Kingdom*
(2) *University of Oxford, Nuffield Department of Clinical Neurosciences and Nuffield Laboratory of Ophthalmology, Oxford, United Kingdom*

Purpose Holly et al. (1984) showed that the wetting length of the Schirmer strip is influenced by evaporation and may be affected by ambient humidity. This could explain poor reproducibility in different environmental conditions. We therefore studied how preventing evaporation affected wetting length in different conditions of relative humidity.
Methods A closed-eye Schirmer test was performed bilaterally in 8 subjects with normal eyes (3 male; mean age 35.5 years SD ± 25), in a Weiss-Gallenkamp controlled environmental chamber, at a temperature of 23°C and with a laminar airflow of 0.08 m/s. Tests were conducted at relative humidities (RH) of 25%, 15% and 5%, with a 10 minute break between each test. Eyes received either a standard Schirmer paper (Whatman No. 41 - Biotech °), or a Schirmer paper clad in a waterproof sheath, on a random basis. Sheaths were constructed from a double layer of laminating plastic (Fellowes ° ImageLast - outer layer: polyethylene terephthalate; inner layer: ethylene-vinyl acetate), heat-sealed to form a lightweight pouch. Papers were inserted, first on the right eye and then on the left. Wetting length was measured at 5 minutes. If full wetting occurred before this time, the time was noted.
Results The wetting length was greater on the sheathed side in 23/24 tests. At 25% RH the mean difference in wetting length was 39.3% SD ± 14.7 (n=8), at 15% RH the mean difference was 44.3% SD ± 17.8 (n=8) and at 5% RH the mean difference was 56.3% SD ± 17.7 (n=7). However, no significant difference was found in % means at different RH, P (0.287) > α (0.05) using a repeated measures ANOVA test.
Conclusions Sheathing of the Schirmer strip frees the test from a dependence on ambient conditions that can vary seasonally, geographically and locally from clinic to clinic. Such standardisation would improve the performance and utility of the test.

• 2234

A Fresh Look at Tear Film Structure and Dynamics

BRON A J (1), Yokoi N (2), Georgiev G (3)
(1) *University of Oxford, Department of Clinical Neurosciences. Nuffield Lab. of Ophthalmology, Oxford, United Kingdom*
(2) *Kyoto Prefectural University of Medicine, Department of Ophthalmology-, Kyoto, Japan*
(3) *University of Sofia "St. Kliment Ohridski", Faculty of Biology- Department of Biochemistry, Sofia, Bulgaria*

Purpose To determine the structure of the precorneal tear film from its behaviour during blinking and eye movements.
Methods The tear film lipid layer (TFLL) and the fluorescein-stained mucoaqueous subphase (MAS) were studied during spontaneous blinking and after vertical or horizontal saccades, using the DR-1TM video-interferometer and video-biomicroscope, respectively.
Results During horizontal saccades, the TFLL and MAS behave as a 'fluid shell' that moves with the cornea (Yokoi et al. Ocul Surf 2014). This cohesion is lost during blinking. In the downstroke, the TFLL is stripped from the MAS and compressed. In the upstroke it spreads, driven by a surface tension gradient, dragging with it the newly deposited MAS. As these layers spread, they are transiently dissociated and also, the MAS is dissociated from the glycocalyx. Cohesion is restored as the tear film stabilises before the next blink. When the tear film forms in the upstroke of the blink, the menisci draw fluid from the tear film until they are separated by a zone of meniscus-induced thinning (MIT) – the "black line" seen in the fluorescein-stained tear film. During pauses at the end of any saccade, this MIT is imprinted onto the MAS and made visible in the fluorescein-stained tear film as ***dark arcs*** on return from horizontal saccades, and ***dark bands*** after vertical saccades. Their persistence in the blink interval, implies that the MAS has viscous, gel-like properties.
Conclusions Just prior to each blink there is cohesion between the tear film and glycocalyx and between each layer of the tear film. Cohesion is broken transiently by blinking. Most of the water intervening between the gel-like MAS and TFLL is drawn off into the menisci at the time of tear film formation.

• 2235

Novel role of PELI3 as a potential biomarker for Sjogren's syndrome related dry eyes

PILSON Q (1,2), Ni Gabhann J (1), Murphy C C (2)
(1) The Royal College of Surgeons in Ireland, Molecular and Cellular Therapeutics, Dublin, Ireland
(2) The Royal College of Surgeons in Ireland, Department of Ophthalmology, Dublin, Ireland

Purpose In Sjogren's syndrome (SS) related dry eyes (SS-KCS), reduced aqueous tear production and tear hyperosmolarity leads to inflammatory damage to the ocular surface. microRNAs (miR) are known to alter the expression of cytokines, which plays an important role in the pathogenesis and progression of SS. The aim of this study was to isolate miRs and mRNA from conjunctival epithelial cells (CEC) of patients with primary SS (pSS) to identify potential biomarkers that might aid diagnosis and future therapy in pSS.
Methods Confirmed SS-KCS and healthy controls were recruited to this study. mRNA isolated from conjunctival impression cytology was sent for miR and mRNA microarray. Bioinformatic analysis was performed to identify predicted targets and comparison was made with the mRNA microarray data. Validation experiments were performed in HeLa cells following transfection with selected miR mimics and predicted genes were detected using qPCR.
Results miR and mRNA microarray found 32 differentially expressed novel miRs and 136 differentially expressed genes in pSS patients compared to healthy controls. Following bioinformatic analysis, novel miR-A was chosen for further analysis. miR-A was significantly increased in pSS (p=0.0079) and bioinformatics suggested Pellino3 (PELI3), a negative regulator of inflammatory cytokines, as a predicted target. The mRNA microarray showed a decrease in PELI3 in pSS patients compared to healthy controls (p= 0.0731). Overexpression of miR-A mimic in HeLa cells resulted in decreased expression of PELI3, suggesting that it is a direct target for miR-A.
Conclusions We have identified differentially expressed miRs and gene targets from CEC in pSS. PELI3, a potential target of novel miR-A which is over expressed in pSS, is a negative regulator of cytokines that might have biomarker and therapeutic potential for pSS related dry eyes.

• 2236

Three dimensional meibography for diagnosis of dry eye syndrome

BYUN Y S (1), Yoo Y S (1), Eom T J (2), Na K S (3), Joo C K (1)
(1) Seoul St. Mary's Hospital, Ophthalmology, Seoul, South-Korea
(2) Gwangju Institute of Science and Technology- School of Information and Communication, Information and Communication, Gwangju, South-Korea
(3) Yeouido St. Mary's Hospital, Ophthalmology, Seoul, South-Korea

Purpose The dysfunction of meibomian glands which secrete components of lipid layer in tears is currently pointed out as one of the main causes occurring dry eye. The distribution of that is more than 70% in Asian, especially. This brought out the importance for the dysfunction of meibomian glands. Our study was aimed to confirm the efficacy of 3D meibography to evaluate the structures of meibomian glands.
Methods This study is a cross sectional study for patients who had diagnosed as dry eye disease associated with the dysfunction of meibomian glands at Seoul Saint Mary's Hospital from July to October, 2014. To confirm the structure of dry eye patients, 3D images using 3D OCT (optical coherence tomography) and 2D images using infrared camera were obtained. Patients who had the drop-out lesion in 3D and 2D images were divided as two groups, and differences between them were analyzed. At the same time, to find the clinical signification for structural changes of meibomian glands, all patients had an ocular surface and a tear function examination to define the degree of dry eye.
Results As compared between 3D and 2D images for dry eye patients who had the drop-out lesion on meibomian glands, 3D images was more useful for diagnosis of dry eye than 2D, especially in dry eye related with mild meibomian gland disease.
Conclusions Our study confirmed that the structural change of meibomian glands was reflected in optical coherence tomography 3D images. Especially, 3D meibography was more powerful than 2D infrared camera to find out the real state of drop-out lesion on meibomian glands. But, there was no statistical significance between the location of drop-out lesions; such as near lid margin, middle area, near superior conjunctival fornix, and clinical features in these study.

• 2237

Randomised, controlled study of the efficacy and safety of a new eye-drop formulation for moderate to severe dry eye syndrome

DOAN S (1), Baudouin C (2), Khairallah M (3)
(1) Hopital Bichat, Ophtalmologie, PARIS, France
(2) CHNO des XV-XX, Service Ophtalmologie III, Paris, France
(3) Hôpital Fattouma Bourguiba, Service d'ophthalmologie, Monastir, Tunisia

Purpose The aim of this study was to compare the efficacy and safety in Dry Eye Disease (DED) of T2762, a new product containing an innovative bioprotective molecule trehalose (molecule finds in plants resistant to dissication with osmoprotectant properties) and hyaluronic acid, to Vismed®.
Methods Phase III, randomized, active-controlled, Investigator-masked, multicentric study in France and Tunisia. 105 Adult patients (≥18 years) with moderate to severe DED were included and received one drop of either T2762 (N=52) or Vismed® (N=53) 3-6 times per day for 84 days. The primary efficacy variable was the Oxford grading score at Day 35. Ocular Surface Disease Index (OSDI), dry eye symptoms, Schirmer test, TBUT, conjunctival hyperaemia, and global performance were assessed as secondary efficacy criteria at baseline, Day 35 and Day 84. Safety assessments were standard.
Results Non-inferiority of T2762 to Vismed® for Oxford grading score was demonstrated at Day 35. For secondary efficacy parameters, reductions in OSDI, dry eye symptoms and investigator/patient assessments of global performance were better for T2762. There were no clinically meaningful between-group differences for the other secondary criteria. Both treatments were well tolerated. Interestingly, there were fewer ocular symptoms upon instillation and fewer AEs with T2762.
Conclusions T2762 is effective and safe, with better patient satisfaction than existing hyaluronate-only eye drops, and offers a therapeutic advancement in the treatment of moderate to severe DED

• 2238

Efficacy of Dry Eye Disease Treatment based on the 2007 Report of the International Dry Eye WorkShop (DEWS)

UTHEIM O (1), Ræder S (2), Utheim T P (3), Eidet J R (3), Badian R (4), Stojanovic A (5), Chen X (3)
(1) Oslo University Hospital, Ophthalmology Department, Oslo, Norway
(2) The Norwegian Dry Eye Clinic, Oslo, Norway
(3) Oslo University Hospital, Department of Medical Biochemistry, Oslo, Norway
(4) Elverum Hospital, Department of Ophthalmology, Oslo, Norway
(5) University Hospital of North Norway, Department of Ophthalmology, Tromsoe, Norway

Purpose To assess the effect of dry eye disease (DED) treatment according to the guidelines reported by the International Dry Eye WorkShop (DEWS) in 2007.
Methods Dry eye disease patients with or without meibomian gland dysfunction (MGD), treated at the Norwegian Dry Eye Clinic, with at least 6 months follow-up time were consecutively included in the study. The choice of treatment for DED was based on the dry eye severity level (DESL), according to the 2007 Report of the International Dry Eye WorkShop (DEWS). The values of tear film break-up time (TBUT), Schirmer I test, ocular surface staining (Oxford scale), and dry eye severity level (DESL) on the right eye at 1, 3, 6, 12, and 24 months after the treatment were compared with those prior to treatment.
Results A total of 237 eyes were included. At 6 months follow-up, TBUT increased from 5.07±3.63s to 8.54±5.12s (p<0.001); Schirmer I test did not show significant change; ocular surface staining decreased from 1.64±2.13 to 0.76±1.20; and DESL decreased from 2.08±0.47 to 1.72±0.54 (p<0.001). The improvement of TBUT, ocular surface staining, and DESL remained significant at 24 months follow-up.
Conclusions Treatment based on the 2007 Report of the International Dry Eye WorkShop (DEWS) was effective in a Norwegian cohort of DED patients with significant improvement in key parameters for assessing DED.

• 2241

SRPK1 inhibitors as novel anti-angiogenic therapeutics for wet age-related macular degeneration (wAMD)

BATSON J (1), Toop H (2), Rowlinson J (1), Allen C (3), Gibbons B (1), Zhang J (2), Wearmouth S (2), Knapp S (4), Morris J (2), Bates D (1)
(1) University of Nottingham, School of Medicine/Exonate, Nottingham, United Kingdom
(2) University of New South Wales, Chemistry, Sydney, Australia
(3) University of Nottingham, School of Medicine, Nottingham, United Kingdom
(4) University of Oxford, Structural Genomics Consortium, Oxford, United Kingdom

Purpose Anti-angiogenic VEGF inhibitors are the standard of care for wAMD but must be administered by intraocular injection and non-specifically inhibit all VEGF isoforms. We aim to develop SRPK1 inhibitors as eye drops that specifically inhibit pro-angiogenic VEGF-A isoform-driven angiogenesis underlying wAMD.
Methods Novel compounds, synthesized based on the structure of SRPK1, were tested in kinase assays, thermal shift binding assays and immunoprecipitation, immunoblotting and immunofluorescent assays. Retinal toxicity and efficacy were evaluated by Ganzfeld ERG and laser-CNV. PK was evaluated in vivo and in ex vivo penetration assays using mass spectrometry.
Results Novel compounds selectively bind to SRPK1 and dose-dependently inhibit SRPK1 kinase activity (IC50s<10 nM), SRSF1 phosphorylation and nuclear localization and increase anti-angiogenic VEGF-A165b levels. SRPK1 inhibitors did not inhibit retinal function yet potently inhibited laser-CNV following eye drop administration in mice (EC50s<0.5μM, n=6-8, P<0.05, One-way ANOVA). Compounds were detected in the sclera, choroid and retina following eye drop administration in vivo in rat and mouse and in ex vivo penetration assays in human, pig and rabbit eyes.
Conclusions We developed SRPK1 inhibitors that specifically target pro-angiogenic VEGF-A-driven choroidal neovascularization and can be delivered to the retina following eye drop administration. These compounds potentially offer more specific, efficacious and safer therapeutics for patients with wAMD.

Commercial interest

• 2242

Ghrelin inhibits choroid-retinal cell migration, proliferation and in vitro angiogenesis, under a high glucose environment

ROCHA DE SOUSA A (1,2), Silva-Gomes R (2), Conceição G (2), Moleiro A (2), Santos C (2), Leite-Moreira A (2)
(1) Department of Senses Organs- faculty of Medicine- University of Porto, Ophthalmology, Porto, Portugal
(2) Faculty of Medicine- University of Porto, Department of Physiology and Thoracic Surgery, Porto, Portugal

Purpose Ghrelin is a peptide expressed in many organs and tissues. Recently, ghrelin has been implicated in the pathophysiology of proliferative retinopathy, although its true involvement remains unclear. The aim of this study is to test the effect of ghrelin in the migration, proliferation, apoptosis and ***in vitro*** angiogenesis of primate choroid retinal endothelial cells (RF/6A), cultured under high glucose conditions.
Methods RF/6A cells were incubated for 24 hours with different glucose concentrations (0-300mM). Cell migration was assessed using wound-healing assay. Colorimetric immunoassay was used for the quantification of cell proliferation, based on the measurement of BrdU incorporation. Cell apoptosis was assessed by TUNEL technique. For each glucose concentration, the effect of ghrelin (10-10 to 10-5nM) was determined after 24 hours of incubation. The ***in vitro*** angiogenesis was assessed by tube formation assay after exposure to the same glucose concentrations and ghrelin (10-7nM) for 4 hours.
Results Ghrelin significantly inhibited RF/6A cell migration at every glucose concentrations, although this effect is more consistent under low glucose environment. Ghrelin, at the concentration of 10-7nM, significantly reduces cell proliferation at every glucose concentration. ***In vitro*** angiogenesis is decreased by ghrelin under a high glucose environment. No differences on the apoptosis assay were seen.
Conclusions In conclusion, ghrelin significantly inhibits RF/6A cells migration, proliferation and in vitro angiogenesis, under high glucose environment.

• 2243

Surface modification of intraocular lenses towards controlled drug delivery

FILIPE H P (1), Bozukova D (2), Pimenta A (3), Vieira A P (4), Alves P (5), Coimbra P (5), Guiomar A J (5), Gil M H (5), Mata J L G (5), Serro A P (3,6)
(1) IOGP, Ocular Surface- Ocular Imaging- Cataract Surgery, Lisboa, Portugal
(2) PhysIOL, PhysIOL, Liége, Belgium
(3) Instituto Superior Técnico, Centro de Química Estrutural, Lisboa, Portugal
(4) Universidade de Coimbra, CIEPQPF Dep. Engenharia Química, Coimbra, Portugal
(5) Universidade de Coimbra, CIEPQPF Dep. Engenharia Química, Coimbra, Portugal
(6) IST CII Egas Moniz, ISCSEM CIIEM, Lisboa, Portugal

Purpose Ocular drug delivery systems replacing or complementing the usual therapeutics after cataract surgery have been the focus of several studies. A possible solution could be implanting intra-ocular lenses (IOLs) also acting as drug carriers. The main challenge is to obtain IOLs that besides providing the best refractive outcome release the drug at a suitable rate. The purpose of our research was to design an effective strategy to incorporate the drug and study the release profile.
Methods IOL surface was modified with PHEMA [poly(2-hydroxyethyl methacrylate)] by treatment with argon plasma and subsequent immersion in a HEMA solution with moxifloxacin (MFX; Vigamox®), followed by a final immersion in an MFX solution. Drug release profiles were obtained ***in vitro*** under hydrodynamic conditions, which simulate those found in the eye for the aqueous humor. A microfluidic cell with a volume of 250 μL was designed and used with a continuous flow of saline solution, at 37ºC, with a renovation rate similar to the physiological one.
Results Results showed that MFX was released with concentrations above the minimum inhibitory concentrations for ***S. aureus, S. epidermidis*** and ***S. pneumoniae*** for 11 days.
Conclusions In the conditions described, IOLs surface modification with PHEMA has allowed an extended drug release effective to prevent post cataract surgery endophthalmitis.

• 2244

Use of retinal oximetry in estimating cerebral tissue oxygenation

VAN KEER K (1), Abegão Pinto L (2), Stalmans I (1), Vandewalle E (1)
(1) University Hospitals Leuven, Department of Ophthalmology, Leuven, Belgium
(2) Centro Hospitalar Lisboa Norte, Department of Ophthalmology, Lisbon, Portugal

Purpose To investigate the correlation between cerebral tissue oxygenation (SctO2) and retinal vessel oxygen saturation (SO2) using non-invasive spectroscopy in healthy individuals.
Methods Retinal and cerebral oxygen saturations were measured in dark-adapted, healthy volunteers breathing ambient air in a seated position using dual wavelength retinal oximetry and transcranial near-infrared spectroscopy (NIRS) respectively. Correlations between SO2 and SctO2 were analyzed using Pearson correlation coefficients. Multivariate analysis was performed to determine the relative contribution of the arterial and venous vessels to SctO2. Using this model, SctO2 was estimated based on retinal arterial and venous oxygen saturation. Pearson correlation coefficients, paired sample t-test and Bland-Altman analysis were used to assess the agreement between the measured and the predicted SctO2.
Results Twenty-one young healthy individuals aged 26.4±2.2 years were analyzed. SctO2 showed a significant positive correlation with both arterial and venous SO2 (r=0.442, P=0.045 and r=0.434 P=0.049 respectively). In multivariate analysis, the relative contribution of arterial and venous SO2 to SctO2 was significantly correlated with diastolic blood pressure, retinal venous oxygen saturation and retinal venous diameter (R2=0.60, P<0.001). The measured SctO2 (72.2±3.5%, range 67.3–80.1) correlated well with estimated SctO2 (72.2±2.6%, range 67.6–77.5) (r=0.774, P<0.001). Bland–Altman plots showed 95% agreement within ±6.8%.
Conclusions In this pilot study, retinal oximetry showed promising as an estimate of cerebral tissue oxygenation as measured by NIRS.

• 2245

The diameter regulation of retinal arterioles during systemic hypoxia is impaired in diabetic patients without retinopathy

PETERSEN L , Bek T
Aarhus University Hospital, Department of Ophthalmology, Aarhus, Denmark

Purpose Diabetic retinopathy (DR) is characterized by retinal lesions related to disturbances in retinal vascular supply that may lead to retinal hypoxia. Additionally, the metabolic activity of cyclooxygenase (COX) and nitric oxide synthase (NOS) have been found to be changed in patients with diabetes mellitus. Therefore, the purpose of the present study was to investigate the effects of inhibiting the COX and the NOS enzymes during hypoxia.
Methods Twenty patients with type 1 diabetes mellitus and no visible diabetic retinopathy were studied. Using the Dynamic Vessel Analyzer the diameters of retinal arterioles at rest and during isometric exercise and flicker stimulation were studied before and during systemic hypoxia induced by breathing a hypoxic gas mixture. The examinations were performed before and during i.v. infusion of the NOS inhibitor L-NMMA and all examinations were repeated on a second day after topical administration of the COX-inhibitor diclofenac.
Results Hypoxia reduced the vasodilatation induced by flicker stimulation ($p=0.0003$) and the vasocontraction induced by both isometric exercise ($p=0.001$) and NO synthesis inhibition ($p<0.0001$), whereas COX inhibition had no significant effects on the diameter responses.
Conclusions In diabetic patients, hypoxia reduces the diameter response of retinal arterioles secondary to changes in blood pressure and retinal metabolism, and the response depends on nitric oxide synthesis. This may potentially point to targets for intervention on retinal flow disturbances in patients with diabetic retinopathy.

• 2251

Matrix metalloproteinase in diabetic retinopathy

OPDENAKKER G
Rega Institute, Leuven, Belgium

The inflammatory processes in diabetic retinopathy (DR) are executed by leukocytes and their molecules. An important class of leukocyte effector molecules are the matrix metalloproteinases (MMPs), which are used by leukocytes to penetrate sites of inflammation. More than 20 MMPs are counteracted by 4 natural tissue inhibitors of metalloproteinases (TIMPs). By analysis of vitreous fluids of patients with diabetic retinopathy and ophthalmological controls, MMP-9 has been detected as a disease marker of eye inflammations. MMP-9 is a gelatinase and cleaves denatured and not intact collagens. For collagenolysis, one of the collagenases (MMP-1, MMP-8 and MMP-13) need to be present. In DR, MMP-1 levels are increased in the vitreous and may execute collagenolysis. In addition, MMP-9 also cleaves the neuroprotective factor prominin-1/CD133, abundantly present in photoreceptors. The fact that MMP-9 gene knockout mice are resistant to the development of DR suggests MMP-9 inhibition may be beneficial. The techniques to detect various forms of MMPs and the relevance of inhibitors will be discussed. References: (1) PLoS One (2013) 8: e85857; (2) Progress in Retinal and Eye Research (2014) 43: 76-91; (3) Nature Methods (2013) 10: 211-220

• 2252

Role of chemokines in diabetic retinopathy

STRUYF S *(1), Mohammad G (2), Imtiaz Nawaz M (2), Van Raemdonck K (1), De Hertogh G (3), Van Damme J (1), Abu El Asrar A (2,4)*
(1) Laboratory of Molecular Immunology, Rega Institute for Medical Research, Dept. of Microbiology and Immunology
(2) Dept. of Ophthalmology, College of Medicine, Kind Saud University
(3) Laboratory of Histochemistry and Cytochemistry, University of Leuven, KU Leuven
(4) Dr. Nasser Al-Rashid Research Chair in Ophthalmology, ,

We have detected altered expression of chemokines in the vitreous fluid of patients with proliferative diabetic retinopathy (PDR). In the early phase of disease chemokines (CXCL8, CCL2) are involved in leukocyte attraction. Later, CXCL12 may attract progenitor cells (endothelial cell precursors and fibrocytes) involved in establishment of neovessels and in formation of fibrovascular membranes. The myofibroblasts producing ECM in the fibrovascular membranes of the diabetic patients can originate from endothelial (precursor) cells via endoMT, from fibrocytes or from leukocyte-like precursors. During the active disease stage also angiostatic chemokines (CXCL4, CXCL4L1 and CXCL10) are upregulated, probably in an attempt to counteract the stimulatory effects (angiogenesis and increased vascular permeability) of VEGF. Finally, CCL2 and CXCL10 have been reported to induce fibrosis and might play a role in the later stages of the pathology. Recently, we have demonstrated that CXCL4L1, a most potent angiostatic chemokine can be applied therapeutically as VEGF-inhibitor in diabetic rats. Indeed, intraocular injections of CXCL4L1 early after the onset of diabetes protected animals against diabetes-induced blood-retinal barrier breakdown.

• 2253

Inflammatory mediators of diabetic retinopathy: lessons from proteomic analysis

SIMO R *(1), Simó-Servat O (2), Hernández C (3)*
(1) Vall d'Hebron Research Institute and CIBERDEM, Diabetes and Metabolism Research Unit, Barcelona, Spain
(2) Vall d'Hebron Research Institute, Diabetes and Metabolism Research Unit, Barcelona, Spain
(3) Vall d'Hebron Reseach Institute and CIBERDEM, Diabetes and Metabolism Research Unit, Barcelona, Spain

Vitreous fluid obtained from diabetic patients undergoing vitreoretinal surgery is currently used to explore the events that are taking place in the retina for clinical research. However, several confounding factors such as vitreous haemorrhage and concentration of vitreous proteins should be considered in the analysis of the results. In addition, the volume of vitreous fluid obtained after vitrectomy is approximately 1mL and, therefore, only few peptides can be analysed simultaneously. The recent development of proteome analysis has made it feasible to analyse protein profiles with only a small sample. We have used this approach for exploring pathogenic candidates in both proliferative DR (PDR) and DME. Regarding mediators of inflammation involved in PDR, it is worthy of mentioning that several factors of the complement system have been found increased in the vitreous fluid from PDR patients in comparison with control subjects. There is scarse information on this issue in DME. However, an overview will be given and our results showing that hemopexin is a candidate in the pathogenesis of DME will be presented.

• 2254

Immune cell activation in diabetic retinopathy

XU H *(1), Chen M (2)*
(1) Queen's University Belfast, Center for Experimental Medicine, Belfast, United Kingdom
(2) Queen's University Belfast, Centre for Experimental Medicine, Belfast, United Kingdom

Inflammation plays an important role in the pathogenesis of diabetic retinopathy (DR), although the detailed pathways involved remain poorly defined. Inflammation may occur intravascularly at the early stages of DR in the form of leukocyte-endothelial interaction (leukostasis). As the disease progresses, this intravascular inflammation damages the integrity of the blood retina barrier resulting in the infiltration of circulating immune cells and plasma proteins that are often toxic to various retinal cells, including the vascular cells as well as various neurons. The presentation will discuss how the phenotype and function of circulating immune cells is affected by diabetes and the contribution of systemic immune activation to retinal degeneration during diabetes.

• 2261

Extraocular phenotyping of mitochondrial optic neuropathy

MARTINUZZI A (1), Vavla M (2), Papayannis A (3), Petacchi E (4), Carraro E (4), Paparella G (4), Privato F (5), Prosdocimo G (3)

(1) IRCCS "Medea", Conegliano and Pieve di Soligo Research Centre, Conegliano, Italy
(2) IRCCS "E. MEDEA", Conergliano and Pieve di Soligo research Centre, Conegliano, Italy
(3) ULSS7 PIEVE DI SOLIGO, OPHTALMOLOGY UNIT, CONEGLIANO, Italy
(4) IRCCS "E. MEDEA", CONEGLIANO AND PIEVE DI SOLIGO RESEARCH CENTRE, CONEGLIANO, Italy
(5) IRCCS "E. MEDEA", CONEGLIANO AND PIEVE DI SOLIGO RESEARCH CENTRE, pIEVE DI SOLIGO, Italy

The presence of clinical neurophtalmologic manifestations in neurodegenerative disease of early onset such as the hereditary spastic paraplegias (HSP), spino cerebellar ataxias (SCA) or hereditary sensory motor neuropathies (HSMN) has been an inconstant element often reported in case descriptions. A more widespread and subclinical involvement of the retina and the optic nerve however is suspected in most of these conditions. Mitochondrial dysfunction is frequently recognized in the pathophysiology underlining the above mentioned neurodegenerative genetically determined conditions. Retina and the optic nerve are privileged target tissues where mitochondrial pathology is expressed. We systematically explored in a cohort of patients with early onset molecularly defined HSP, SCA or HSMN the occurrence of subclinical involvement of the visual system, with the aim of establishing its real prevalence and its correlation with functional and neuroimaging data. The definition of a typical pattern of alteration may contribute to the inclusion of neuro-ophtamological measures as sensible objective biomarkers of disease and indicators for disease severity and progression.

• 2262

LHON and extraocular features

YU-WAI-MAN P

Institute of Genetic Medicine Newcastle University, Wellcome Trust Centre for Mitochondrial Research, Newcastle upon Tyne, United Kingdom

LHON is typically a monosymptomatic disease but additional features such as cardiac conduction defects, peripheral neuropathy, dystonia, and myopathy have been reported as occurring more frequently among LHON carriers. There is also a well-reported association between the three primary mitochondrial DNA LHON mutations and a multiple sclerosis-like illness, especially among female carriers (so-called Harding's disease). This presentation will critically appraise the extraocular features that have been associated with LHON and how these atypical phenotypes are potentially informing us about important disease mechanisms.

• 2263

Vascular supply in mitochondrial optic neuropathy and glaucoma

BARBONI P

Bologna, Italy,

To quantitatively evaluate the vascular supply in patients at different stages of Leber's hereditary optic neuropathy (LHON). Twenty-six LHON patients were recruited for the study. LHON patients were sub-grouped in: acute (aLHON), chronic phase (chLHON) and asymptomatic carriers (LHON carriers). All subjects had an extensive ophthalmological examination, including Enhanced depth imaging-optical coherence tomography (EDI-OCT). Macular choroid thickness was significantly increased in aLHON patients and this was most evident nasally and superiorly. On the contrary, choroidal thickness was significantly reduced in chLHON patients in all measurement but the 1500 nasal. In comparison, LHON carrier subjects showed a significant increase of choroidal thickness in the 1500 inferior measurement. In the present study we show that choroidal thickness follows a pattern similar to that observed in RNFL, increasing in the pre-symptomatic and acute stages and decreasing in the chronic stage. This feature might be explained by different hypotheses including: (1) a peripapillar microangiopathy, typical of the acute stage, involving the choroidal vessels; (2) increased blood flow through a thickened choroid in response to inefficient metabolism of the retina requiring more oxygenation or a greater heat state.

• 2264

Early-onset Behr syndrome due to compound heterozygous mutations in OPA1

BONNEAU D , Lenaers G , Procaccio V , Amati-Bonneau P , Reynier P

Pôle de Recherche et d'Enseignement en Médecine Mitochondriale PREMMI, UMR CNRS 6214 - INSERM 1083, Angers, France

Behr syndrome is an early-onset and severe syndromic optic atrophy which is probably heterogeneous. Recently, a heterozygous mutation in *OPA1* was reported in an adult-onset Behr-like syndrome. Heterozygous mutations in *OPA1* are the main causes of autosomal dominant optic atrophy (DOA). As many as 20% of patients with DOA exhibit extra-ocular signs including deafness, external ophthalmoplegia, ataxia, peripheral neuropathy and, myopathy. Aside from these autosomal dominant forms, only few syndromic cases have so far been linked to compound heterozygous *OPA1* mutations suggestive of either recessive or semi-dominant inheritance. However, the clinical spectrum of these emerging double-mutant *OPA1*-related disorders remains to be characterized. We report on four children affected with Behr syndrome associated with compound heterozygous *OPA1* mutations. These children were similarly affected with an early-onset neurological syndrome associating a severe optic atrophy (4/4), cerebellar ataxia (4/4), peripheral neuropathy (4/4), digestive involvement (2/4) and deafness (1/4). This report confirms the importance of searching an *OPA1* compound heterozygosity in paediatric cases of syndromic optic neuropathy.

• 2265

Leber's Hereditary Optic Neuropathy (LHON) mtDNA mutations cause cell death by overproduction of reactive oxygen species

SADUN A (1), Carelli V (2), La Morgia C (2), Karanjia R (1)
(1) Doheny Eye Center UCLA, Ophthalmology, Los Angeles, United States
(2) University of Bologna, Neurology, Bologna, Italy

LHON cases are due to point mutations of mtDNA affecting Complex I.
Complex I is the first in a series of redox reactions along the mitochondrial inner membrane in which electrons are transferred. In LHON, ATP may be reduced and reactive oxygen species (ROS) overproduced.
The actual pathophysiology of Complex I is just starting to be understood. In the Wallace mouse model, the mtDNA ND6 mutation in Complex I produces defects in oxidative phosphorylation and RGC loss. .
However the mouse synaptosomes demonstrated increased ROS without diminution of ATP production.
Hence, ROS production at Complex I is important. We propose that alterations of the Complex I proteins disrupt the distance of electron transfer at the iron-sulfate clusters. Mathematical analysis shows that if electrons only cross < 14 angstroms, then quantum electron tunneling (QET) is possible. The criticality of this distance may depend upon proteins that surround the cluster. Mutations that increase this critical distance may convert a QET electron transfer to a traditional chemical one. Thermodynamically, this will not only decrease the efficiency of electron transfer but also produce free electrons which lead to ROS overproduction and RGC death.

• 2271

Tear proteomics in health and disease

BEUERMAN R
Singapore Eye Research Institute, Singapore,

Purpose: To evaluate the tear proteins in normal and diseased eyes to determine how the tear proteins reflect the health of the ocular surface. The tear proteome in normal and in specific pathological conditions has been determined using mass spectrometry. Methods: Tears were collected by either fire polished micropipettes of 1-10µl or Schirmer's Type I tear test, and prepared for mass spectrometry on a AB Sciex 5600. Results: The normal tear proteome has been found to contain more than 1300 proteins. Proteomic studies have been particularly successful in revealing key molecules associated with inflammatory diseases such as dry eye, Meibomium gland disease (MGD) and pterygium. In these studies S100 proteins were found to be upregulated, In MGD, levels of S100A8 and S100A9 were correlated to disease severity and levels of S100A8 protein were significantly correlated to sensations of grittiness, whereas S100A8 and S100A9 were correlated to symptoms of redness and transient blurring. Conclusions: In each disease, the changing levels of disease associated inflammatory markers were found to be unique. Generally, more than one proteomic signal was useful for characterizing the disease state. Proteomic biomarkers must undergo thorough clinical trials for validation, but in the future could augment lengthy and often inconclusive clinical observations.

• 2272

Environmental factors in ocular surface disease

CALONGE M *(1,2), Gonzalez-Garcia M J (1,2), Enriquez de Salamanca A (1,2), Fernandez I (2,1), Pinto-Fraga J (1,2), Teson M (1,2), Martin-Montanez V (1,2), Stern M E (3,1), Lopez-Miguel A (1,4)*
(1) IOBA, University of Valladolid, Valladolid, Spain
(2) CIBER-BBN, Carlos III National Institute of Health, Spain
(3) Allergan Biological Sciences, Irvine, CA, USA
(4) Vision I+D, Valladolid, Spain

It is well known the unquestionable influence of the environment in the prevalence/severity of certain ocular surface diseases such as vernal keratoconjunctivitis, pterigium, allergic conjunctivitis or certain infectious diseases. Our research has been focused however on the effects of indoor artificial environments on the ocular surface. These indoor facilities in which we spend a large percentage of our lives (i.e. work places, homes, shopping centers, recreational facilities, air plane cabins) have in common a low relative humidity and an air flow. These conditions are being shown to greatly influence one of the most prevalent diseases worldwide, Dry Eye Disease (DED). We have recreating these artificial environments in an environmental chamber in a Controlled Environmental Laboratory (IOBA-CERLab) located in our Institute. Our research group has demonstrated how not only DED patients' but even contact lens wearers' or healthy subjects' lacrimal functional unit worsens when exposed to adverse conditions simulating desiccating stress. The main damage was increase in corneal staining, but also some tear molecules had significant altered levels, showing potential as biomarkers of disease activity. More recently, we have demonstrated how topical steroids can ameliorate that damage provoked by desiccating stress, opening an interesting possibility of studying drug efficacy by using these artificially recreated environments.

• 2273

Inflammation, wound healing and tear proteomics in glaucoma

UUSITALO H
Department of Ophthalmology, University of Tampere, Tampere, Finland

Wound healing is a complex process involved in ocular surgery, trauma and pathogenesis of several eye diseases. Due to the delicate and sensitive structures of the eye wound healing is playing a essential role in ophthalmology. In glaucoma surgery well controlled wound healing process is as important for the creation of a functioning passage to aqueous humor out of the eye. The state of the ocular tissues is of great importance for the success of ocular surgeries. Chronic topical glaucoma medication is an important risk for the ocular surface disease. It is also a risk for the failure in glaucoma surgery. The mechanism of failing glaucoma surgery is related to the presence inflammatory cells, accumulation of extracellular matrix proteins in the conjunctiva and the site of surgery, activation of matrix metalloproteinases and their tissue inhibitors and accumulation oxidized lipids in the conjunctiva and around the site of operation and glaucoma shunts. Tear fluid proteome is a novel technique to get detailed information about the processes of the anterior surfaces of the eye and could easily be performed. It has also proven to be a promising technique for detecting biomarkers for ocular surface disease, ocular inflammation and predicting thus the success of glaucoma surgery.

• 2274

Bioinformatics in tear proteome

NYKTER M
University of Tampere, BioMediTech, University of Tampere, Finland

Tear is a complex fluid containing rich mixture of biomolecules. Current mass spectrometry based proteomic techniques are able to capture the expression of thousands of proteins from small tear volumes, opening possibility for data driven identification of predictive biomarkers. We have developed a bioinformatic approach for biomarker discovery that effectively finds associations between time course proteomic data and clinical phenotypic data. We first construct a feature matrix that contains the data and clinical information as well as various computationally derived features, for example pathway enrichments scores across thousands of pathways and various biologically motivated activity scores for master regulators. These feature matrices that can contain categorical, discrete or continuous data are then computationally analyzed to identify the strongest statistical associations with the phenotypes of interest. Cross validation strategy is utilized to make sure the identified associations are robust. Our approach has been applied to data from clinical patient samples to identify new candidate biomarkers.

• 2331

New paradigm in Dry Eye Disease (DED)

BAUDOUIN C
Boulogne Billancourt, France,

Abstract not provided

• 2332

Visual function impairment in Dry Eye Disease (DED)

PISELLA P J
Tours, France,

Abstract not provided

• 2333

MEIBUM survey: a closer look at the eyelids

DIAZ VALLE D
Hospital Clinico San Carlos, Servicio de Oftalmologia, Madrid, Spain

Abstract not provided

• 2334

New treatment to improve Tear film thickness in Dry Eye Disease (DED)

SCHMETTERER L
Medical University of Vienna, Clinical Pharmacology, Vienna, Austria

Abstract not provided

• 2411

The "complete vitrectomy performed early" treatment philosophy

ROCHA DE SOUSA A (1), Gouveia P (2), Correia-Pinto Jr J (2), Alves P (2), Falcao-Reis F (2)
(1) Department of Senses Organs- Faculty of Medicine- University of Porto, Ophthalmology, Porto, Portugal
(2) Department of Ophthalmology, Centro Hospitalar de São João, Porto, Portugal

Purpose To compare the impact of early *versus* late complete vitrectomy in the management of acute postoperative endophthalmitis (PE).
Methods Retrospective study.
Results 57 eyes from 57 patients were included in this study. 49.1% of patients were males. Baseline characteristics were similar in all groups (VIT, NVIT, VIT_early and VIT_late). Mean visual acuity at presentation was hand movements (2.3 logMAR) in all groups. After treatment mean visual acuity was 1.2 ± 1.1 logMAR in the NVIT group and 1.9 ± 1.2 logMAR in the VIT group (p=0.075). The differences between visual outcomes in VIT_early and VIT_late groups, however, achieved statistical significance (p=0.012): 0.8 ± 1.1 logMAR in the VIT_early group whereas in the VIT_late group it was 2.2 ± 1.0 logMAR. Significant differences between visual outcomes were also encountered when comparing NVIT and VIT_late groups (p=0.008). The difference in final visual acuity between VIT_early and NVIT didn't not attain statistical difference (p=0.459).
Conclusions This study highlights the impact of a complete early vitrectomy in the management of PE. A complete vitrectomy didn't surpass the visual results of intravitreal antibiotics alone (p=0.075). Howeverm a complete vitrectomy performed within the first 24 hours after presentation was clearly beneficial when compared to vitrectomy performed later (p=0.012). Furthermore, our series suggests that a late vitrectomy is detrimental to visual results when compared to intravitreal antibiotics (p=0.008).

• 2412

Early experiences with intravitreal ocriplasmin: a series of cases with vitreomacular traction

SCHULZ C , Saunders D , Lockwood A , Begum S
Portsmouth Hospitals NHS Trust, Eye Department, Portsmouth, United Kingdom

Purpose Ocriplasmin is a vitreolytic agent that may improve the chances of non-surgical resolution of vitreomacular traction (VMT), based on phase III trials. Since it gained regulatory approval, only a handful of small retrospective studies have reported its efficacy. To date, no study has commented on the chronicity of VMT prior to treatment.
Methods Case notes were examined for all patients with VMT that underwent intravitreal ocriplasmin injection at a single district general hospital. Baseline characteristics were recorded including patient demographics, sub-classification of VMT, and the length of time from diagnosis to treatment with ocriplasmin. The main outcome was non-surgical resolution of VMT within 28 days.
Results All 9 eligible cases were included. The mean length of time between diagnosis of VMT and treatment with intravitreal ocriplasmin was 655 days. Only 1 patient (11%) experienced non-surgical resolution of VMT within 28 days of treatment. This patient had the shortest time between diagnosis and treatment (17 days), and this was significantly distant from the sample mean (p=0.01). The mean age of our sample (81) was higher than that reported in other studies. All other baseline characteristics were consistent with prior studies.
Conclusions This study adds to the limited dataset regarding treatment of VMT with ocriplasmin since it gained regulatory approval. While the small sample size of this study is appreciated, the rate of success is disappointing when compared to phase III trials. The observations of this series raise the possibility that prolonged vitreomacular adhesion may limit the efficacy of non-surgical resolution with ocriplasmin.

• 2413

Anatomic and functional follow-up of foveal microstructures after macula-off retinal detachment surgery

DESCHASSE C (1), Kauffmann Y (1), Frérot M (2), Chiquet C (3), Berrod J (4), Le Mer Y (5), Arndt C (6), Tadayoni R (7), Korobelnik J F (8), Weber M (9), Gaucher D (10), Delbosc B (11), Bron A M (1), Creuzot C (1)
(1) University Hospital, Ophthalmology, Dijon, France
(2) university hospital, INSERM U866- Registre bourguignon des cancers digestifs- ResAM, Dijon, France
(3) University Hospital, Ophthalmology, Grenoble, France
(4) University hospital, Ophthalmology, Nancy, France
(5) Fondation Rothschild, Ophthalmology, Paris, France
(6) University Hospital, Ophthalmology, Reims, France
(7) Lariboisière, Ophthalmology, Paris, France
(8) University Hospital, Ophthalmology, Bordeaux, France
(9) University Hospital, Ophthalmology, Nantes, France
(10) University Hospital, Ophthalmology, Strasbourg, France
(11) University Hospital, Ophthalmology, Besançon, France

Purpose To describe the course of functional and anatomical damage after successful repair of macula-off rhegmatogenous retinal detachment (RRD).
Methods This was a prospective multicenter study including patients with successful surgery for macula-off RRD between October 2011 and April 2014. Patients with pre-existing macular diseases or with surgery failures were excluded. Each patient underwent a complete ophthalmologic exam at baseline and at one, three and six months after the surgery (M1, M3, M6), with an assessment of the best-corrected visual acuity (BCVA) at 4 m using the standard Early Treatment Diabetic Retinopathy Study chart, and with Spectral-Domain Optical Coherence Tomography (SD-OCT) macular imaging.
Results One hundred and three eyes of 103 patients from ten French centers, with a 63-years median age (IQR: [58; 69]), were included. The median BCVA increased significantly from 63 [46; 73] letters at M1 to 73 [62; 80]) at M6, p<0.01). SD-OCT morphologic lesions in the outer retina significantly improved between M1 and M6: irregular hyporeflectivity of the photoreceptor outer segments (76.7% vs 61.5%, p<0.01) and disruption of the inner/outer segment junction line (51.5% vs 26.2%, p<0.01). The rate of epiretinal membrane did not significantly increase between M1 and M6 (9.7% vs 20.4%, p<0.67).
Conclusions These preliminary results of the study « DécOllement de REtine : Fonction et Anatomie (DOREFA)» show a slow recovery of the external retinal layers after a successful RRD surgery. These observations seem to be parallel to the progressive recovery of the visual function after the intervention. A better knowledge of functional and anatomical kinetics after macula-off RRD constitutes a preliminary step to the study of factors influencing the visual prognosis.

• 2414

Anterior chamber aqueous flare in retinal detachment surgery.

BERROD J P , Kurun S , Mouna A , Jeancolas A L , Ferte A , Conart J B
CHU Nancy Brabois, Ophtalmologie, Vandoeuvre les Nancy, France

Purpose To investigate preoperative aqueous flare as a predictive factor for proliferative vitreoretinopathy (PVR) leading to relapse in patients with primary rhegmatogenous retinal detachment repear.
Methods Preoperatively, the aqueous flare of 100 consecutive patients with unilateral rhegmatogenous retinal detachement (RD) was measured with Kowa FM-500 laser flare-cell meter. All patients were evaluated at 1 month and 6 months or just after recurence.
Results Twenty eyes underwent redetachment secondary to PVR developpement. The mean value of flare of patients that redetached was 48.12 pc/ms versus 17.74 pc/ms for those who did well (p=0.002). We observed that 17/20 recurrences with PVR (85%) and 24 / 76 that did well (31.6%) had flare greater than 15 pc/ms (p=0.0355). Moreover in patients without preoperative clinical signs of PVR, the sensitivity of the laser cell flare to predict post operative PVR when flare reached 15 pc/ms was 100% with 77.5% specificity and 31.25% positive predictive value.
Conclusions Our study shows the effectiveness of the laser flare cell meter in detecting eyes at risk of developing post operative PVR leading to recurrences. The laser flare-cell meter is a non invasive tool that informs the surgeon on the potential severity of the detachment.

• 2415

Improvement in retinal vessel oxygen saturation after vitrectomy

LIM S L (1), Tan L (2), Perera S (3)
(1) Singapore National Eye Centre, Vitreoretina, Singapore, Singapore
(2) Singapore National Eye Centre, Training and Education, Singapore, Singapore
(3) Singapore National Eye Centre, Glaucoma, Singapore, Singapore

Purpose To evaluate the effects of vitrectomy on retinal vascular oxygen saturation.
Methods This was a prospective observational study. 27 eyes of 27 patients who underwent vitrectomy for macular conditions were included. Retinal oximetry was performed using the Oxymap (Oxymap Inc., Reykjavik, Iceland) prior to vitrectomy and 3 months after surgery. The mean retinal arterial and venous oxygen saturation were measured and the arterial-venous difference (AVD) was calculated as the difference between the arterial and venous saturations.
Multivariate linear regression models were constructed to compare oxygen saturation before and after surgery, with adjustments for age, sex, hypertension, hyperlipidemia, diabetes mellitus and indication for surgery.
Results The mean age of the subjects was 68.4±8.9 years, 15 (55%) were male and the majority were of Chinese ethnicity (93%). The mean arterial saturation increased significantly after vitrectomy (101.93 ± 8.36% vs 96.16 ± 14.14%, p = 0.01). The mean venous saturation also increased significantly after surgery. (59.76 ± 8.52% vs 50.40 ± 11.72%, p = 0.02). The mean AVD significantly decreased from 45.76 ± 12.18% before surgery to 42.17 ± 10.94% after surgery (p= 0.02).
Conclusions Retinal arterial and venous oxygen saturation are significantly increased after vitrectomy, while the AVD is decreased after vitrectomy. Our results suggest that vitrectomy enhances retinal oxygenation. This may account for the apparent benefit of vitrectomy on conditions with retinal hypoxia such as diabetic retinopathy.

• 2416

Imaging of intravitreal injected solution dispersion.

WILLEKENS K (1), Reyns G (2), Jonckx B (2), Feyen J (2), Yewei L (3), Coudyzer W (3), Yicheng N (3), Stalmans P (1)
(1) UZ Leuven, Ophthalmology, Leuven, Belgium
(2) Thrombogenics, Research and development, Leuven, Belgium
(3) UZ Leuven, Radiology, Leuven, Belgium

Purpose The extent of activity of an intravitreal injected drug is linked to its dispersion within the vitreous body. Researchers have been trying to visualize dispersion of intravitreal injected solutions using Indian ink or fluorescein, either with subsequent dissection or with endoillumination, both invasive methods that could influence the dispersion pattern. Therefore, this pilot study aims at investigating and identifying the best minimal invasive imaging method for visualizing the dispersion of an intravitreal injected solution.
Methods To determine the optimal imaging concentration, a series of 5 enucleated porcine eyes were injected with 0.1cc of 100%, 50%, 25%, 20% and 10% standard iodium contrast medium, respectively. Injections were made using a standard 1cc syringe and 30 gauge needle at 3.5mm from the limbus aiming at the center of the globe. Subsequently, the dispersion of the contrast agent was monitored using high resolution imaging methods: mammography and ultra high resolution computed tomography (UHRCT). For the latter, 3D reconstructions were rendered.
Results A 1:10 dilution mixture combined optimal visualization contrast with low viscosity of the injection solution using radiographic ultrahigh resolution mammography. Both mammography and UHRCT images were taken from two eyes; one with a slow injection, the other with a fast injection.
Conclusions 3D reconstructed UHRCT images were favored over 2D mammography images for dynamic imaging of the intravitreal solution dispersion.

• 2417

The use of intraoperative spectral domain optic coherence tomography in vitreoretinal surgery: The evaluation of efficacy.

LYTVYNCHUK L (1), Glittenberg C (2), Binder S (2)
(1) Lviv Regional Clinical Hospital, Department of Ophthalmology, Lviv, Ukraine
(2) Rudolf Foundation Hospital- Karl Landsteiner Institute for Retinal Research and Imaging, Department of Ophthalmology, Vienna, Austria

Purpose To evaluate the feasibility of intraoperative spectral domain optic coherence tomography (iSD-OCT) in challenging cases during pars plana vitrectomy (PPV).
Methods Intraoperative imaging was performed using the first commercially available iSD-OCT system Rescan 700, fully integrated into the surgical microscope OPMI Lumera 700 (Zeiss, Oberkochen, Germany). The feasibility of iSD-OCT was assessed during three 23-gauge PPV cases: large macular hole (MH) with inverted internal limiting membrane (ILM) flap technique (Case #1), vitrectomy for asteroid hyalosis with age-related macular degeneration (Case #2), vitrectomy for morning glory syndrome with retinoschisis and exudative retinal detachment (Case #3).
Results Case #1. The use of iSD-OCT facilitated to safely initiate ILM flap, to form inverted flap, to invert the flap into the MH, to control position of the forceps concerning retinal layers, and to confirm the MH covering with the ILM remnants at the end of the surgery. Case #2. Standard OCT was not available before the surgery due to opaque vitreous. Intraoperative SD-OCT imaging assisted to reveal epiretinal membrane (ERM), retinal pigment epithelium detachment, intraretinal fluid and drusen. These findings required additional surgical steps: ERM removal and injection of anti-VEGF at the end of the surgery. Case #3. In the case of morning glory syndrome iSD-OCT facilitated to remove the strongly adherent posterior hyaloid, to control ILM flap initiation, to perform the peeling over the detached retina, to aspirate residual fluid after fluid/air exchange.
Conclusions The use of iSD-OCT facilitates real-time simultaneous to surgical workflow visualisation of tissue behaviour and surgical manoeuvres during pars plans vitrectomy. The obtained information can improve surgical technique and influence the decision making in difficult cases.

• 2418

Epiretinal membrane peeling for eyes with asteroid hyalosis: a case-control study

MOUNA A , Conaert J B , Kurun S , Ameloot F , Berrod J P
NANCY regional university hospital, ophthalmology, Vandœuvre-lès-Nancy, France

Purpose To evaluate anatomical and functional results of epiretinal membrane peeling for patients with asteroid hyalosis (AH) comparing with those of a control population without AH.
Methods Retrospective, case-control study, of a cohort of 1104 patients operated from an epiretinal membrane(EM) between January 2002 and February 2014. Forty four consecutive patient were included in the EM associated with AH group and were compared to 44 control patient without AH, matched for: age, sex, date of surgery, and axial length. The best corrected visual acuity (BCVA) and central macular thickness on OCT (CMT) were measured at baseline and postoperatively at 1, 6 and 12 months. intraoperative and/or postoperative complications were also analyzed.
Results 34 men and 10 women were included in the AH group. Respectively, the mean initial BCVA was 0.49+/-0.21 logMar for the AH group Vs 0.44+/-0.21 logMAR for the control group (p = 0.2), and the mean initial CMT was 415 +/- 71 µm Vs 422+/-73 µm (p = 0.6). No significant difference was found regarding the final BCVA, with respectively a mean of 0.37 Vs 0.24 logMAR(p=0.26) at 1month, 0.27 Vs. 0.23 logMAR(p=0.5) at 6 months, and 0.17Vs 0.2 logMAR(p=0.26) at 12 months. Also, no difference was found regarding the evolution of CMT, with respectively a mean of 368 Vs 353 µm(p=0.5) at 1 month, 347 Vs 358 µm(p=0.61) at 6 months, 345 Vs 349 µm (p =0.87) at 12 months. Only a single macular hole was recorded in the AH group in the follow up.
Conclusions The presence of asteroid hyalosis does not constitute a factor of poor prognosis for visual recovery after epiretinal membrane peeling

• 2421

Transneuronal degeneration in human glaucoma: A novel multiphoton-DAPI approach

MORGAN J E
School of Optometry, Cardiff University, Cardiff, United Kingdom

Abstract not provided

• 2422

Ocular hypertension in adult rodents does not affect non-RGC neurons in the ganglion cell layer but results in severe loss of cone-photorreceptors

VIDAL-SANZ M , Rodríguez-Llarena S , Ortín-Martínez A , Salinas-Navarro M , Nadal-Nicolás F M , Valiente-Soriano F J , Villegas-Pérez M P
University of Murcia, Department of Ophthalmology, Murcia, Spain

We investigate short and long-term effects of laser photocoagulation (LP) of the limbal tissues-induced ocular hypertension (OHT) in the innermost and outer layers of the retina (OLR). Adult albino rats or mice were examined 2 weeks to 6 months after LP-induced OHT. Brn3a-immunodetection was used to identify retinal ganglion cells (RGCs) and DAPI-staining to identify all cell nuclei in the ganglion cell layer. Retinas were cut in cross sections for morphometric analysis or prepared as wholemounts to study the entire population of RGCs or L- and S-cones (immunolabeled). OHT resulted in pie-shaped retinal areas lacking Brn3a+RGCs but with large numbers of DAPI+nuclei. Cross-sections showed focal regions of degeneration affecting the ORL that became evident by 2 m and progressed up to 6 months after LP. Rat retinal wholemounts showed RGC diminished to 20-25% by 1 m with no further loss, whereas the L- or S-cones showed progressive loss up to 6 months that amounted to 19% or 33% by 1 m, to 62% or 51% by 3 m, and to 66% or 59% by 6 m, respectively.
LP-induced OHT results in selective loss of RGCs within the ganglion cell layer, but there is progressive severe damage of the ORL up to 6 m.

• 2423

Anatomic, biochemical and functional evidence for cone injury in glaucoma

NORK T M , Kim C B Y , Nickells R W , Ver Hoeve J N
University of Wisconsin--Madison, Ophthalmology and Visual Sciences, Madison, United States

Purpose: To investigate outer retinal injury in glaucoma.
Methods: Studies were done on human glaucomatous eyes as well as eyes from a laser trabecular meshwork destruction model of experimental glaucoma (EG) in non-human primates (NHPs), including light microscopy and ***in situ*** hybridization (ISH) for mRNA using probes specific for rod, S-cone and M/L-cone opsins. Choroidal blood flow (ChBF) was measured using non-recirculating fluorescent microspheres. Functional studies on the NHP eyes included multifocal and full-field electroretinography (mfERG and ffERG).
Results: Swelling of M/L-cones) was a common finding in both the glaucomatous human and NHP EG eyes. Cone loss was also observed in some of the human eyes. ISH for mRNA showed reduced levels in both the S- and M/L-cones in human glaucoma and NHP EG. Supranormal mfERG waveforms were a common feature of the NHP EG eyes. ChBF was greatly reduced in eyes with EG. The ffERG in NHP eyes with advanced EG showed larger reductions in photopic than in scotopic a- and b-wave single-flash responses; particularly at higher intensities.
Conclusion: Multiple lines of evidence show cone injury in human glaucoma and in NHP EG. Reduced ChBF could be the cause.

• 2431

Mass production of high quality corneal endothelial cells from old donors

HE Z (1), Forest F (1), Perrache C (1), Cognasse F (2), Cognasse H (3), Gain P (1), Thuret G (4)

(1) Laboratory BiiGC- EA2521, Faculty of Medicine- Jean Monnet University, Saint Etienne, France
(2) Eye Bank of Saint-Etienne, French Blood Centre, Saint Etienne, France
(3) Laboratory GIMAP- EA3064, Faculty of Medicine- Jean Monnet University, Saint Etienne, France
(4) IUF, Institut Universitaire de France, Paris, France

Purpose In vitro expansion of human corneal endothelial cells (CECs) possessing differentiation status and high endothelial cell density (ECD) is the key for the future cell therapies addressing endothelium dysfunctions. A few recent successes were reported using young donors (<30 years old (yo), by definition scarce), but an efficient technique is lacking for current donors over 55 yo. We present a protocol for mass production of very high quality CECs from old donors.
Methods The Descemet membrane of 35 organ cultured corneas from donors over 55 yo were peeled and digested in collagenase to separate the CECs. Primary cultures were grown in fibronectin-coated wells for 1 month with low concentrations of growth factors. Cells were then trypsinized and subcultivated for 1 month in a second medium enriched with growth factors. The whole process was animal compound free. Only cultures with small regular cells without mesenchymal transition were further subcultured in T25 flasks. At 5th passage, the culture yield and cell characteristics were assessed.
Results Cultures with monolayer of small polygonal cells were obtained for 7 donors (mean age 71±13 yo). ECD was ≥4000 cells/mm2. At 5th passage, each cornea gave more than 160 million of CECs. They strongly expressed ZO1, Na/K ATPase, NCAM, Ncadherin and Vimentin as expected. After ex vivo re-endothelialization of denuded corneas of their own CECs, a new endothelium with high ECD (>2500 cells/mm2) was obtained. Alizarin red staining showed typical morphology of CECs.
Conclusions This new protocol provided a very high quality of cultured CECs from old donors. The satisfying yield and high ECD allows us to plan its transfer to a clinical grade process.

• 2432

Epithelial wound healing in a model of porcine corneas stored in an innovative bioreactor

GUINDOLET D. (1), He Z (2), Bernard A (2), Regeade D (2), Piselli S (2), Perrache C (2), Forest F (2), Peoch M (3), Gain P (2), Gabison E (1), Thuret G (2)

(1) Fondation Ophtalmologique Rothshild, Cornea and External Diseases, PARIS, France
(2) Corneal Graft Biology- Engineering and Imaging Laboratory, EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine- Jean Monnet University, Saint-Etienne, France
(3) Department of Pathology, University Hospital of Saint-Etienne, Saint Etienne, France

Purpose Experimental models of corneal epithelial healing are critically important to study cellular mechanisms and new therapeutics. We designed a bioreactor (BR) for exvivo corneal storage. It restores a pressure equivalent to the intraocular pressure in the endothelial chamber while allowing continuous renewing of media in both epithelial and endothelial chambers. It comprised 2 transparent windows for direct observation of epi and endo layers. Initially designed for human corneas, we adapted a prototype for porcine corneas to develop a new experimental platform. Aim: to study epithelial wound healing in the BR compared to a standard ex-vivo model of porcine corneas.
Methods Porcine eyeballs were obtained from a local slaughterhouse within 4 hours after death. Excised corneas were stored either in a BR or in a Petri dish with culture medium and agar for 4 weeks. A 5mm epithelial debridmentulcer was performed. Exposition of the epithelium to various conditions was assessed in parallel: air-lifting, immersion in different media, alternating media and air. Experiments were done in triplicate. Healing rate was monitored with fluorescein staining, digital pictures, and image analysis with ImageJ. After complete healing, corneas were processed for histology and immunolabelling with K3-K12, laminin-5, 5-ethynyl-2'-deoxyuridine (EdU), ABCB5, and PAX6.
Results Faster epithelial healing was observed for cornea stored in bioreactor. In bioreactor epithelial layer was mature (K3-K12 immunostaining) and multi-layered. Basement membrane was also restored (laminin-5 immunostaining). Repeated epithelial debridement successfully healed indicating adequate survival of progenitors
Conclusions This innovative porcine bioreactor could be a new ex-vivo assay to study corneal wound healing and to assess efficacy or toxicity of new therapeutics. Grant: UJM, ANSM

• 2433

Ultrastructural maintenance of decellularized corneas using dextran

LYNCH A (1), Wilson S (2), Ahearne M (1)

(1) Trinity College Dublin, Trinity Centre for Bioengineering, Dublin 2, Ireland
(2) University of Nottingham, Division of Clinical Neuroscience, Nottingham, United Kingdom

Purpose Corneal decellularization has emerged as a promising alternative to traditional tissue-engineering strategies for the creation of corneal replacements for transplantation. However, decellularization methods can lead to swelling of the cornea, limiting its potential use as a scaffold. In this study, we propose the use of a complex polysaccharide, dextran, to reduce this swelling and maintain the native dimensions and architecture of the cornea.
Methods Porcine corneal buttons were treated with Triton X-100, SDS and nucleases under constant rotation followed by a washing step. To prevent corneal swelling, the decellularization solution was supplemented with dextran. This solution was added to one group throughout the decellularization process and to a second group during the washing cycle. The resulting acellular scaffolds were systematically evaluated by histological and biochemical analyses, in addition, the ultrastructure of the cornea was examined by transmission electron microscopy (TEM).
Results Results demonstrated that the combination of detergents and nucleases effectively removed the majority of cellular material from the cornea. Furthermore, the addition of dextran prevented significant swelling when used throughout the protocol or only during the washing process. After soaking in glycerol a degree of transparency was returned to all decellularized corneas suggesting maintenance of the extracellular matrix. However, TEM analysis confirmed that dextran must be present throughout the decellularization process to preserve the native ultrastructure of the cornea.
Conclusions The findings of this study indicate that the addition of dextran to the decellularization process not only prevents significant corneal swelling but also enhances the maintenance of the native ultrastructure of the cornea.

• 2434

Self-complementary vectors for optimization of AAV2-mediated gene-therapy of corneal endothelial cells

GRUENERT A (1), Buening H (2), Schnoedt M (2), Schmeer M (3), Schleef M (3), Kruse F E (1), Fuchsluger T (1)

(1) Friedrich-Alexander Universität Erlangen-Nürnberg, Ophthalmology, Erlangen, Germany
(2) University of Cologne, Center for Molecular Medicine Cologne CMMC- Laboratory for AAV vector development, Cologne, Germany
(3) PlasmidFactory GmbH & Co. KG, PlasmidFactory, Bielefeld, Germany

Purpose Recombinant adeno-associated viruses 2 (rAAV2) represent a nonpathogenic and safe alternative to other viral delivery systems. However, their transduction efficiency in corneal endothelial cells (CEC) is limited. As the level of transgene expression is dependent on the conversion of single-stranded (ss)- into double-stranded (ds)-DNA, self-complementary (sc)-AAV vectors have been developed to circumvent this problem. The aim of this study was to evaluate the use of scAAV2 in terms of transduction efficiency in CEC. Additionally, the impact of transduction on cell viability was investigated.
Methods A human corneal endothelial cell line (HCEC-12) as well as organ-cultured human donor corneas were transduced with different titers of ss- or sc-AAV2. Transduction efficiencies were compared by means of GFP-transgene expression. GFP-expression in HCEC-12 cells was evaluated by flow cytometry over a period of 28 days. GFP-expression in human donor corneas was analyzed by confocal microscopy on day 6. 7-AAD staining and flow cytometry as well as MTT-assay were performed to determine cell viability after transduction.
Results GFP-expression was significantly higher in cells transduced with scAAV2 than in cells transduced with ssAAV2. The difference in transduction efficiency decreased with increasing vector titer. The highest transgene expression rate using scAAV2 was 86.9% compared to 80.5 % using ssAAV2. In human donor corneas GFP-expression was observed in 72.2% (scAAV) and 44.1% (ssAAV) of CEC respectively. There was no significant difference between viability of transduced and untreated cells.
Conclusions ScAAV2 vectors are an effective tool to enhance transduction efficiency in CEC. Allowing higher transduction rates with lower vector titers, this could improve AAV2-mediated gene therapy to protect CEC in corneal allografts.

• 2435

Designing an innovative bioreactor destined to improve the endothelial viability of stored corneas

RAGEADE D (1), Bernard A (1), Nangoum-Fosso T (1), Herbepin P (1), He Z (1), Perrache C (1), Piselli S (1), Acquart S (2), Thuret G (1,3,4), Gain P (1,3)

(1) *Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering, Faculty of Medicine- Jean Monnet University, Saint-Etienne, France*

(2) *Eye Bank, French Blood Centre, Saint-Etienne, France*

(3) *Department of Ophthalmology, University Hospital of Saint-Etienne, Saint-Etienne, France*

(4) *Institut Universitaire de France, Bd St Michel, Paris, France*

Purpose Loss of intraocular pressure (IOP) after death and after corneo-scleral procurement triggers a stromal swelling causing posterior folds in which endothelial mortality is increased. We hypothesized that restoration of IOP after procurement will be key for long-term corneal storage with preserved endothelial functions.

Methods We designed two bioreactors (BR) (for human and porcine corneas) and their control units. The BR presented as a sterile disposable cassette comprising a corneal chamber with transparent windows surrounded by the fluidic system. Sterile sampling sites were added in the circuit for monitoring physiochemical parameters as well as sterility without risk of contamination.

Results After insertion of the corneo-scleral rim, the system was closed and the cassette connected to its control unit, comprising a peristaltic pump driven by a microcontroller. In a comparative study (ongoing) on paired corneas, the BR maintained a normal corneal thickness and transparency during the storage, while reducing the number of endothelial folds and increasing the endothelial viability.

Conclusions The innovative BR restores IOP while ensuring a continuous medium renewal in a fully transparent chamber. The BR will be available for eye banks, research laboratories, contract research organizations, and cosmetic industry. GRANTS: AP looks for from ANSM, EFS, UJM.

• 2436

Systemic immunosuppression with mycophenolate mofetil to prevent corneal graft rejection after high risk penetrating keratoplasty: a 2-year follow-up study

SZAFLIK J P , Major J , Izdebska J , Lao M , Szaflik J

Medical University of Warsaw, Department of Ophthalmology, Warszawa, Poland

Purpose The study aimed to evaluate the efficacy and safety of systemic immunosuppression with mycophenolate mofetil (MMF) to prevent corneal graft rejection after high risk penetrating keratoplasty.

Methods One hundred ninety-six consecutive patients who underwent high risk penetrating keratoplasty defined as the presence of deep vascularization in more than two quadrants, keratouveitis, emergency keratoplasties, and retransplantations were enrolled in the study. Ninety-eight prospectively followed-up patients were treated with MMF (with dose adjustment based on mycophenolic acid [MPA] serum concentration), and 98 patients were in the non-MMF-treated retrospectively assessed control group.

Results During a mean of 24 months' observation, immune reactions occurred in 8 cases (8%) and graft rejection with subsequent graft failure occurred in 3 cases (3%) in the MMF group. In the control group, graft rejection occurred in 76 cases (78%) and failure due to graft rejection occurred in 30 cases (31%). Kaplan-Meier analysis showed that after a year 93% of the grafts in the MMF-treated group and 47% in the control group showed no immune rejection ($p < 0.01$, log-rank test). Cox regression analysis showed that MMF treatment decreased the risk of graft rejection 11 times (RR = 11, 95.0% CI 4.8-25, $p < 0.0001$). Among 98 MMF-treated patients, 13 had gastric discomfort, 3 developed leucopenia, and 2 had anemia that resolved after MMF dose reduction.

Conclusions MMF treatment after high risk penetrating keratoplasty is safe and reduces the incidence of immune graft rejection and graft failure. Side effects were rare and reversible in all but one case.

• 2441

Sensory and motor fusion

HOUTMAN A C

Universitair Ziekenhuis Vrije Universiteit Brussel, Ophthalmology, Brussel, Belgium

The basis of our understanding of binocular vision and amblyopia in clinical practice has not changed much since Claud Worth formulated three grades of binocular vision in 1903 – well over a century ago. Despite many scientific advances in the neuroanatomical and neurophysiological aspects of binocular vision it may - or may not - come as a surprise that the treatment of strabismus and amblyopia has not fundamentally changed since.

This part of the Special Interest Symposium "contains nothing new" [p.1 Squint: its causes, pathology and treatment. Worth C. London, John Bale, Sons & Danielsson Ltd, 1903], to an extent, but is intended as a refresher of the anatomical and physiological basis of binocular vision and to prime the attendants for the symposium's subject: the presentation of recent advances in the research of the corpus callosum and its role in binocular vision.

• 2442

Normal vision, strabismus and the corpus callosum in animals

MILLERET C

Collège de France, Center for Interdisciplinary Research in Biology CIRB, Paris, France

In the primary visual cortex of higher mammals, both the retino-geniculo-cortical (RGC) and the interhemispheric callosal pathways contribute to the unification of the visual hemifields that project separately within the two hemispheres. Anatomical and functional studies performed on animals reveal that each pathway complements each other both spatially and in terms of binocularity. They also reveal that this pattern emerges progressively with age during the critical period, proving however postnatal visual experience has been normal. In case of abnormal postnatal vision such as the one led by strabismus, both pathways develop abnormally. In particular, we have shown recently that asymmetrical callosal connections develop and this prevents the establishment of a unifying representation of the two visual hemifields. As a general rule, we suggest that crossed and uncrossed RGC pathways contribute successively to all this.

Refs.

C. Milleret et al. Eur. J. Neurosci. 1994, 6:193; JC Houzel et al. 1994, Eur. J. Neurosci. 6: 898; C. Milleret & J.C. Houzel. Eur. J. Neurosci. 2001, 13:137; N. Rochefort et al. Neuroimage, 2007, 36:804; E. Bui Quoc et al. Frontiers in Neuroanat. 2011, 5: 1-29; Ribot et al. J. Neurosci. 2013, 33:13326.

• 2443

The origins of strabismus and loss of binocular vision. Implication of the corpus callosum

BUI QUOC E

France

Strabismus and loss of binocular vision (BV) are often linked disorders because the parallelism of the eyes is necessary for a proper BV. But no BV may exist in the absence of strabismus. If the question of the consequences of strabismus and loss of BV on the brain has been explored for decades, the core question of their origins is less understood. Strabismus is a developmental disorder which causes are numerous as assessed by the various forms of strabismus. Peripheral causes are sometimes responsible. But central causes are mostly the ***primum movens*** of strabismus and loss of BV. Normal interhemispheric callosal connections (CC) being necessary for a proper unification of both visual hemifields and for normal BV along the vertical meridian, we propose here that an abnormal development of the CC might be responsible for strabismus and loss of BV. A misrouting of ganglion cell axons or abnormal development of neuronal activity in the visual system or abnormal development of neuronal activity in the oculomotor system are also proposed to be implicated.

Ref. - Bui Quoc E, Milleret C. Origins of strabismus and loss of binocular vision. Front Integr Neurosci. 2014 Sep 25;8:71. doi: 10.3389/fnint.2014.00071. eCollection 2014.

• 2444

The corpus callosum in human binocularity and strabismus

TEN TUSSCHER M

UZ Brussel, Brussel, Belgium

Intercortical visual transfer has been shown important in mammalian binocularity. The present study aims at demonstrating intercortical visual callosal transfer in 16 human subjects using DTI, fMRI and connectivity. With fMRI brain activation was analysed during central and peripheral retinal stimulation. These were compared with right and left sided stimuli during RE and LE fixation. Results were analysed in a 2X2X2 ANOVA with p=0.005. Callosal fiber tracts were visualised with DTI. With fMRI it showed that RE fixation is associated more with significant signal changes in the corpus callosum, both with right and left V1 co-activation. Connectivity from the left V1 showed mostly de-activation in the corpus callosum and activation if the eye is stimulated from the contralateral central area of the visual field. Callosal activity is associated stronger with stimulation of the temporal central retina and right eye fixation. The stronger trigger from the right eye is likely due to ocular dominance: during central stimulation of the temporal retina of the RE, activation in the left V1 is associated with de-activation in the corpus callosum.

• 2451

Role of High-mobility group box-1 in diabetic retinal vasculopathy and neuropathy

ABU EL ASRAR A
King Saud University, Department of Ophthalmology- College of Medicine, Riyadh, Saudi Arabia

High-mobility mobility group box-1 (HMGB1) is a non-histone DNA-binding protein that plays an important role in chromatin organization and transcriptional regulation. Extracellular HMGB1 functions as a proinflammatory cytokine and triggers the inflammatory response through the activation of multiple receptors such as the receptor for advanced glycation end products (RAGE), toll-like receptor-2 (TLR2), TLR4 and TLR9. We demonstrated that HMGB1 and RAGE were expressed in fibrovascular epiretinal membranes from patients with proliferative diabetic retinopathy (PDR). In addition, we demonstrated increased levels of HMGB1 in the vitreous samples from patients with PDR and that there were significant positive correlations between the vitreous levels and HMGB1 and the levels of the biomarkers of inflammation and oxidative injury. Furthermore, we demonstrated that diabetes induced significant upregulation of the expression of HMGB1 and RAGE in the retinas of rats and mice and that HMGB1 mediates diabetes-induced oxidative stress, activation of inflammatory signaling pathways, breakdown of the blood-retinal barrier and neuropathy in the retina. Therefore, compounds inhibiting HMGB1 may be novel therapeutic agents for diabetic retinopathy.

• 2452

Bioactive Lipids and Early inflammatory Response in diabetic Retinopathy

AL-SHABRAWEY M , Ibrahim A , Beasley S , Wang F , Tawfik A
Georgia Regents University, Oral Biology- Culver Vision Discovery Institute and Ophthalmology, Augusta, United States

Diabetic retinopathy (DR) is a leading cause of blindness primarily due to hyperpermeability and subsequent macular edema. Recent studies showed association between dyslipidemia and DR. Diabetic dyslipidemia is characterized by increased arachidonic acid which is converted to inflammatory bioactive lipids via lipoxygenases (LOX), cycloxygenase, and cytochrome P450 enzymatic pathways. Our studies focus on the role of 12/15-LOX in DR. We have demonstrated upregulation of retinal 12/15-LOX and its products, 12- and 15-hydroxyeicosatetraenoic acids (HETEs), in retina of diabetic human and animals. Interestingly, 12- and 15-HETEs were the main bioactive lipids generated in cultured human retinal endothelial cells (HREC) under hyperglycemia. Intravitreal injection of 12-HETE induced DR phenotype in normal mice. Contrary, pharmacological inhibition or genetic deletion of 12/15-LOX attenuated retinal hyperpermeability and inflammation in diabetic mice. 12- and 15- HETEs also disrupted HREC barrier function, increased leukocyte adhesion, migration and tube formation. This was associated with increased oxidative stress, nitric oxide generation and inflammatory cytokines. Thus, targeting 12/15-LOX is a novel therapeutic strategy to treat DR.

• 2453

Mutual enhancement between high-mobility group box-1 and NADPH oxidase-derived reactive oxygen species mediates diabetes-induced upregulation of retinal apoptotic markers

GHULAM M , Abu El Asrar A
King Saud University, Ophthalmology, Riyadh, Saudi Arabia

We hypothesized that a novel mechanism exists where HMGB1and NADPH oxidase (NOX)-derived ROS are mutually enhanced in the diabetic retina, which may be a novel mechanism for promoting upregulation of retinal apoptotic markers induced by diabetes. To test this hypothesis we analyzed the vitreous samples from PDR and nondiabetic patients, retinas from rats and human retinal microvascular endothelial cells. We found that HMGB1 and the oxidative stress marker protein carbonyl content levels in the vitreous fluid from PDR patients were significantly higher than in controls. There was a significant positive correlation between vitreous fluid levels of HMGB1 and the levels of protein carbonyl content. HMGB1 enhanced interleukin-1β, ROS, NOX2, and PARP-1 and cleaved caspase-3 expression by HRMEC. Diabetes and intravitreal injection of HMGB1 in normal rats induced significant upregulation of ROS, NOX2, PARP-1 and cleaved caspase-3 in the retina. Constant glycyrrhizin and apocynin intake from onset of diabetes did not affect the metabolic status of the diabetic rats, but restored these increased mediators to control values. Our results suggest that there is a mutual enhancement between HMGB1 and NOX-derived ROS in the diabetic retina.

• 2454

Evaluation of T-cell related cytokines in the vitreous of proliferative diabetic retinopathy

TAKEUCHI M
National Defense Medical College, Saitama, Japan

Macrophages are involved in low-grade inflammation in diabetes, and play pathogenic roles in proliferative diabetic retinopathy (PDR) by producing proinflammatory cytokines. T cells as well as other cells are activated by proinflammatory cytokines, and the infiltration into the vitreous of patients with PDR has been shown. We have recently found that both positive rates and levels of IL4, IL-6, IL-10, IL-17A, IL-21, IL-22, and TNFα in the vitreous of PDR patients were significantly higher than those in the serum, and that vitreous levels of these cytokines and IL-31 were significantly higher in PDR patients than in epiretinal membrane or macular hole patients. In addition, although vitreous of IFN-g and sCD40L in the vitreous of endogenous uveitis (EU) patients were significantly higher than those of PDR patients, vitreous levels of IL-4, IL-17A, IL-22, IL-31, and TNFa were conversely higher in the vitreous of PDR patients than those of EU patients. Although it is unclear whether these cytokines synergistically play facilitative roles or inhibitory roles for the progression of PDR, our study suggested that Th2- and Th17-related immune responses are involved in the pathogenesis of PDR.

• 2461

Dominant Optic Atrophy plus phenotype caused by a deep intronic mutation and a modifier variant in the OPA1 gene

WISSINGER B (1), Bonifert T (1), Gonzalez-Menendez I (1), Theurer Y (2), Synofzik M (2), Schoels L (2)

(1) University of Tuebingen, Molecular Genetics Laboratory- Institute for Ophthalmic Research, Tuebingen, Germany

(2) University of Tuebingen, Department of Neurodegenerative Diseases- Hertie-Institute for Clinical Brain Research, Tuebingen, Germany

Mutations in OPA1 are a common cause of dominant optic neuropathy (DOA). Recent studies suggest that ~20% of patients carrying OPA1 mutations have additional neurological deficits (DOAplus phenotype). Such patients frequently carry missense mutations in the GTPase domain of OPA1 suggesting a gain-of-function effect as a major mechanism. We and others recently reported a series of DOAplus patients with biallelic OPA1 mutations as an alternative disease mechanism. Notably most cases were compound heterozygous for a null allele and the Ile382Met variant. The latter is not ***per se*** pathogenic but rather acts as a hypomorphic modifier allele that reinforces phenotypic expression in patients with ***null*** mutations on the opposite allele. In one biallelic DOAplus family we identified a deep intronic mutation (DIM) that causes a constitutive activation and inclusion of a cryptic frameshift-inducing exon into OPA1 mRNA. Consistent with the DIM representing a null allele we observed reduced OPA1 protein amounts to about 50% of normal. Applying antisense oligonucleotides targeting the splice acceptor site of the DIM in patient fibroblasts we could efficiently rescue splicing of the mutant mRNA and re-establish intermediate OPA1 protein levels.

• 2462

Involvement of mitochondrial dynamics in the physiopathology of Dominant Optic Atrophy

LENAERS G

INSERM U583, Institut des Neurosciences de Montpellier, Montpellier, France

Dominant Optic Atrophy is a blinding disease due to the degeneration of the Retinal Ganglion Cells (RGC) that form the optic nerve. Since our discovery of OPA1 gene in 2000 and novel genes more recently, we now know that mitochondrial dynamic is a key process for RGC physiology, as all DOA genes are primarily or secondarily related to mitochondrial dynamics. I shall present these genes and their respective involvement in mitochondrial fusion or fission, and then put emphasis on the importance of mitochondrial dynamics for the maintenance of RGC physiology, taking into account the two different myelinisation status of RGC axons in the retina and optic nerve. Analysis of these parameters in wild type mice and animals mutated for the DOA genes will be presented to illustrate the consequences of impairing mitochondrial dynamics on mitochondrial structure in axons and RGC survival. We believe that our data provide the first example of a mitochondrial disease, for which a clear rational explanation can justify the high specificity of the cell type affected in this disease.

• 2463

Genetic landscape of Leber's hereditary optic neuropathy: reflection on pathogenic mechanisms

CARELLI V (1,2), La Morgia C (1,2), Caporali L (1,2), Maresca A (1,2), Giordano L (3), Valentino M L (1,2), Barboni P (4), Cantatore P (3), D'Adamo P (6), ()

(1) IRCCS Institute of Neurological Sciences of Bologna, Bellaria Hospital, Bologna, Italy

(2) Neurology Unit, Dept. of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna

(3) Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari

(4) IRCCS Istituto Scientifico San Raffaele, Milan, Italy

(5) Doheny Eye Institute, UCLA, Los Angeles

(6) IRCSS-Burlo Garofolo Children Hospital, University of Trieste, Trieste, Italy

Leber's Hereditary Optic Neuropathy (LHON) is a mitochondrial disease due to homoplasmic mtDNA point mutations in complex I, affecting prevalently young males with incomplete penetrance. We recently documented that increase of mitochondrial biogenesis drives incomplete penetrance in LHON, further enhanced by estrogen protection in females. To shed light on nuclear genetic modifiers of LHON penetrance, we combined linkage analysis and association studies with tag and functional SNPs, MitoExome and microarray expression analysis. After computation of relevant co-variates (age, sex, smoke and mtDNA copy number) we obtained a list of candidate genes, the most interesting being implicated in ROS detoxification, mitochondrial biogenesis and cell quality control. A prevalent role of tobacco smoking in penetrance also emerged from our studies, showing that tobacco toxicity triggers LHON by depressing mtDNA copy number and oxidative phosphorylation. Overall, our results indicate that penetrance in LHON is modulated by variants in different genes rather than by a single mutation, and that a complex interaction with environmental factors such as tobacco smoking plays also a major role, representing a confounder for genetic studies. Supported by Telethon-Italy, grant #GGP11182 to VC.

• 2464

Update on treatment strategies for LHON

YU-WAI-MAN P

Institute of Genetic Medicine Newcastle University, Wellcome Trust Centre for Mitochondrial Research, Newcastle upon Tyne, United Kingdom

Leber hereditary optic neuropathy (LHON) is an important cause of severe bilateral visual loss among young adults. This presentation will review the evidence base for the various treatment strategies that have been put forward to treat this mitochondrial disorder, including future developments. Innovative IVF techniques to prevent the maternal transmission of pathogenic mitochondrial DNA mutations will also be discussed.

• 2465

Gene therapy in LHON

VIGNAL-CLERMONT C *(1,2), Corral Debrinski M (3,4,5), Sahel J A (4,6,7,8,9)*

(1) Fondation Ophtalmologique A de Rothschild, 75019, Paris, France
(2) Centre Hospitalier National d'ophtalmologie des Quinze Vingts, 75012, Paris, France
(3) INSERM- U968-, 75012, Paris, France
(4) CNRS- UMR_7210, 75012, Paris, France
(5) Sorbonne Universite´s- UPMC universite´ Paris 6- UMR_S 968- Institut de la vision-, 75012, Paris, France
(6) INSERM- U968, 75012, Paris, France
(7) Fondation Ophtalmologique Adolphe-de-Rothschild, 75019, Paris, France
(8) Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts- INSERM-DHOS CIC 503-, 75012, Paris, France
(9) Sorbonne Universite´s- UPMC universite´ Paris 6- UMR_S 968- Institut de la vision, 75012, Paris, France

Gene therapy is a promise for the treatment of Leber hereditary optic neuropathy (LHON). The techniques required for introducing genes into mitochondria have not yet been developed and allotopic expression is one means of circumventing this barrier. To ensure efficient mitochondrial uptake of the nuclear expressed mtDNA gene, the protein should have a mitochondrial targeting signal (MTS). We have optimized allotopic expression by targeting the mRNAs to the mitochondrial surface with a specific 3'UnTranslated Region (UTR) which can cooperate with the MTS for ensuring the localization of ND4 mRNA to the mitochondrial surface. After having collected data proving that an AAV2/2 vector carrying this therapeutic ND4 gene meets the criteria of robust, long-duration gene expression, and safety in LHON rat model and non human primate retinas, we are leading a phase I/II, open-label, prospective clinical trial with dose escalation, which intends to evaluate safety of this gene therapy administered in one single intravitreal (IVT) injection in humans with chronic ND4 LHON. Actually 9 patients were included and no SAE or treatment-related systemic AE occurred. At last, we look forward to be successful in the generation of a treatment for patients suffering from ND4 LHON.

Commercial interest

• 2471

Is there something like a "Healthy Contact Lens" ?

KNOP E , Knop N
Ocular Surface Center Berlin OSCB, Dept. for Cell- and Neurobiology- Center for Anatomy- Charité - Universitätsmedizin Berlin, Berlin, Germany

Contact lenses (CL) are popular. Soft CL are in the vast majority in spite of severe inherent risk factors. On the other hand, design, materials & properties of scleral CL have greatly improved and they are used as therapeutic devices . This leads to the question whether there is something like a "healthy" CL.
CL history is reviewed with changes in designs, materials & properties over the last century together with the implications of the term "healthy" CL.
Scleral lenses that cover the complete ocular surface (OS) with a rigid spherical material are almost lost in favor of CL from soft materials. Even though the adaptation to soft CL is short & wearing is easy they are still not a toy. Apart from the ability to correct refraction they cannot improve the health of the OS in terms of anatomy & physiology. Careless use can have severe risks to OS health as detailed in a vast body of literature. In particular for children and teenagers it is made easy to view soft CL as must-have life style devices and they come into the focus of a advertisements.
For principal reasons, a "healthy" CL is almost a contradiction in terms. However, scleral lenses that cover the complete OS, have a therapeutic potential in many OS disease conditions.

• 2472

Longterm restoration of ocular surface function with scleral lenses

CARRASQUILLO K G
Boston Foundation for Sight, Ophthalmology, Needham, United States

The ocular surface ecosystem is altered when any of its components becomes compromised. In order to have a stable and healthy ocular surface, there has to be good lid function, healthy and functioning lacrimal and accessory glands, healthy and functional limbal stem cells to allow corneal regeneration and prevention of corneal conjunctivalization, a healthy tear film, and adequate sensory innervation. Without these, the ocular surface, in particular the cornea is vulnerable to severe desiccation, vascularization, opacification, conjunctivalization, chronic epithelial breakdowns, chronic exposure, amongst other sequela; ultimately resulting in compromised vision, severe forms of pain, and light sensitivity. Scleral lenses play an important role in restoring the ocular surface function of compromised ocular surfaces, even when other topical or surgical approaches have failed. Not only are they a viable option, but they are able to provide long-term support of the ocular surface. We report on various cases where long-term restoration of ocular surface function was achieved with the use of prosthetic replacement of the ocular surface ecosystem (PROSE) treatment and use of BostonSight® PROSE devices.

• 2473

Scleral lenses in the management of exposure/neurotrophic keratopathy in patients with cranial nerve palsy

SCHORNACK M
Minnesota, United States

Scleral lenses are increasingly being recognized as a viable option for management of exposure keratopathy.
Unlike more aggressive surgical interventions, the lenses can provide complete protection of the ocular surface without compromising visual clarity or restricting visual field. Preservation of corneal epithelial integrity is of utmost importance when lid function is compromised or absent. The fluid reservoir between the posterior surface of a scleral lens and the anterior corneal surface provides continuous hydration of the corneal epithelium and allows for healing of any epithelial defects. Furthermore, the lens itself protects fragile epithelial tissue from shear forces arising from lid movement over the cornea during the blink. Preservation of visual function is also important for these patients. Those who suffer from decreased vision due to irregularity of a desiccated ocular surface frequently note improvement in visual function with scleral lens wear, because the lens provides a smooth optical surface and neutralizes any corneal irregularity. This presentation will review and summarize visual and ocular outcomes of scleral lens therapy for management of exposure keratopathy at the Mayo Clinic.

• 2474

Scleral lens as a first therapeutic weapon in severe ocular burns

MEKKI M B (1), Yahiaoui S (1), Titah O (1), Belaoudmou R (2)
(1) Ibn Al Haythem Center, Eye surgery and contact lens fitting, Algiers, Algeria
(2) Epidemiology Unit- CHU Lamine Debaghine, INESSM, Algiers, Algeria

PURPOSE:To demonstrate the spectacular effect of therapeutic scleral lens in healing severe ocular burns.
METHODS: Retrospective study of 6 eyes with severe ocular burns, complete limbal stem cell deficiency with limbal ischemia in 360°, corneal anaesthesia and resistant to medical treatment for more than 2 weeks without healing tendancy, presenting large complete corneal and limbal ulcer, fitted with therapeutic scleral lens Misa lens (Microlens®, The Netherlands) for continuous daily wear and filled with saline solution and daily control with fluid exchange.
RESULTS: All eyes had complete re-epithelialisation in 1 to 3 weeks under therapeutic scleral lens alone, The healing proccess began from peripheral conjunctival epithelial cells.
CONCLUSIONS: Therapeutic scleral lens is magic solution to manage severe ocular burns and may be used as first therapeutic weapon.These cases show that epithelial stem cells are presents in all ocular surface not only limbus.

Commercial interest

• 2475

Indications for scleral lenses

LEYSEN I
Antwerp University Hospital, Ophthalmology, Edegem, Belgium

In several cases of high irregular astigmatism such as advanced keratoconus, postkeratoplasty and pellucid marginal degeneration scleral lenses are the only nonsurgical solution to improve vision. In addition to correction of irregular astigmatism the large size and scleral bearing surface of these lenses can also be beneficial in the management of certain ocular surface disorders. They can prevent exposure keratitis and enhance epithelial healing. In this part of the session the different indications for scleral lens fitting are discussed and demonstrated by several case reports. This will show the clinical success and many opportunities of these lenses.

Commercial interest

• 2476

Improving vision and comfort of patients with corneal deformations with implementation of ultraHealth and ultraHealth FC S-H Hybrid Lenses

MANCZAK H
Specialty Medical Contact Lens Practice, Poznan, Poland

In spite of the quadrant specific lens designs, fitting GP lenses to protruded corneas is a greater fitting compromise compared with fitting regular shaped corneas with GP corneal lenses. Also as GP corneal lenses have direct mechanical impact on unhealthy, more vulnerable KC epithelium, they are more likely to induce erosions, abrasions and other mechanical changes. Additionally, due to lack of centration evoked by misalignment of the tip of the cone and optical axis of the cornea, the visual outcome of GP corneal lens wear in patients with corneal irregularity in comparison to GP wear in regular shape corneas patients is usually worse. Synergeyes UltraHealth and UltraHealth Flat Curve hybrid lenses are designed to reduce or eliminate interaction between the part of the cornea within the area of the protrusion, and the back surface of the lens. In addition, size of Synergeyes hybrid lenses is 14.5mm what usually results in better centration over the visual axis which leads to a reduction of HOA; thus they give a better visual quality outcome. Hypoxia, one of major drawbacks of former hybrid lenses, is greatly alleviated with the new materials that are available. Therefore, currently it is possible to diminish or in some cases entirely exclude complications enhancing the visual outcome at the same time.

• 2511

Pathogenesis of diabetic retinopathy and macular edema

BEHAR-COHEN F
INSERM U 598, Paris, France

Abstract not provided

• 2512

Classification of diabetic retinopathy : from screening to diagnosis

WIEDEMANN P
Universität Leipzig, Augenklinik, Leipzig, Germany

The global incidence and prevalence of diabetes mellitus have reached epidemic proportions. Estimates indicate that more than 350 million people will be affected by diabetes mellitus by 2030. All of these individuals will be at risk of developing diabetic retinopathy (DR). It is necessary to categorize, classify and stage the severity of DR in order to provide adequate therapy. With proper management more than 90% of cases of visual loss can be prevented. The purpose of this presentation is to review the classification of DR with a special emphasis on the International Clinical Disease Severity Scale for DR. This new classification is simple to use, easy to remember and based on scientific evidence. It is based on clinical examination and applying the Early Treatment of Diabetic Retinopathy Study 4:2:1 rule. Together with general medical information it allows a risk based assessment. Specialized examinations such as optical coherence tomography or fluorescein angiography support treatment decisions.

• 2513

Macular complication: from edema to ischemia

MIDENA E
University of Padova, Department of Ophthalmology, Padova, Italy

The pathophysiology of macular complications in diabetic retinopathy is multifactorial. Diabetic macular edema and ischemia (both macular and peripheral) are the major drivers of macular involvement in diabetes. Macular edema may be both intra and extra-cellular and it is clinically characterized by different aspects, mainly detected by an accurate qualitative analysis of spectral domain OCT data. This approach allows to identify different phenotypes of diabetic macular edema, providing a track to a personalized treatment. Macular ischemia has always been considered a negative prognostic factor in the treatment of macular edema, and this aspect has been recently re-confirmed. Peripheral retinal ischemia, easily documented by wide field retinal angiography, is emerging as a "new" driver of macular edema. All these new aspects, better defined by a multimodal imaging approach, are the essential to plan an adequate treatment.

• 2514

Therapautic options: how does it work?

POURNARAS C J
La Colline, Ophthalmology Center, Geneva

Visual acuity, in diabetic patients, is decreased due to the development of macular edema (DMO), capillary non-perfusion, and vitreous hemorrhage secondary to retinal neovascularization. Clinical therapeutical approaches using focal photocoagulation and intravitreal treatments offer new insights for the managmenet of DMO and the preservation of vision. The inhibition of the endothelial growth factor (VEGF) and the inflammatory factors, alone or in association to focal laser, have an important impact on the reversal of the inner blood-retina barrier (BRB) diabetic abnormalities. Laser photocoagulation induces in addition, an improvement of the macular hemodynamics, a reversal of tissue hypoxia, a downregulation of the VEGF and inflammatory factors expression and an occlusion of the permanent microvascular abnormalities.

• 2515

Clinical cases

CREUZOT C

Department of Ophthalmology, Dijon, France

Clinical cases of diabetic retinopathy will be considered: diabetic retinopathy with macular edema, macular edema and cataract surgery, proliferative diabetic retinopathy, diabetic retinopathy and pregnancy...

• 2521

Dietary interventions for age-related macular degeneration: a review of the evidence

LAWRENSON J (1), Evans J (2)
(1) City University London, Division of Optometry and Visual Science, London, United Kingdom
(2) London School of Hygiene and Tropical Medicine, Cochrane Eyes and Vision Group, London, United Kingdom

Purpose To summarise the findings of three recently published Cochrane systematic reviews, conducted by the authors that investigated whether taking nutritional supplements can prevent or slow the progression of age-related macular degeneration (AMD).
Methods The systematic reviews were performed using standard Cochrane methodology. We included randomised controlled trials (RCTs) where increased dietary intake of omega 3 fatty acids or antioxidant vitamin or mineral supplements were compared to placebo or no intervention with the aim of preventing the development of AMD, or slowing its progression.
Results There is no good evidence from RCTs that the general population should be taking antioxidant vitamin supplements to reduce their risk of developing AMD later on in life. By contrast, there is moderate quality evidence that people at high risk of developing advanced AMD may experience a delay in progression by taking specific antioxidant vitamin and mineral supplements. This finding is drawn from trials conducted in the USA in a relatively well-nourished population. Although observational studies have shown that the consumption of dietary omega 3 fatty acids may reduce the risk of progression to advanced AMD, two recently published RCTs failed to show any benefit of omega 3 supplements on AMD progression.
Conclusions There is no high quality experimental evidence that nutritional supplementation is beneficial for the primary prevention of AMD. However, people at high risk of developing advanced AMD may benefit from taking antioxidant vitamins. There is currently no evidence to support increasing levels of omega 3 long chain polyunsaturated fatty acids in the diet for the explicit purpose of preventing or slowing the progression of AMD.

• 2522

Prevalence of age-related macular diseases in an old French population (the MONTRACHET Study)

DE LAZZER A (1), Dossarps D (1), Gabrielle P H (1), Pallot C (1), Daniel S (2), Binquet C (2), Tzourio C (3), Bron A M (1), Creuzot C (1)
(1) CHU Dijon, Service d'Ophtalmologie CHU Dijon, Dijon, France
(2) CHU Dijon, Service d' Epidémiologie- Inserm unité 866, Dijon, France
(3) CHU Bordeaux, Service d'Epidémiologie- Inserm unité 708, Bordeaux, France

Purpose To describe the prevalence of age-related macular diseases in a French population-based study (the Montrachet study) older than 74 years.
Methods The Three City study (3C) was a prospective study including 9294 patients aged of 65 years or more from three French cities (Dijon, Bordeaux, and Montpellier) at enrolment in 1999. After 10 years of follow-up, an eye examination was proposed to participants of the 3C cohort in Dijon and 1153 participants were included in the so-called Montrachet study. All patients underwent a complete eye examination including nonmydriatic color retinal photographs. The photographs were classified according to the type of abnormality (intermediate soft drusen, large soft distinct or indistinct drusen, reticular drusen or large area of soft drusen reaching 500µm in diameter, hyperpigmentation or hypopigmentation), and their location (central or pericentral) using the classification of the Multi-ethnic Study of Atherosclerosis (MESA) and that used in the Rotterdam Study. Patients were then classified into 3 categories : early age-related macular degeneration (AMD), late AMD (atrophic or neovascular).
Results Data were available for 1069 patients: 396 men (37.0%) and 673 women (63.0%). The mean age was 82.2 ± 3.8 years. The prevalence of healthy subjects was 56.0%. Stages 1, 2 and 3 accounted for 32.6%, 7.7% and 1.5%, respectively. The late AMD stages represented 2.2% (24 patients). Smoking was not significantly associated with AMD categories.
Conclusions The prevalence of AMD grading in our population is consistent with the literature. The classification of participants according to different macular abnormalities may predict the populations at risk of developing an advanced grade and can help to adapt the management. The relationship with other risk factors will be the next step of this analysis.

• 2523

Subretinal drusenoid deposits in an elderly population with age-related macular degeneration (MONTRACHET study: Maculopathy, Optic Nerve, nuTRition, neurovasCular and HEarT diseases)

GABRIELLE P H (1), DeLazzer A (1), Koehrer P (1), Devilliers H (2), Arnoult L (1), Danielle S (3), Binquet C (4), Tzourio C (3), Bron A M (1), Creuzot C (1)
(1) CHU DIJON, Ophtalmologie, Dijon, France
(2) CHU DIJON, Epidémiologie - Médecine interne, Dijon, France
(3) CHU BORDEAUX, Epidémiologie, Bordeaux, France
(4) CHU DIJON, Epidémiologie, Dijon, France

Purpose To determine the frequency of subretinal drusenoid deposits (SDD) in a French population of elderly patients presenting an age-related macular degeneration (AMD) in the MONTRACHET study.
Methods The three-city study (3C) was a population-based study including 9294 patients older than 65 years from three French cities (Dijon, Bordeaux and Montpellier) at baseline in 1999. After 10 years, the cohort of Dijon benefited from a complete ophthalmologic examination as part of the MONTRACHET study. Each patient underwent a non-mydriatic retinophotography associated with a spectral-domain OCT examination (SD-OCT) of the macula. AMD classification was established according to the classification of the Multi-Ethnic study of Atherosclerosis (MESA) for the retinophotography analysis and with the E3 CONSORTIUM classification for the SD-OCT analysis. Patients with uninterpretable images of both eyes were excluded from statistical analysis.
Results One thousand one hundred fifty three subjects were included. 62.7% were female and the mean age was 82.2 ± 3.8 years. With retinophotography analysis, the frequency of SDD was 1.9% (n=38 eyes). With the SD-OCT macular analysis, the frequency of SDD was 14.8% (n=342). In patients presenting with SDD, 68.8% (n=137) had a bilateral involvement. The relative risk (RR) of presenting SDD lesions in patients older than 80 years old was 2.6 (p<0.001) and in women at 1.3 (p<0.045). An interruption of the ellipsoide line and an alteration of the retinal pigment epithelium were statistically associated with the presence of SDD : RR = 5.9 (p<0.001) and RR = 2.8 (p<0.001), respectively. The average thickness of the subfoveal choroid was thinner in subjects presenting SDD (174.9µm with SDD vs 209.8µm without SDD, p<0.001).
Conclusions Few population-based studies have established the frequency of SDD in an elderly population.

• 2524

Lens status and macular pigment optical density in an old French population (MONTRACHET's study: Maculopathy, Optic Nerve, nuTRition, neurovAsCular and HEarT diseases)

FLECK O (1), Koehrer P (1), Alassane S (2), Binquet C (2), Bretillon L (3), Acar N (3), Tzourio C (4), Bron A M (1), Creuzot C (1)
(1) CHU Dijon, Ophthalmology, Dijon, France
(2) CHU Dijon, Epidemiology, Dijon, France
(3) CNRS UMR6265, CSGA, Dijon, France
(4) CHU Bordeaux, Inserm unité 708, Bordeaux, France

Purpose The aim of our study was to compare macular pigment optical density between pkakic and pseudophakic eyes in a population-based study in the elderly.
Methods The hree city study (3C) included 9294 participants aged 65 years or more from three cities (Bordeaux, Dijon and Montpellier) in 1999. After a 10-year follow-up, Dijon's cohort had a complete ophthalmic examination in the MONTRACHET study; 1153 participants older than 75 years were included. Every participant had fundus photographs, macular pigment optical density measured by two-wavelength autofluorescence. We retained only one eye for each subject, the one with the best image quality. An experimented investigator recorded macular pigment optical density at 0.5, 1, 2, and 6° eccentricity and classified images into one of the three patterns: no ring, ringlike or intermediate. Subjects with age-related macular degeneration were excluded.
Results We included 534 participants with good image quality. The age was 82.3 ± 3.7 years. There were 247 (46.3%) phakic and 287 (53.7%) pseudophakic. Mean macular pigment optical density was significantly higher in pseudophakic eyes at 0.5° (0.66 ± 0.25 vs 0.44 ± 0.23 density units) at 1° (0.56 ± 0.21 vs 0.39 ± 0.19 density units) at 2° (0.35 ± 0.14 vs 0.25 ± 0.13 density units) and at 6° (0.08 ± 0.04 vs 0.06 ± 0.04 density units), p<0,0001. There were no significant differences of macular pigment pattern between whatever the lens status (p=0.64).
Conclusions Macular pigment optical density measurement by two-wavelength autofluorescence is dependent on the lens status so that it should be taken into account when used in elderly where cataractarct surgery is common.

• 2525

The Protective Effect of Anti-blue Lens Against Photo-induced Cell Death

YU W Y , Shan S W , To C H , Chan H H L
The Hong Kong Polytechnic University, School of optometry, Hong Kong, Hong Kong-China

Purpose Anti-blue lenses that selectively block the harmful portion of the blue light spectrum become commercially available recently. This study aimed to evaluate the protective effect of anti-blue lens on cultured porcine primary retinal pigmented epithelial (RPE) cells against photo-irradiation.
Methods Primary RPE cells were isolated from porcine eyes and cultured to confluence. The cells were characterised by RPE65 using Western Blot. White and blue light emitting diode (LED) light sources as well as the transmittance of the anti-blue and anti-UV lenses were characterised by a spectroradiometer. The RPE cells were exposed to ~1.8x104 cd/m2 white (peak wavelength at 443 and 533nm) or blue (peak wavelength at 448 and 523nm) LED light for 16 hours, with anti-blue, anti-UV lens or without lens. Control cells were incubated in the dark. Cellular viability under the different lighting conditions with the anti-blue or anti-UV lenses were compared using trypan blue staining and MTT assay.
Results Trypan blue staining showed that the RPE cellular viability under no light, white light and blue light conditions without any lenses were 94.8±0.4%, 93.7±1.1% and 88.7±2.0% respectively. Blue light irradiation significantly induced more cell death when compared to no light (p=0.001) and white light (p=0.005) conditions. MTT assay also revealed significant difference under blue light when compared to no light (p=0.002) and white light (p=0.014) conditions. When comparing the effect of anti-blue and anti-UV lenses on cell survival, we found that anti-blue lens showed significantly elevated viability (93.4±1.4% vs 90.6±1.4%) using trypan blue (p=0.022) and MTT assay (p=0.029).
Conclusions Blue light exposure induced significant cytotoxicity on RPE cells. The anti-blue lens significantly reduced the harmful blue spectrum and showed protective effect on RPE cell survival.

• 2526

Age Macular Degeneration-Lipidomic Study: Relevance and interest of Lipidomic study in screening, follow-up and etiopathogeny of AMD

GONZALEZ C (1), Bertrand-Michel J (2)
(1) Cabinet du Dr Corinne Gonzalez, FUTUROPHTA, Toulouse, France
(2) I2MC INSERM U1048 ss Bat L3, plateau MetaToul-LIPIDOMIQUE, TOULOUSE, France

Purpose To evaluate the lipidomic study impact on AMD diagnosis, screening, etiopathogenie and interrelations,correlations between those 2 entities
Methods AMD:30 AMD patients.3 Groups:A:10 first stage AMD patients,B:10 Atrophy AMD patients, C:10 Neovascular AMD patients. Ophthalmologic exam:ETDRS visual acuity (VA), complete ophthalmic examination,Fundus examination, autofluorescence imaging (FAF),optical coherence tomography (Spectral Domain OCT) and fluorescein angiography (FA) and ICG when Neovascular complication.Lipidomic Study:Blood tests and analysis, all lipids qualitative, quantitative analysis, all the same for all patients,whatever group. Blood test is done during ophthalmologic exam. Plasma congelation "snap frost" in liquid nitrogen after total blood centrifugation, then liquid-liquid extraction for lipids analysis:neutral lipid by GC,as well as fatty acid but after BF3 methanol derivation,phospholipids by LC-MS directly,as sphingolipids but firstly hydrolysed. Polyinsatured fatty acids metabolites preparation: protein precipitation then pre-concentration by SPE(solid phase extraction) before m'analyses by LC-MS
Results Analysis will determine qualitative,quantitative lipids values in each patients group, each of them proportion, characterization, singularity; so, characterization, prevalence, specifics of and for each group. Lipidomic study'evaluation, identification, classification in AMD patients groups allow AMD screening,follow-up, particularly according to AMD type and stage. Lipidomic study have biomarker feature, let AMD prevention, etiopathogenic concept
Conclusions Lipidomics study and so better AMD characterization allow better diagnosis, follow-up, screening of AMD. Interrelations and correlations between AMD and Lipidomics lead to better etiopathogenie understanding and therapeutics prospects

• 2527

Endophthalmitis associated with intravitreal Ranbizumab: Microbiology and visual outcomes.

PENWARDEN A , Weston K , Lockwood A
Queen Alexandra Hospital NHS Trust, Ophthalmology, Portsmouth, United Kingdom

Purpose The purpose of this study was to examine the spectrum of pathogenic organisms isolated from all cases of endophthalmitis identified during an 11 year period (2003-2014) at a single eye unit. The study was undertaken at the Queen Alexandra Hospital in Portsmouth, UK.
Methods Eye casualty and theatre data bases (HICCS, Medisoft) were used to capture cases of endophthalmitis. Case notes were reviewed to identify whether an intravitreal tap had been taken and to note visual acuities prior to ranibizumab treatment as well as the best visual acuity achieved post endophthalmitis treatment. Microbiological data was gathered for these cases by using the pathology database (ICE).
Results There were 8 cases of endophthalmitis in the 11 year period. All except 1 had an intravitreal tap taken for gram staining and microbiological culture. 4 cultures grew coagulase negative Staphylococcus, 1 grew a Streptococcus species, 1 grew the gram negative organism Haemophilus influenza and 1 culture was sterile. All cases were treated with the intravitreal antibiotics Vancomycin and Ceftazidine. 5 patients had a starting visual acuity 6/12 or better and 3 were 6/18 or worse. Post recovery from endophthalmitis 4 patients had VA of 6/24 or better and 2 had Hand Movements or worse. The patient with the gram negative culture had NPL (no perception of light) vision.
Conclusions The proportion of coagulase negative Staphylococci was slightly higher than other published reports. 2 patients had a poor visual outcome of Hand Movements or worse despite treatment with intravitreal antibiotics, one of which had a gram negative culture. However, half of the patients retained a reasonable vision of 6/24 or better.

• 2528

Microbiology of conjunctiva sac in intravitreal injections.

GRZYBOWSKI A (1), Gaca-Wysocka M (2), Paluch M (2)
(1) University of Warmia and Mazury, Dept. of Ophthalmology, Olsztyn, Poland
(2) Poznan City Hospital, Dept. of Ophthalmology, Poznan, Poland

Purpose To evaluate the conjunctival sac flora before and after intravitreal injection (IVI) in eyes with no prophylactic antibiotic use.
Methods 37 eyes of 37 patients not using systemic or local antibiotics for at least 30 days were included. Microbiological culture from conjunctiva sac to nutrient media was taken twice: before IVI and before any topical medications were given and 30 minutes after anty-VEGF IVI. Topical antibiotics were not used neither before, nor after IVI. Shortly before IVI conjunctival sac was rinsed with 5% povidone-iodine (PVI). Control group constituted eyes not treated with IVI of the same patients.
Results Negative microbiological cultures before and after IVI were noted in the studied group in 15 patients (40.5%) and in 9 control eyes (24,3%). Coagulase-negative Staphylococci (CNS) were cultured in 13 eyes (35.1%) before IVI and in 8 eyes (21.6%) after IVI. In 3 eyes (8.1%) Staphylococcus aureus was shown before IVI, with subsequent negative cultures. In the control group CNS was shown in 14 eyes (37.8%) before IVI and in 7% (18.9%) after IVI. Microbiological flora was identical in studied and control groups in 14 cases (37.8%). There was no case of post-IVI endophthalmitis.
Conclusions About 50% of cultures were negative, in 35% - CNS, and in 15% - other bacteria were cultured, including Staphylococcus aureus in 8%. The number of negative cultures after IVI (the use of PVI) was higher than before IVI, and all Staphylococcus aureus were eliminated. The eye antisepsis based on PVI in IVI is an effective and efficient prophylaxis method.

• 2531

Bilateral acute iris transillumination

TUGAL-TUTKUN I
Istanbul University Istanbul Faculty of Medicine, Istanbul, Turkey

Atrophy and/or depigmentation of the iris is seen in a number of inflammatory and noninflammatory conditions, including viral iridocyclitis, Fuchs uveitis syndrome, Vogt–Koyanagi–Harada disease, pigment dispersion syndrome, acute angle closure glaucoma, and trauma. An acute onset of severe photophobia associated with bilateral acute iris transillumination with variable sphincter paralysis and pigment dispersion has been recently reported as an adverse effect of oral moxifloxacin. In our experience, only 23% of patients presenting with these findings report moxifloxacin use while more than 60% report a preceding viral illness. Pigment dispersion may persist for several months, refractory glaucoma may develop, and diffuse iris transillumination and syphincter paralysis are irreversible in this entity.

• 2532

Cystoid macular oedema in endstage glaucoma

BIFRARE D
Microcystic macular changes associated with optic neuropathy

Microcystic macular edema has been first described in association with multiple sclerosis in 2012. Since then many papers have emerged, describing microcystic macular changes mainly in connection with inflammatory or non-inflammatory optical neuropathy, suggesting the neuropathy to be the origin of these microcystic macular changes.
The different neuropathies and the pathomechanism possibilities will be discussed according to recent litterature.

• 2533

Radius Maumenee Syndrome

KESTELYN P
UZ Gent, Ophthalmology, Gent, Belgium

Ocular injection and increased IOP from elevated episcleral venous pressure are most frequently caused by carotid cavernous fistula. Other causes include large vessel venous obstruction (venous sinus thrombosis and superior vena cava syndrome), Sturge–Weber syndrome, scleritis, thyroid-related orbitopathy and orbital tumours or orbital varices (Radius &Maumenee 1978; Rhee et al. 2009). Additionally, idiopathic rise in episcleral venous pressure, known as Radius–Maumenee syndrome, can lead to ocular injection with elevated IOP (Radius & Maumenee 1978). The syndrome was originally described by Minas & Podos (1968). The diagnosis is based on the clinical findings of elevated IOP causing glaucomatous optic nerve and visual field damage in association with an open angle and dilated episcleral veins. The diagnosis of Radius–Maumenee syndrome can only be made with confidence after intra-orbital and intracranial pathology mentioned above has been excluded by MRI. Two case reports will illustrate the typical features of this rare cause of glaucoma.

• 2534

Drug induced glaucoma: old and new drugs

LAMBRECHT P
UZ Gent, Gent, Belgium

Some drugs have the ability to cause ocular hypertension and glaucoma as a consequence. This lecture discusses the old and new drugs that have the ability to cause an ocular hypertension side effect and classifies them according to the mechanism of action.

• 2541

Influence of intraocular pressure in anterior lamina cribrosa depth – a prospective observational study in a healthy Portuguese population

CORDEIRO SOUSA D (1,2), Leal I (1,2), Pinto Ferreira N (1), Pinto J (1), Abegao Pinto L (2), Pinto F (1,2), Marques-Neves C (1,2,3)
(1) Hospital Santa Maria - Lisbon Academic Medical Center, Ophthalmology, Lisboa, Portugal
(2) Faculty of Medicine - Lisbon Academic Medical Center, Ophthalmology, Lisboa, Portugal
(3) Centro de Estudos das Ciencias da Visao, Ophthalmology, Lisboa, Portugal

Purpose To investigate the association between anterior lamina cribrosa depth (ALCD) determined with enhanced depth imaging spectral-domain optical coherence tomography (EDI-OCT) and IOP in a healthy Portuguese population.
Methods Prospective observational study conducted between January and April 2015 of 44 subjects with a irrelevant ophthalmologic history. EDI-OCT of optic nerve head (ONH) was performed in all participants (2 cross scans: vertical and horizontal). ALCD was defined as the perpendicular distance between the line connecting both edges of Bruch's membrane and the anterior border of the lamina cribrosa, at the maximum depth point. An experienced operator manually segmented ALCD and a mean of the two consecutive blinded measurements was computed. To guarantee observations' independence, only one eye was considered per subject. Only high-quality images were accepted. The tenets of the Declaration of Helsinki were followed. Statistical analyses were performed using STATA 13.0.
Results Studied population included 44 subjects (26 women), with a mean age of 62.9 ± 14.3 years. Mean vertical and horizontal maximum ALCD was 453.3 ± 88 µm and 436.1 ± 78.7 µm, respectively. Neither gender nor age were associated with these ALCD scans (p>0.05). When controlling for gender, age and spherical equivalent, maximum vertical and horizontal ALCD increased, respectively, by 8.8 µm (95% confidence interval [CI], 0.6-17.0 µm; p=0.04) and 8.1 µm (95% CI, 0.4-15.7 µm; p=0.04) per mmHg increase in IOP.
Conclusions Our sample of healthy subjects presented a statistically significant positive linear relation between IOP and ALCD, when controlling for possible confounding factors. Our results may trigger furthers studies to better elucidate the role of IOP in morphological and functional dynamics of the ONH.

• 2542

Intra and inter-rater agreement of anterior lamina cribrosa depth measurements using enhanced-depth imaging optical coherence tomography

LEAL I (1,2), Cordeiro Sousa D (1,2), Couceiro R (1,2), Barata A (1,2), Abegao Pinto L (2), Pinto F (1,2), Marques-Neves C (1,2,3)
(1) Hospital de Santa Maria - Lisbon Academic Medical Center, Ophthalmology, Lisbon, Portugal
(2) Faculty of Medicine of Lisbon, Ophthalmology, Lisbon, Portugal
(3) Centro de Estudos das Ciencias da Visao, Ophthalmology, Lisbon, Portugal

Purpose To determine intra and inter-rater agreement of anterior lamina cribrosa depth (ALCD) manual measurements using enhanced depth imaging spectral-domain optical coherence tomography (EDI-OCT).
Methods Double blind prospective observational study between Dec/14-May/15. EDI-OCT of optic nerve head was performed in subjects with an irrelevant ophthalmologic history (2 cross scans: vertical and horizontal). ALCD was defined as the perpendicular distance between the line connecting both edges of Bruch's membrane and the anterior border of the lamina cribrosa, at the maximum depth point. Two double-blinded experienced operators manually measured ALCD twice, with a one-month interval. Intra and inter-rater agreement was evaluated using intraclass correlation coefficients (ICC), concordance correlation coefficients (CCC) and Bland-Altman (BA) plots for the right eye vertical (RV) and horizontal (RH) scans and left eye vertical (LV) and horizontal (LH) scans. Statistical analyses were performed using STATA 13.0.
Results Studied population included 44 subjects (26 women), with a mean age of 62.9 ± 14.3 years. Mean vertical and horizontal maximum ALCD was 453.3 ± 88 µm and 436.1 ± 78.7 µm, respectively. Intra-rater ICC for ALCD in RV, RH, LV and LH were 0.98, 0.94, 0.97 and 0.96, respectively. Inter-rater ICC for ALCD in RV, RH, LV and LH were all 0.99. Intra-rater CCC for ALCD in RV, RH, LV and LH were 0.98, 0.93, 0.97 and 0.96. Inter-rater CCC for ALCD in RV, RH, LV and LH were all 0.99. Bland-Altman plots suggested that almost all observations were within the 95% limits of agreement.
Conclusions ALCD manual measurements with EDI-OCT showed high agreement among intra and inter-rater measurements in healthy eyes. EDI-OCT is a reliable tool for ALCD measurement, which can provide potentially useful information for integrated glaucoma management.

• 2543

Evaluation of the lamina crivosa thickness and depth, the prelaminar nerve tissue thickness and the Bruch's membrane opening-based minimum rim width in eyes with and without primary open-angle glaucoma: an enhanced depth imaging OCT study of the optic nerve head and the correlation between anatomy and function

GAMA I , Almeida L , Gonçalves I , Monteiro-Grillo M
Hospital Santa Maria — Centro Hospitalar Lisboa Norte, Ophthalmology, Lisboa, Portugal

Purpose To evaluate the lamina crivosa(LC)thickness(LCT), depth(LCD), prelaminar thickness (PLTT) and Bruch's membrane opening-based minimum rim width (BMO-MRW) in primary open-angle glaucoma(POAG) and normal eyes(NE) and their correlation with function(MD).
Methods This observational study included 45 eyes(25 eyes with POAG;20 normal eyes),which were evaluated clinically,by applanation tonometry, pachymetry,Octopus perimetry and by enhanced depth imaging-optical coeherence tomography(EDI-OCT).A grid scan of the optic herve head(ONH),averaged 80scans,to image the LCT,LCD and PLTT in center, mid-inferior(I-ONH), and superior positions and a nerve fiber layer (NFL) scan were done.LCT was the distance between borders of the LC. LCD was the distance between BMO reference line-anterior LC border. BMO-MRW was the shortest distance between BMO and internal limiting membrane.All values were compared between both groups and correlations between variables were tested.
Results Global LCT was lower in POAG(132,9±40,1µm) than in control group(235,9±36,8µm,p<0,05).Mean LCD was higher in POAG (572,2±195,2µm).Mean PLTT was lower in POAG (91,9±49,9µm,p<0,05),as occurred with BMOMRW.In all eyes,the global LCT was correlated to NFLT(R=0,61)and BMOMRW(R=0,67;p<0,001). In POAG eyes, global NFL was correlated to BMOMRW (R=0,67) and the PLTT(R=0,386).In I-ONH scan,PLTT was correlated with LCD (R=-0,502) and inferior-temporal(IT)-NFLT(R=0,479,p=0,015).MD was correlated with PLTT(R=-0,597)and MBOMRW (R=-0,670,p<0,01).
Conclusions Glaucoma can cause a decrease in LCT,PLTT,BMOMRW and increase in LCD,being potential markers of glaucomatous damage.Some ONH-OCT parameters correlated with function,as measured by the MD. ONH EDI-OCT imaging with automatic segmentation would be useful in glaucoma evaluation.

• 2544

Pigment epithelium central limit - Inner limit of the retina, Minimal Distance, PIMD, a morphometrical variable for glaucoma follow-up

SANDBERG MELIN C (1,2), Malmberg F (3), Malmqvist L (1), Talebizadeh N (1), Yu Z (1), Söderberg P (1)
(1) Uppsala University, Gullstrand lab-Opthalmology- Neuroscience, Uppsala, Sweden
(2) Uppsala University, Region Gavleborg, Gävle, Sweden
(3) Uppsala University, Information Technology, Uppsala, Sweden

Purpose To establish the resolution of measurements of the minimal distance between the central limit of the pigment epithelium and the inner limit of the retina (PIMD) as measured with OCT.
Methods The optic nerve head was topographically recorded with OCT (Topcon 3D, OCT-2000, protocol: 6x6 mm 3D disc cube). The minimal distance between the inner limit of the retina and the central limit of the pigment epithelium was sampled 8 times resolved in 500 angles.
Results The angular minimal distance was longer in the upper and the lower meridian and averaged 0.21 mm. An analysis of the consequence of the resolution demonstrated that the minimal relevant significant average difference at $\alpha = 0.05$ and aiming for $\beta = 0.02$ was 0.11 change (mm)/Average (mm). Thus, a change of 0.024 mm integrated over 2π is the detection limit at the selected statistical parameters. This corresponds to a local average change within one quadrant of 0.006 mm.
Conclusions PIMD has the potential to be a useful variable for follow-up of nerve fiber loss in the optic nerve head.

• 2545

Subjective versus objective vertical cup-disc-ratio assessment in open angle glaucoma patients.

VANDEWALLE E (1), Willekens K (1), Van Keer K (1), Abegao Pinto L (2), Stalmans I (1)
(1) UZ Leuven, Ophthalmology, Leuven, Belgium
(2) Centro Hospitalar Lisboa Norte, Ophthalmology, Lisbon, Portugal

Purpose To evaluate the difference in assessment between fundoscopic and confocal scanning vertical cup-disc-ratio (VCDR) in open angle glaucoma patients.
Methods Data from a single eye of normal tension (NTG) and primary open angle glaucoma (POAG) patients from the Leuven Eye Study were included: age, gender, visual field mean deviation (MD), fundoscopic and HRT III VCDR assessment as well as mean retinal nerve fiber layer thickness (mRNFL). Differences within groups were assessed by paired sample t-tests. Receiver operator curves (ROC) were constructed to assess and compute the likelihood ratio and positive predictive value.
Results 303 eyes (161 POAG and 142 NTG) were included. The average VCDR clinically assessed was significantly larger than the value derived from the HRT III software (0.81 ±0.14 versus 0.61±0.16, p<0.001) and this difference remained statistically significant in both groups. In advanced glaucoma (MD>-12dB) , the area under the curve for HRT III and fundoscopic VCDR was respectively 0.80±0.05 versus 0.84±0.04 for NTG and 0.66±0.044 versus 0.82±0.033 for POAG. To predict a MD of maximum -12dB with 80% certainty in NTG patients the VCDR needs to be at least 0.79 and 0.88 for HRT III and fundoscopic VCDR values, whereas in POAG patients these numbers are 0.88 and 0.93, respectively.
Conclusions Clinical assessment of VCDR renders significantly higher values than HRT III derived values. Fundoscopic assessment of the optic nerve can predict better the visual field damage compared to the HRT III assessment.

• 2546

Gender specific IOP measurement using induced corneal vibration analysis - a multicenter clinical trial

BITOUN P (1), Bouafia K (2), Khoueir Z (3), Haouchine B (2), Hammoud S (3), Chapelle P (4), Chambard J P (5), Jourot P (5), Lachkar Y (3), Benzacken L (2)
(1) GROUPE MEDICAL, Genetique, Paris, France
(2) Robert Ballanger Hospital, Ophthalmology, Aulnay s/b, France
(3) Institut du Glaucome- Hopital St Joseph, Ophthalmology, Paris, France
(4) Agilite, Engineering, Gif s/y, France
(5) HOLO3 Laboratories, Engineering, Saint Louis, France

Purpose Novel non-contact, non-invasive Vibration Tonometry using analysis of induced corneal vibrations and their correlation to GAT IOP was tested in a large multicenter clinical trial .
Methods 470 eyes in 236 volunteers from various ethnic origins at Paris area hospital eye clinic and Glaucoma Institute were studied. History, vibration tonometry measurements in triplicate GAT, NIDEK air puff IOP, refractometry, keratometry and non-contact pachymetry. Algorithm discovery was performed by random draw splitting runs into a discovery sample and a separate validation sample performed 10 times separately in men and women
Results In 236 patients, 34.6% of eyes had glaucoma, 51% of which women. 1311/1772 (76%) vibration tonometry measurements were in correct position. Population aged 20-92 yo with 48.7% females with mean of 62.1(+/-13.5) in women and 62.5 (+/-12.7) in men. CCT mean was 531.2µ (+/-37.3) in women and 534.8µ (+/-38.5) in men. 207 patients AL mean was 23.29 mm (+/-1.68) in women and 23.73 mm (+/-1.68) in men. GAT IOP ranged from 5.3 to 34 mm Hg, mean was 15.2 mm Hg (+/-3.1) in women and 15.2 (+/-3.52) in men -No significant differences . No adverse events during or post trial. Algorithm for women yielded 98,6% of IOP mean within 5 mm Hg of mean GAT IOP and 86% within 3 mm Hg. For men 96.4% of IOP mean was within 5 mm Hg of mean GAT IOP and 84.2% within 3 mm Hg from GAT IOP mean. Using the mean of 2 closest measures was used .
Conclusions Current algorithm shows no influence of CCT on IOP. Gender Specific algorithm concurrs with previous publications of different corneal hysteresis (lower) in women. Vibration tonometry is a valuable method for measurement of IOP without contact with precision and reproducibility independently of CCT. It may be a valuable tool for IOP measurement in thin and surgical corneas.

Commercial interest

• 2551

Three-dimensional structure of the mammalian limbal stem cell niche

BORDERIE V (1), Grieve K (1), Ghoubay D (1), Georgeon C (1), Thouvenin O (2), Bouheraoua N (1), Pâques M (1)
(1) Institut de la Vision- CHNO des XV-XX, Ophthalmology, Paris, France
(2) Institut Langevin- 1 rue Jussieu, Physics, Paris, France

Purpose Although the existence of the limbal stem cell (LSC) niche is accepted, precise knowledge of its 3D architecture remains incomplete.
Methods The LSC niche was explored on freshly excised corneoscleral rims from human donors (n=47), pigs (n=15) and mice (n=27) with full-field optical coherence microscopy (FFOCM).
Results Limbal crypt features were detected in 90% of human corneoscleral rims, extending between the palisades of Vogt as radial (74%) and/or rounded (23%) forms, often branching off to or becoming interconnected by sub-scleral radially or circumferentially oriented crypts (56%). [kg1] Mean crypt volume represented 16% of sampled limbal volume on the vertical axis and 8% on the horizontal axis. In pigs, palisades were finer and crypts wider with relatively uniform distribution around the eye, and radial orientation, connecting to numerous narrow criss-crossing invaginations beneath the sclera. In mice, only a circumferential limbal trough was detected. Mean crypt volume represented 13% of limbal volume in humans, 9% in pigs and 7% in mice. FFOCM combined with fluorescence showed presence of p63-α+ cells and cytokeratin-3+ cells in the limbal crypts. LSC density increased with percentage limbal volume occupied by crypts. Colony Forming Efficiency increased with limbal crypt volume.
[kg1]See how to rephrase all this
Conclusions Crypt architecture in the three species appears associated with eye exposure to light. Clone production correlated strongly with the limbal crypt volume in humans indicating that limbal crypts constitute a niche for adult limbal stem cells. FFOCM imaging could assist in assessment of the richness of the limbal crypts and targeted biopsy for cell culture.

• 2552

Assessing the microstructures of the human cornea using Gabor-Domain optical coherence microscopy with large field of view and high resolution

THURET G (1), Tankam P (2), He Z (3), Lanis M (4), Canavesi C (5), Lepinet T (6), Hindman H (7), Topham D (8), Gain P (3), Rolland J P (2)
(1) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA 2521- SFR143- Faculty of Medicine- and Institut Universitaire de France- Paris, Saint Etienne, France
(2) University of Rochester, The Institute of Optics and Center for Visual Science, Rochester- NY, United States
(3) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA 2521- SFR143- Faculty of Medicine, Saint Etienne, France
(4) University of Rochester, Department of Biomedical Engineering, Rochester- NY, United States
(5) LighTopTech Corp., R&D, West Henrietta- NY, United States
(6) University Jean Monnet, Laboratoire Hubert Curien UMR-CNRS 5516 and Biology- engineering and imaging of the corneal graft laboratory EA2521, Saint Etienne, France
(7) University of Rochester Medical Center- School of Medicine and Dentistry, Ophthalmology, Rochester- NY, United States
(8) University of Rochester Medical Center, Department of Microbiology and Immunology-, Rochester-NY, United States

Purpose To investigate the performances of a new large field of view and high volumetric-resolution Gabor-Domain Optical Coherence Microscope (GD-OCM) in imaging human corneal microstructures
Methods The GD-OCM combined the high sectioning capability of optical coherence tomography with the high lateral resolution of confocal microscopy. We developed a system that achieved high-contrast imaging with a field of view of 1x1 mm2 and volumetric cellular resolution of 2 µm across a thickness of up to 2 mm in tissue. The system fitted on a movable cart and the handheld scanning probe was attached to an articulated arm that may be adjusted to image different locations of the cornea without contact. For real time visualization, we implemented a parallelized Multi-Graphic Processing Units architecture to speed up the processing of data. In this investigation, we focused on imaging the microanatomy of the corneal stroma keratocytes as well as corneal endothelial cells of ex vivo human corneas maintained in an innovative bioreactor
Results The overall time to 3D visualization, including acquisition that is 1.5 minutes, processing and rendering of a 1000x1000x400 voxels, was less than 2 minutes compared to 2 hours on a conventional CPU. The system produced 3D high-resolution images of the distribution of epithelial cells, stromal keratocytes and endothelial cells, comparable to standard in vivo confocal microscopy
Conclusions This innovative GD-OCM allows pseudo histology of the cornea in an unprecedented wide field and a short acquisition time compatible with analysis of ex vivo living corneas

• 2553

Posterior corneal surface: new insights in curvature and astigmatism

PATEL S , Wacker K
Mayo Clinic College of Medicine, Ophthalmology, Rochester, United States

Purpose In normal eyes, a fixed relationship between anterior and posterior corneal astigmatism is assumed, especially for lens power calculations. This study assessed the association between anterior and posterior corneal astigmatism and thickness.
Methods Normal corneas were examined by slit-lamp microscopy and Scheimpflug imaging. The differences between vertical and horizontal thicknesses at 4-mm and 6-mm-diameters were calculated. Anterior and posterior astigmatism were calculated as the difference between steep and flat powers based on the corresponding radii of curvature and refractive indices. Comparisons and significances of correlations were assessed by using generalized estimating equation models.
Results Fifty-four subjects (101 corneas) aged 18–80 years were included. Peripheral corneas were thicker vertically than horizontally ($p < 0.001$) at 4 mm by 13.4 ± 9.4 µm (mean ± standard deviation) and at 6 mm by 8.6 ± 4.8 µm. Anterior corneal astigmatism was 1.08 ± 0.57 D and was aligned vertically (73%), horizontally (6%), or obliquely (21%). Posterior corneal astigmatism was -0.31 ±0.13 D and was aligned vertically (94%) or obliquely (6%). Anterior and posterior astigmatism were correlated in eyes with vertical anterior astigmatism ($r = 0.65$; $p < 0.001$), but not in eyes with oblique or horizontal anterior astigmatism. The difference between vertical and horizontal corneal thickness correlated with posterior astigmatism at 4 mm ($r = -0.58$; $p < 0.001$) and at 6 mm ($r = -0.61$; $p < 0.001$).
Conclusions The posterior cornea is normally ellipsoid in shape with a steep vertical meridian that corresponds to the cornea being thicker in the vertical paracentral region. Understanding the normal relationship between anterior and posterior corneal surfaces is important when assessing the same in corneal diseases.

• 2554

Computerized analysis of human corneal endothelium morphology

RUGGERI A , Scarpa F
University of Padua, Department of Information Engineering, Padua, Italy

Purpose Corneal images acquired by in-vivo microscopy provide clinical information on the cornea endothelium health state. The reliable estimation of the 3 clinical morphometric parameters (endothelial cell density, pleomorphism, polymegethism) requires the accurate detection of cell contours in a large number of cells. Thus for the practical application of this analysis in clinical settings an automated method is needed.
Methods The contours of cells are detected using a genetic algorithm. It randomly modifies individuals from the current population to produce the children for the next generations, which evolve toward an optimal solution. We start with a small set of vertexes forming regular hexagons, which in successive generations evolve into polygons with possibly different number and positions of vertexes. Each vertex is positioned by considering both its correspondence with the actual image (pixels intensity) and the regularity of the resulting polygons. The goal is to obtain a final population of vertexes forming polygons that best fit the cells contours in the actual image.
Results 15 images were acquired with a specular endothelial microscope (SP-3000P, Topcon Co, Japan) in healthy and pathological subjects. Ground truth values for the 3 parameter were obtained from manually drawn cell contours. Differences between this manual estimation of the parameters and the automated one were always less than 8%.
Conclusions These preliminary results show the ability of the proposed algorithm to adapt to different shapes and sizes of cells and to allow the reliable estimation of the morphometric parameters used in clinical practice.

• 2555

Differential molecular signature of ectatic and non-ectatic areas from Keratoconus patient corneas.

PAHUJA N (1), Rajiv Kumar N (2), Shetty R (1), Shroff R (1), Ghosh A (2)
(1) Narayana Nethralaya, Cornea, Bangalore, India
(2) Narayana Nethralaya, GROW lab, Bangalore, India

Purpose To evaluate if the gene expression profile of corneal epithelium from the cone area in Keratoconus (KC) differs from the peripheral non-ectatic areas Hypothesis: The ectasia in Keratoconic cornea is localized to the cone while the peripheral areas are apparently normal. Hence we hypothesized that within the cone of a KC patient cornea, the structural weakness may be a function of localized gene expression differences
Methods Study group contained 54 KC patients undergoing epithelium off corneal collagen crosslinking (CXL) and 9 non-ectatic subjects undergoing photo refractive keratectomy (PRK) as controls. The cone vs periphery distinction is based on keratometry and location of the cone based on elevation map. Using a 4.5 mm trephine centered on the cone, epithelium was scraped separately for cone and rest as periphery. In non-ectatic controls, the central 4.5 mm area was taken as cone. Gene expression profiling was performed for each pair of cone and periphery samples by quantitative PCR.
Results Lysyl oxidase levels were significantly reduced in the cone of KC patients (p=0.002). Structure related genes COL1(p=0.01) and COL4(p=0.008) were also reduced significantly in KC patient cones. The cytokines IL6, TGFβ and TNFα did show an increased trend; regulatory cytokine IL10 did not show significant trend. Matrix remodeler MMP9 showed an increasing trend at the cone while its inhibitor TIMP1 showed a reducing trend that was not significant(p=.09).
Conclusions Ectasia in KC may be driven by local molecular factors at the cone that possibly spreads to other parts of cornea as disease progresses

• 2556

Assessment of the performances of a handheld in vivo confocal microscope for the analysis of human corneal innervation

BREHON A (1), Perrot J L (2), Cinotti E (2), Labeille B (2), Grivet D (3), Crouzet E (1), Gain P (1), Thuret G (4)
(1) Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering, Faculty of Medicine- Jean Monnet University, Saint-Etienne, France
(2) University Hospital, Department of Dermatology, Saint-Etienne, France
(3) University Hospital, Department of Ophthalmology, Saint-Etienne, France
(4) Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine- Jean Monnet University- Saint-Etienne- France- and Institut Universitaire de France, Bd St Mich,

Purpose We previously reported, for the first time, the use of a dermatological handheld in vivo confocal microscope (IVCM), VivaScope 3000 (Lucid, NY), for the imaging of the ocular surface and ocular adnexa (AmJOphthalmol2015;159:324). Aim: to further assess its performances for qualitative and quantitative analysis of corneal innervation.
Methods Clinical interventional prospective single-center study comparing the first version of the handy handheld VivaScope 3000 with the Heidelberg Retina Tomograph (HRTIII-RCM) as a reference. The right central subbasal plexus (SBP) of healthy corneas of non-diabetic patients, diabetic patients without peripheral neuropathy and diabetic patients with peripheral neuropathy was analyzed the same day with both IVCMs by the same observer. The three best images were selected for each device and the nerve density, the number of nerves by frame, the number of branch per frame, and tortuosity of the nerves of the central SBP were calculated using NeuronJ. Analyzes were done on similar areas, blind to the IVCM type, then on full fields.
Results The VivaScope provided 920 x 920 µm images versus 400 x 400 µm for the HRTIII-RCM. Images of the SBP were easily obtained but the 4 parameters were significantly lower in the 3 populations with the VivaScope despite a larger field of view. Comparisons between populations are ongoing.
Conclusions This handheld dermatological IVCM is able to image the SBP but is less informative than the static HRTIII-RCM. For SBP, the larger field is not an advantage because most of the field is out of focus. Improvements of the IVCM objective are proposed. GRANT: project INNOVEYE GIRCI RAA.

• 2557

Contribution of Optical Coherence Tomography (OCT) with real-time OCT of the Femtosecond laser, and per operative OCT of the microscope in deep anterior lamellar keratoplasty (DALK) for keratoconus: a new technique

NGUYEN D T (1), Stephan S (1), Gleize S (2), Cochereau I (1), Gabison E (1)
(1) Hopital Fondation Rothschild, ophthalmology, Paris, France
(2) French Bank of Eyes, grafts, Paris, France

Purpose Deep anterior lamellar keratoplasty (DALK) is a treatment of choice for keratoconus. We evaluate the contribution of a new technique associating femtosecond laser with real-time OCT, and per-operative OCT on the microscope, in DALK surgeries forkeratoconus.
Methods After training on artificial anterior chambers of corneal grafts to evaluate the reproducibility of cuts, pre-cuts of human anterior corneal lamellae during DALK of keratoconus were realized using the femtosecond laser (Victus, Bausch and Lomb) with real-time OCT and a curved applanation's surface. The depth was caculated around 60% of the thinnest pachymetry. Surgeries were realized using the per-operative OCT with the Rescan system of the microscope (Lumera 700, Zeiss).
Results Curved applanation and visualization with real-time OCT of the cuts' depth enabled the realization of reproducible lamellar cuts on 200µ thick corneas, without modifying the laser-cornea interface neither using masking agents. Femtosecond laser cuts allowed the big-bubble formation on 10/10 ex-vivo corneas. In human surgeries, real-time OCT visualization allowed controlling non-penetrating cuts, and the curved applanation limited folds formation on the residual stroma. Each surgical step was controlled by per-operative OCT, with visibility of tissues' structure and thickness, and instruments in cross section. The Anwar-air dissection technique permitted the "big-bubble" formation in 7/7 case, clearly visible on OCT, with only 1 or 2 injections of air. Residual posterior stroma was resected realizing pre-descemetic lamellar grafts.
Conclusions This new technique, femtosecond laser associated with per-operative OCT, appears to be safe, effective, reproducible and time-saving in DALK surgeries, facilitating the "big-bubble"formation. It may be proposed for the management of keratoconus and other indications.

• 2561

Review of the anatomical and physiological bases of stability of gaze

BORRUAT F X
Hopital Ophtalmique Jules Gonin, Neuro-Ophthalmology, Lausanne, Switzerland

In order to benefit from the advantages of a highly developed fovea, steadiness of gaze is mandatory. Visual fixation and gaze stability under static and dynamic conditions is achieved via several pathways : vestibulo-ocular, optokinetic, and smooth pursuit systems. Further a proper control of saccades is necessary. A synthetic review of these systems will be provided. At the end of the session the participants should be able to understand why and how abnormal spontaneous eye movements can be generated.

• 2562

Congenital forms of nystagmus

KAESER P F
Hôpital ophtalmique Jules Gonin, Lausanne, Switzerland

Congenital benign forms of nystagmus have to be recognized and distinguished from acquired forms caused by neurologic lesions, in order to avoid unnecessary investigations. This distinction can usually be made on clinical grounds. Congenital forms of nystagmus include idiopathic infantile, ocular (most commonly associated with albinism, macular or optic nerve hypoplasia, and congenital retinal dystrophies) and latent nystagmus of the congenital esotropia. At the end of the session, participants should be able to identify these specific forms of nystagmus.

• 2563

Acquired forms of nystagmus not to be missed

BORRUAT F X
Hopital Ophtalmique Jules Gonin, Neuro-Ophthalmology, Lausanne, Switzerland

The purpose of this section will be to present and discuss some of the most recognizable forms of acquired nystagmus. The followings will be discussed : vestibular nystagmus, downbeat nystagmus, upbeat nystagmus, and dissociated nystagmus. At the end of the session, participants should be able to identify these specific forms of nystagmus and organize proper investigations accordingly.

• 2564

Alterations of stabilization of the eyes under dynamic conditions

KAESER P F
Hôpital ophtalmique Jules Gonin, Lausanne, Switzerland

Dynamic stabilization of the eyes depends mainly on vestibulo-ocular reflex (VOR). VOR is initiated by the labyrinth of the inner ear and is modulated by the cerebellum. During head motion, the VOR stabilizes the retinal image by producing an opposite synchronized eye movement. If the retinal image is not steady enough on the retina, visual acuity will drop. The cerebellum integrates eye velocity, retinal slip, motor feedback and vestibular afferences to modulate the VOR. Therefore, inadequate VOR generation or modulation will result in visual loss under dynamic conditions. At the end of the session, participants should be able to identify VOR dysfunction and organize proper investigations accordingly.

• 2565

Abnormal non nystagmic spontaneous eye movements

BORRUAT F X
Hopital Ophtalmique Jules Gonin, Neuro-Ophthalmology, Lausanne, Switzerland

When the saccadic system is dysfunctional, an intrusion of spontaneous unwanted saccades can disrupt visual fixation. These can present as square wave jerks, ocular flutter and opsoclonus. Voluntary nystagmus is also a sequence of abnormal saccades. At the end of the session, participants should be able to identify these specific eye movement disorders and organize proper investigations accordingly.

• 2571

Treg-based immunotherapy of non-infectious uveitis (NIU)

ASNAGLI H (1), Jacquin M (1), Belmonte N (2), Gertner-Dardenne J (2), Hubert M F (3), Sales A (4), Foussat A (5)
(1) TxCell, Preclinical Pharmacology and Safety, Valbonne, France
(2) TxCell, New Products, Valbonne, France
(3) COLA, Ophtalmology, Jozerand, France
(4) Vetopath, Histopathology, Antibes, France
(5) TxCell, Valbonne, France

Purpose Col-Treg is a T-cell immunotherapy composed of autologous type-1 regulatory T (Treg) cells specific for collagen-II. Col-Treg are tested in NIU mice as collagen-II is present in the eye, allowing the triggering of their activity in situ. NIU is one of the most common cause of blindness in the developed world.
Methods Col-Treg cells are produced from blood of healthy volunteers or splenocytes of mice transgenic for collagen-II-specific TCR. Cells are characterized for marker expression using FACS and for in-vitro immuno-modulatory function. NIU model was induced by IRPB immunization. In-vivo efficacy was evaluated with ophthalmoscopy histology, pro-inflammatory cytokines analysis. In-vivo tracking was performed using a Col-Treg TCR specific quantitative PCR.
Results Col-Treg secrete IL10, IL13 and express GITR, CD39 and Granzyme B, molecules involved in the control of inflammation. Col-Treg hydrolyse ATP, kill myeloid cells and inhibit T effector cell IL17 and IFNg secretion. Intravenous administration of Col-Treg inhibited ocular inflammation in NUI mice with reduction of cellular infiltrates, IL1β, IL6, TNFα. In-vivo-tracking demonstrated a tropism of Col-Treg for inflammatory eyes. In-vivo GLP toxicity study in healthy mice did not revealed Col-Treg related adverse events. Characterization of human Col-Treg GMP batches demonstrated comparability with mouse Col-Treg for marker expression and in vitro function.
Conclusions These data demonstrate the safety and efficacy of Col-Treg administration for the treatment of NIU in mice, suggesting that Col-Treg could be used as a therapeutic tool for patients with non-infectious uveitis refractory to approved medications.

Commercial interest

• 2572

The role of dendritic cells in non-infectious anterior uveitis

O'ROURKE M (1), Canavan M (2), Sweeney C (3), Fletcher J (4), Fearon U (2), Murphy C (5)
(1) Royal Victoria Eye and Ear Hospital- Dublin, RCSI Dept of Ophthalmology, Dublin, Ireland
(2) St Vincent's University Hospital, Rheumatology Research Group, Dublin, Ireland
(3) St Vincent's University Hospital, Education and Research Centre, Dublin, Ireland
(4) Trinity Biomedical Sciences Institute, Schools of Medicine and Biochemistry & Immunology, Dublin, Ireland
(5) Royal Victoria Eye and Ear Hospital, RCSI Dept of Ophthalmology, Dublin, Ireland

Purpose Noninfectious uveitis is characterised by influx of inflammatory cells into the immune-privileged ocular microenvironment. Dendritic cells (DC) are powerful antigen presenting cells (APCs) and thereby initiate and perpetuate inflammation. Animal models of uveitis have suggested alterations in DC contribute to pathogenesis. Firstly, we examine the phenotype of circulating DC in anterior uveitis (AU). Secondly, we characterise the influxing inflammatory cells in the local micro-environment of inflamed aqueous humor (AqH). Finally, the effect of this inflamed microenvironment on a DC model is examined.
Methods Circulating DC were defined as HLA-DR+, Lineage- and CD11c+. CD40, CD80 and CD83 cell surface expression was used to assess activation and maturation of circulating DC. Cells isolated from AqH obtained from AU patients (n=5) and HC were assessed by flow cytometry based on cell size, granularity and cell surface expression. 1:2 dilution of AqH supernatant was cultured with monocyte derived DC (moDC) model obtained from a healthy donor for 48 hours and activation and maturation markers on moDC assessed.
Results There is a decrease in circulating DC in AU patients compared to HC ($p<0.01$). Circulating AU DC express higher CD40 ($p<0.05$). Inflamed AqH contains >98% CD45+ cells. Populations of neutrophils (CD15+ HLA-DR-), T cells(CD3+ and either CD4+ or CD8+) and APCs (HLA-DR+ CD11c+) were identified. HC AqH is devoid of CD45+ cells. AU AqH induces CD40 ($p<0.01$) and CD80 ($p<0.01$) expression on moDC compared to HC.
Conclusions These results suggest that DC are recruited from the circulation to the eye during AU. AqH from AU patients can activate DC which will lead to initiation and propagation of inflammation. Current work examines functional effects on allogenic CD4+ T cell cocultures. These results suggest DC may be a useful therapeutic target in AU.

• 2573

Interleukin 33/ST2 signaling regulates inflammatory response in choroidal stroma and ocular angiogenesis: implications for age-related macular degeneration.

THEODOROPOULOU S (1), Doyle S (2), Copland D (1), Liu J (1), Wu J (1), Campbell M (3), Dick A (1)
(1) School of Medical Sciences- University of Bristol, Academic Unit of Ophthalmology, Bristol, United Kingdom
(2) Trinity College Dublin, Clinical Medicine, Dublin, Ireland
(3) Trinity College Dublin, Ocular Genetics Unit, Dublin, Ireland

Purpose Age-related macular degeneration (AMD) is a leading cause of irreversible blindness. We wished to elaborate mechanisms that regulate RPE-choroidal microenvironment in AMD. We hypothesize that retinal pigment epithelial cells (RPE) produce interleukin 33 (IL-33) and regulate choroidal stromal fibroblasts and mast cell activation and angiogenesis in an ST2-dependent manner. Through such mechanisms, change in choroidal architecture may contribute to AMD phenotypes observed clinically.
Methods Upon treatment, RPE cells, human choroidal fibroblasts and bone-marrow-derived mast cells (BMMC) were assayed by RT-PCR, Western Blot and ELISA. Choroidal sprouting assay and laser-induced choroidal neovascularization (CNV) were used as models of ocular angiogenesis.
Results TLR-stimulation of RPE significantly up-regulated IL-33 expression. ST2+ BMMC generated a spectrum of inflammatory cytokines when cultured with IL-33 rich RPE supernatant. Pretreatment with IL-33 antagonist markedly inhibited the ability of BMMC to produce inflammatory mediators. Importantly, activation of inflammatory cascade upon RPE supernatant treatment was abrogated in ST2-/- BMMC. In a wound-healing assay, recombinant IL-33 treatment of human choroidal fibroblasts impaired their ability to migrate and contract collagen gel. Furthermore, IL-33 treatment promoted vascular choroidal sprouting in WT and IL33-/- explants. CNV was also regulated by exogenous and endogenous IL-33 in WT and IL33-/- mice respectively.
Conclusions Our data illuminate an endogenous IL-33/ST2 pathway between RPE function and choroidal stroma, influencing tissue remodeling and regulating angiogenesis. Our findings support IL-33/ST2 axis as a therapeutic target in AMD.

• 2574

Systemic IL-1β production as a consequence of corneal HSV-1 infection – contribution to the development of Herpes Simplex Keratitis

MURPHY C , De Chaumont C , Shahnazaryan D , Malone C , Jefferies C , Smith S , Ni Gabhann J
Royal College of Surgeons in Ireland, Ophthalmology, Dublin, Ireland

Purpose Herpes Simplex Virus type-1 (HSV-1) infection can result in keratitis, a sight-threatening disease that is the leading cause of infectious corneal blindness in the western world. HSV-1 can invade the cornea and remain latent after treatment in the trigeminal ganglia. The pathogenesis of HSK involves a complex interaction between cytokines, chemokines and growth factors, either brought in by inflammatory cells or produced locally. Avoidance of these innate anti-viral responses can cause lifelong recurrent infection, which in turn can cause progressive corneal scarring, vascularisation, thinning and the need for corneal transplantation to recover vision, often with poor long-term outcome. This study aimed to investigate peripheral cytokine production in HSK patients with active and inactive infection to identify potential therapeutic targets.
Methods Peripheral blood mononuclear cells and serum were prepared from whole blood taken from both healthy controls and HSK patients during active infection or following treatment. Protein expression levels were analysed by Western Blot. Cytokine levels were determined by multiplex ELISA.
Results Active corneal HSV-1 infection resulted in significantly elevated peripheral levels of the pro-inflammatory cytokine IL-1b in patients compared to healthy controls. IL-1β levels remained significantly increased in these patients following treatment. Impaired production of pro-inflammatory cytokines (including IL-6, IL-8 and TNF-a) and anti-viral factors (including IL-12 and IFN-g) was associated with significantly reduced expression of the transcription factors IRF3 and STAT1 in active patients compared to inactive patients.
Conclusions Our data suggest that dysregulated peripheral production of pro-inflammatory cytokines and anti-viral factors may have implications for HSV-1 viral clearance and recurrent keratitis.

• 2575

Changes in lamina cribrosa and prelaminar tissue in anterior ischemic optic neuropathy

MUNOZ - NEGRETE F J , Rebolleda G , García-Montesinos J , Oblanca-Llamazares N , De Juan V , De Dompablo E
Hospital Ramón y Cajal. IRYCIS, Ophthalmology, Madrid, Spain

Purpose To determine changes in lamina cribrosa (LC) and prelaminar tissue in patients with unilateral non-arteritic anterior ischemic optic neurophaty (NAION) using enhanced depth imaging (EDI) spectral domain optical coherence tomography (SD-OCT).
Methods Seventeen eyes of 17 patients with NAION were prospectively studied. SD-OCT scans using EDI technology were obtained at the acute episode and at two and six months after the ischemic event. The OCT device was set to image a 15x10 degree vertical rectangle centered on the optic disc. The scan in LC was seen clearliest was selected for analysis. The vertical distances from three equidistant points on the reference line (Bruch's membrane opening-BMO) to the anterior prelaminar tissue surface, and to the anterior and posterior surfaces of the LC were measured.
Results At diagnosis, mean prelaminar tissue was significantly thicker and anterior LC surface more posteriorly placed in NAION eyes than in non-involved eyes. During the follow-up, in NAION eyes there was a significant prelaminar thinning and an anterior LCreversal (P=0.001 and P=0.002 at 2 and 6 months respectively). BMO significantly reduced during follow-up (P=0.008 and P=0.034 at 2 and 6 months respectively). Both prelaminar tissue thickness and BMO changes correlated with retinal nerve fiber layer thickness measurements.
Conclusions OHN is a dynamic structure that undergoes biomechanical changes in eyes suffering NAION. A significant prelaminar tissue thickening and posterior lamina cribrosa displacement occurred during the acute ischemic optic neuropathy, that reverse as the edema resolves.

• 2576

The added value of undiluted vitreous biopsy samples processed by the Cellient® tissue processor (Hologic) in unsolved uveitis.

VAN CALSTER J , Van Ginderdeuren R
University Hospitals Leuven, Dept. of Ophthalmology, Leuven, Belgium

Purpose In this prospective study, the added value of undiluted vitreous biopsy samples in the diagnosis of unsolved uveitis was evaluated. Vitreous biopsies are difficult to handle because of the paucity of cells and the gelatinous structure of the vitreous. Histopathological analysis of the vitreous is useful in challenging cases to differentiate uveitis from lymphoma or infection and to define the type of cellular reaction.
Methods 97 consecutive undiluted vitreous samples were isolated in patients with unsolved intermediate or posterior uveitis. A 1.5-2.5cc sample was taken through a single 23G or 27G port using the EVA vitrectomy platform (DORC) with a twin duty cycle high speed cutter. The samples were analysed with the Cellient® tissue processor (Hologic). This machine is a fully automated processor starting from a specified container with PreservCyt® (fixative fluid) with cells to paraffin. Routine histochemical and immunostainings were evaluated.
Results In 94.8% of the cases, sufficient material was found to provide an added value in the diagnostic workup. In 34%, a Cytolyt® mucolytic wash was necessary to prevent clotting of the tubes in the Cellient® tissue processor due to the viscosity of the sample. In 7% the diagnosis was an acute inflammation (presence of granulocytes), in 42% chronic active inflammation (presence of T-lymphocytes), in 36% low-grade inflammation (presence of CD68 cells, with <5% T-lymphocytes); and in 9% a malignant process (lymphoma). In 5% no diagnosis was found. In the chronic active inflammation group 39% was a granulomatous inflammatory process.
Conclusions This standardized protocol for sampling and handling undiluted vitreous biopsies gives a superior result in morphology, number of cells, and possibility of immuno-histochemical stainings. The diagnosis can be established or confirmed in 94.8% of cases.

• 2577

APMPPE as a window on systemic granulomatous inflammation

LABALETTE P (1), Bouabane I (1), Maurage C A (2)
(1) CHRU de Lille, Ophtalmologie, Lille, France
(2) CHRU de Lille, Anatomo-Pathologie, Lille, France

Purpose Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) an unfrequent posterior uveitis presumed to be caused by a general hypersensitivity vasculitis.
Methods Eight patients aged from 12 to 33 years presented with AMPPE were studied. For each patient a systemic work-up for systemic granulomatous disease was performed, including pathologic analysis of accessory salivary glands biopsies.
Results A granulomatous infiltration of the accessory salivary glands biopsies was found in six cases, a feature consistent with a systemic involvement rather than an isolated eye disease. In addition two patients were diagnosed for systemic sarcoidosis.
Conclusions In numerous cases, AMPPE seems to be the eye expression of a systemic granulomatous reaction

Commercial interest

• 2578

Relapsing Polychondritis and its Orbital Manifestations

TEO L (1,2,3), Choo C T (1,2,3)
(1) Singapore National Eye Centre, Oculoplastics, Singapore, Singapore
(2) Duke- NUS Graduate Medical School, Ophthalmology, Singapore, Singapore
(3) Singapore Eye Research Institute, Oculoplastics, Singapore, Singapore

Purpose We describe a 73 year old Chinese Gentleman with bilateral relapsing, remitting orbital inflammatory disease associated with Relapsing Polychondritis (RP).
Methods We reviewed the current literature available on the diagnosis and management of orbital inflamamtory disease in RP.
Results Our patient first presented with right orbital inflammation that did not improve despite antibiotic treatment. Computer tomography (CT) of the orbits showed a soft tissue mass along the roof of the orbit, which was biopsied, revealing acute on chronic inflammation. There was complete resolution of his orbital inflammation within 2 weeks of initiating systemic steroid treatment. He subsequently developed recurrent bouts of left orbital inflammation. One year later, he was diagnosed with relapsing polychondritis and subsequently developed multiple myeloma seven years later.
Conclusions In summary, recurrent orbital inflammatory disease should prompt the Oculoplastics surgeon to exclude a systemic autoimmune disease and hematological malignancy. The course of orbital inflammation in RP can be relapsing and remitting. Co–managementwith a rheumatologist will be helpful to achieve control of the disease with judicious use of immunosuppression. Long-term follow-up of the patient will be necessary to monitor for malignant transformation of the orbital lesion, as well as the development of hematologic malignancies.

• 2611

Principles & Potential application of OCT-Angiography

COSCAS F
CHI de Creteil, Creteil, France

Abstract not provided

• 2612

ANGIO-OCT & DMLA (diagnosis and post-treatment follow-up)

COSCAS G (1), Lupidi M (2), Coscas F (1)
(1) *Universitè Paris XII, Hôpital Intercommunal de Créteil - Service d'Ophtalmologie, Creteil, France*
(2) *University of Perugia, Department of Biomedical and Surgical Sciences- Section of Ophthalmology, Perugia, Italy*

To compare the OCT Angiography (OCT-A) findings to the traditional multimodal imaging (TMI) in patients with exudative AMD (eAMD) in terms of diagnosis and treatment decision.
80 eyes of 73 consecutive eAMD patients diagnosed with different types of CNV were enrolled. The data obtained from the TMI, based on Fluorescein Angiography (FA), Indocyanine green angiography (ICGA) and OCT, were compared with the ones achieved by OCT-A (Spectralis, Heidelberg Engineering, Heidelberg, Germany). The lesion's activity in TMI was established according to leakage on FA, evidence of CNV network on ICGA and fluid accumulation on OCT, while in OCT-A was based on the shape, the branching pattern, the anastomoses, the vessel termini and the perilesional hypo-intense halo. Both OCT-A and TMI allowed the recognition of 5 types of neovascularization (Type I, Type II, Mixed Type I-II, CRA, AMD-related polyps). The two methods achieved the same diagnosis in 95% of cases. The percentage of full agreement in determining the CNV activity between the two imaging protocols was 92.5%. Our study highlights the capability of OCT-A to diagnose, determine the type, grade the activity and guide the treatment of a choroidal neovascular lesion in an eAMD patient.

• 2613

OCT angiography in CNV quantitative follow up

LUMBROSO B
Centro Macula, ophthalmology, Rome, Italy

Optical coherence tomography (OCT) angiography is a novel imaging modality that uses intrinsic flow contrast and does not require any dye injection. It is a less invasive alternative to fluorescein angiography that is 3 dimensional. It is used to image and measure retinal, choroidal and optic disc circulations. Quantitative applications are possible. The angiograms are visualized as cross sections and en face views of separate retinal and choroidal layers. SSADA technology is used in this study.

• 2614

OCT angiography for the evaluation of macular ischemic micro-angiopathies

POURNARAS C J , Frountzou E , Donati G ,
La Colline, Ophthalmology Center, Geneva

The management of maculopathies related to the retinal vascular micro-angiopathies, has been significantly improved since the initiation of intravitreal therapeutical approaches. A detailed evaluation of the vascular abnormalities by Optical coherence tomography (OCT) angiography offers an accurate evaluation of the therapeutical indications and their beneficial anatomical effects. OCT angiography has several advantages, such as 3D visualization of retinal and choroidal circulations (including the choriocapillaris). Using this non-invasive alternative method, ischemia, microaneurysms, intraretinal microvascular abnormalities and the detection of neovascularization can be clearly visualized by a closer observation of each layer of the retinal capillaries. As an alternative to dye-based angiography, in addition to the 3D tomographic macular imaging, OCT angiography may be clinically useful to evaluate the microvascular status and therapeutic effect of treatments for macular ischemic microangiopathies.

• 2615

En Face OCT and OCT-Angiography in ocular oncology

ZOGRAFOS L

Cabinet Privé du Prof. L. ZOGRAFOS, Jules-Gonin Eye Hospital, Lausanne, Switzerland

En Face OCT and OCT Angiography are two innovative diagnostic modalities which were adapted for the diagnosis, therapeutic decision and observation of the evolution following conservative management in ocular oncology. En Face OCT is particulary useful for (1) The definition of the extend of serous retinal detachment and the documentation of its variations (2) The definition of the internal anatomical structure of unpigmented choroidal tumors (3) The definition of the limits of flat and diffused choroidal melanomas in order to define the target volume of the irradiation. Angio-OCT in ocular oncology is mainly used for the definition of retinal vascular lesions observed in radiation induced optic neuropathy and radiation induced maculopathy. This allows a better definition of the therapeutic strategies with anti-VEGF drugs in order to preserve visual function.

• 2621

Is it becoming or coming of age

CORDEIRO M F
Glaucoma & Retinal Neurodegeneration Research Group, UCL Institute of Ophthalmology, London, United Kingdom

The realisation that lowering IOP is unable to prevent progressive vision loss in all glaucoma patients, has led to investigation of neuroprotection as an alternative or additional treatment option. Neuroprotection has gained renewed interest recently as a therapeutic approach to prevent neuronal degeneration and loss of function in glaucoma. Although confirmation of neuroprotective effects by randomized clinical trials is needed, there is now a demonstration of positive non-IOP dependent effects in the LoGTS study. Furthermore, it has been proposed as a treatment strategy in other ocular diseases, such as AMD. Neuroprotection has been advocated for many years in neurodegeneration. Indeed, the therapies that have been suggested in Alzheimer's and Parkinson's Disease are similar to those investigated in ophthalmology. This talk will review the evidence for neuroprotection that led to our assessment of its role in glaucoma now and its application as treatment strategy.

• 2622

Are we there yet?

LEVIN L A
McGill University, Montreal, Canada

It is the rare parent who has failed to hear the plaintive cry of their child asking "Are we there yet?" on a car trip to distant (or near) sites. Similarly, the field of translational research relevant to neuroprotection in glaucoma has asked the same question for more than a decade, perhaps silenced only by the blown cylinder of one famous failed trial. Meanwhile, basic and clinical science have continued to progress despite several potholes along the way. Now that the smoke has cleared and the engine retooled, we are able to see that we currently possess the tools for successfully carrying out trials in glaucoma neuroprotection. This talk will discuss why this is so, focusing on advances in detecting clinically relevant effects, improving the reliability of preclinical data, imaging sensitive biomarkers for "microprogression," and managing the spread of variability associated with translational research. These recent developments will be used to make the argument that not only is the journey to neuroprotection nearing its completion, but it may even be time to start identifying a parking spot.

• 2623

To the clinic and back

GANDOLFI S
University of Parma, Parma, Italy

For a clinician, neuroprotection in glaucoma means "decreasing vision loss without affecting intra ocular pressure". In recent years, translational research on neuroprotection has offered several molecules for clinical testing. Unfortunately, after evaluation via randomized clinical trials, their efficacy is still a matter of debate. We are presently left with excessive patients' attrition, poorly defined outcomes, borderline significances, clinically unrelevant results etc. A re-thinking of the general approach to the issue of neuroprotection in glaucoma is then necessary. The molecules, before being chosen for evaluation in humans, should offer a more striking and unquestionable pre-clinical efficacy profile. New outcomes, on top of the traditional standard automatic perimetry, are needed in order to shorten the duration of the trials and to reduce the "noise" of the system. New study designs, properly tailored on neurodegenrations, together with new strategies for data analysis are needed: futility trials, Bayesian approach and adaptive study designs will extensively be discussed as potential tools to return from the bench to the bedsite.

• 2631

Corneal Imaging Modalities - from Basic Science to Clinical Application

STACHS O
University of Rostock, Department of Ophthalmology, Rostock, Germany

There are many modalities that acquire data about the cornea: shape, power, morphology, biomechanics, and so forth. This talk will review the technologies on corneal assessment techniques and devices available in experimental and clinical practice. Specifically, it will be discussed slit lamp biomicroscopy, ultrasound, magnet resonance tomography, confocal microscopy, ultrasound biomicroscopy, optical coherence tomography, keratometry, Scheimpflug imaging, and dynamic applanation procedures. In addition, I discuss the necessity of developing new technologies for assessing both the morphology and the physiology of the cornea.

• 2632

Corneal ultra-high relocation OCT

SCHMETTERER L
Medical University of Vienna, Medical Physics and Biomedical Engineering and Clinical Pharmacology, Vienna, Austria

Optical coherence tomography (OCT) has revolutionized ophthalmology. Since its introduction more than 20 years ago there was an enormous improvement in resolution, speed and sensitivity. We present a method for imaging the human cornea with a resolution of approximately 1.3 micrometers. This allows for the visualization of corneal tissues with unprecedented precision enabling visualization of structures that could not be seen before. Most importantly the pre-corneal tear film can be visualized and quantified. Data in patients with dry eye syndrome are presented as well as data on the effect of lubricants on tear film thickness. Furthermore the present talk will focus on the imaging of corneal pathologies using this novel device.

• 2633

Clinical use of in vivo confocal microscopy

GUTHOFF R.F.
Germany

Abstract not provided

• 2634

Recent advantages in the imaging of human corneal endothelial cells

THURET G
University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA 2521- SFR143- Faculty of Medicine- and Institut Universitaire de France- Paris, Saint Etienne, France

Sixty years after the understanding of their crucial role in corneal transparency maintenance, endothelial cells (ECs) are back under the spotlight since the development of endothelial keratoplasty and since new drugs and bioengineering techniques are in the pipeline. Accurate and informative imaging techniques are necessary to objectively assess the efficacy of each new therapeutic option. We will describe 3 recent advances in this field. 1/a simple laboratory assay coupled with image analysis that facilitates the assessment of toxicity of any kind of process liable to interfere with ECs. 2/a software that uses optimized algorithms of 3D reconstruction and of cell segmentation in order to increase the accuracy of EC count in eye banks by avoiding parallax errors that occur when ECs are counted in the deep posterior folds of stored corneas. 3/a 3D mapping of the subcellular localization of a set of proteins characteristic of ECs (in absence of a unique marker). We used confocal imaging of fluorescence immunolabelling of structural and functional proteins of normal human ECs. This 3D map could prove useful to characterize cells obtained during bioengineering processes that are candidate to become advanced-therapy medicinal products

• 2641

Masquerade syndromes in children

DESJARDINS L (1), Cassoux N (2)
(1) Institut Curie, Paris, France
(2) Institut Curie, Ophtalmology Oncology, Paris, France

In children the main diagnosis problem are represented by retinoblastomaand rhabdomyosarcoma. Retinoblastoma can sometimes present as an inflammatory disease withconjunctival and orbital inflammatory reactions.Some tumors can be the cause of major vascular dilatation and exudation which can simulate coats disease. Diffuse infiltrating retinoblastoma can simulate uveitis. All these aspects will be described extensively. One has to keep in mind the necessity of complete fundus examination in case of strabismus orleukocoria. In case of unilateral retinal detachment or uveitis, thepossibility of retinoblastoma should always be ruled out before any surgery. Rhabdomyosarcoma usually presents like a rapid exophtalmia withinflammation but can also appear as a conjunctival or palpebral mass. Itshould not be mistaken for infectious disease and orbital biopsy should beperformed promptly.

• 2642

Blepharitis, chalazion, stye - or rather not?

LOEFFLER K
Augenklinik, University Klinikum, Bonn, Germany

Chronic blepharitis and asociated inflammatory alterations of the eyelids are frequent and usually innocuous. However, inflammation can mimic a variety of malignant lesions. By presenting several clinical cases and the corresponding histology, criteria shall be compiled to allow for a more reliable and possibly earlier clinical diagnostic classification.

• 2643

Photopsia, floaters, cataract - a systematic approach to correct diagnosis

TALL M
Helsinki, Finland

It is a well-known fact that more common disease occur more often, but less common ones should not be forgotten about. Photopsia, floaters and cataract – are some of the most common symptoms in patients ophthalmologist see daily. These symptoms are not always worrying, although in reality they can withhold nearly any ocular disease. Uveal melanoma (UM) is one of the rear possibly deadly disease that often lurks behind innocent symptoms. As it is known that earlier treatment of the UM can enhance survival it is essential to recognize the disease at first glance and refer patient quickly to specialized clinic. There are some nuances in the usual symptoms that should ring the alarm bell of every careful eye care professional and prompt a thorough ophthalmic examination.

• 2644

Uveitis - the classic masquerade in adults

KIVELÄ T
Department of Ophthalmology, Helsinki University Central Hospital, Helsinki, Finland

The classic masquerade syndrome in adults is vitreoretinal lymphoma mimicking bilateral uveitis – in about one third of cases, before any evidence of an intracranial lymphoma. It is, however, not the sole neoplastic disease that can lure the clinician to diagnose uveitis. Other examples include posttransplant lymphoproliferative disorder, multiple myeloma, leukemia, histiocytosis, and carcinoma or another amelanotic tumour metastatic to the anterior segment of the eye, and certain paraneoplastic disorders. Making the correct diagnosis needs prior knowledge, a high index of suspicion, careful systemic workup and, quite often, a confirmatory fine needle aspiration biopsy. A further caveat is that in some of these disorders, immunosuppressive treatment may initially appear to be effective. Notably, this apparent effect will prove only temporary, whereas posttransplant lymphoproliferative disorder actually calls for less intensive immunosuppression. This talk will introduce these principles using clinical examples.

• 2645

It is a masquerade! A potpourri of rapid cases

KIVELÄ T
Department of Ophthalmology, Helsinki University Central Hospital, Helsinki, Finland

In this slot, all the speakers will – time permitting – show a quick cavalcade of misleading clinical presentations from ophthalmic neoplasms, different from the most common ones highlighted in preceding talks.

• 2651

Limbal stem cell transplant technology

LAUIDERDALE J
Georgia, United States,

Abstract not provided

• 2652

PAX6 and corneal homeostasia

GABISON E
Fondation A. de Rothschild, Paris, France

Abstract not provided

• 2653

Syndromic manifestations in aniridia patients with PAX6 point mutations

CALVAS P (1), Chassaing N (2), Kaplan J (3), Rozet J M (4)
(1) *Hôpital Purpan, Toulouse, France*
(2) *CHU & Université de Toulouse, Génétique Médicale, Toulouse, France*
(3) *Institut Imagine- UMR1163 INSER-Univ Paris V, Laboratory of Ophthalmic Genetics, PARIS, France*
(4) *Institut IMAGINE- UMR1163 INSERM-Univ Paris V, Lab. of Ophtalmic Genetics, PARIS, France*

The ***PAX6*** gene is associated with various congenital ocular defects. Aniridia is typically associated with mutations introducing a premature STOP codon, whereas missense mutations, of which the majority are located in the paired domain, lead to variant phenotypes. The study provides a survey of ***PAX6*** mutations in patients presenting with extraocular features. We performed sequencing of ***PAX6*** exons and boundaries, search for intragenic rearrangements (QMPSF/qPCR) and CNV analysis (aCGH) in 127 index cases. Genotype-phenotype correlations were searched.We identified mutations in 90% of patients. Yet, a high inter- and intra-familial clinical variability, we noted that heterozygous missense mutations (Asn64, Gly65, Cys66) in Paired-Domain medial 3rd helix were associated with severe phenotypes (e.g. anophthalmia, & CNS malformations). Cases bearing compound heterozygous mutations were affected with severe malformations. Consistent with previous studies, mutations introducing a premature stop codon and gene rearrangements made up the majority. Some genotype-phenotype correlations could be drawn. It is necessary to better delineate the expression of ***PAX6*** mutations to provide patients with a prognosis and to set up a tailor-made follow-up.

• 2654

Pluripotent stem cells, cornea fate and physiopathology

ABERDAM D

The human corneal surface epithelium is continuously repopulated by limbal stem cells (LSCs). Limbal Stem Cell Deficiency (LSCD) can lead to corneal opacity and vascularization, with consequent visual impairment or blindness. Chemical or thermal trauma and congenital diseases, such as congenital aniridia, can lead to LCSD by destruction of the LSC niche. Grafted autologous limbus or cultivated LCS can restore the vision, unless the two eyes are affected. We have recently developed novel culture systems to reprogram hair follicles into induced pluripotent stem cells (iPSCs) and differentiate them into LSC that could become an alternative to animal models for drug cytotoxicity and an alternative autologous source to the shortage of post-mortem cornea transplantation.
Moreover, we identified miR-450 as specific repressor of PAX-6, the eye master gene responsible for proper embryonic eye formation and LSC pool maintenance. As most of the aniridia patients carry mutations on PAX-6 that lead to haploinsufficiency, we are testing if manipulating the level or activity of miR-450 could be used as a therapeutic strategy in aniridia.Thus, iPSCs are valuable for modeling corneal pathologies, and pave the way for future therapy.

• 2655

Aniridia and ocular surface: new insight (part 1)

BREMOND-GIGNAC D (1,2)
(1) APHP- Hôpital Universitaire Necker Enfants Malades, Pediatric Ophthalmology, Paris, France
(2) CNRS Unit FR3636, Binocular vision, Paris V University, France

Abstract not provided

• 2656

Aniridia and ocular surface: new insight (part 2)

CHIAMBARETTA F
University Hospital of Clermont-Ferrand, Service Ophtalmologie, Clermont Ferrand, France

Abstract not provided

• 2661

Lack of correlation between calcium activity in perivascular cells and prostaglandin induced changes in the tone of porcine retinal arterioles in vitro

KUDRYAVTSEVA O , Bek T
Aarhus University Hospital, Department of Ophthalmology, Aarhus, Denmark

Purpose Recently, a population of perivascular cells (PVCs) was identified external to the vascular smooth muscle cells in retinal arterioles. However, it is unknown whether the pattern of Ca2+ activity in the PVCs can support the role of these cells in the regulation of tone in retinal arterioles. Therefore, the purpose of the present study was to identify whether Ca2+ activity in PVCs correlated with contraction of porcine retinal arterioles induced by prostaglandin F2a (PGF2a) and relaxation of these vessels induced by prostaglandin E2 (PGE2).
Methods Porcine retinal arterioles were mounted in a confocal myograph and loaded with the Ca2+-sensitive fluorophore Oregon Green. Ca2+ activity in the PVCs was studied after pre-constriction with U46619 (10-6 M) followed by relaxation induced by PGE2 (10-5 M), or constriction induced by PGF2a (10-5 M). Arteriolar tone and fluorescence from PVCs were recorded in the absence and in the presence of the Ca2+ channel blockers (ryanodine, nifedipine, LOE908, CPA and 2-APB).
Results PGE2 induced significant relaxation and PGF2a significant contraction of retinal arterioles in vitro, but the PVC Ca2+ responses were similar during the two interventions. The percentage of active PVCs and the number of Ca2+ waves were significantly reduced by CPA and 2-APB for both prostaglandins, while the tone responses were unaffected.
Conclusions The effects of PGE2 and PGF2a on the tone of retinal arterioles involve other cell types than PVCs or is active downstream of the PVC pathway, e.g. by a direct effect on the vascular smooth muscle cells.

• 2662

New generation analysis of thrombin generation in retinal vein thrombosis

FRUSCHELLI M (1), Capozzoli M (2), Scapellato C (3), Calzoni P (4), Puccetti L (1)
(1) *University of Siena, Scienze Mediche Chirurgiche e Neuroscienze, Siena, Italy*
(2) *University of Siena, Scuola di Specializzazione in Oftalmologia, Siena, Italy*
(3) *University of Siena, U.O.C. LABORATORIO PATOLOGIA CLINICA AOUS, Siena, Italy*
(4) *University of Siena, U.O.C. EMATOLOGIA E COAGULAZIONE AOUS, Siena, Italy*

Purpose To investigate potential mechanisms involved in retinal vein occlusion (RVO) we evaluated thrombin generation and soluble CD40 ligand (sCD40L) with respect to other known thrombophilic factors.
Methods 68 patients affected by RVO (28 central, 40 branch) and 60 healthy controls were evaluated for endogenous thrombin potential (ETP) by a chromogenic method and sCD40L by ELISA technique. Polymerase chain reaction (PCR) was employed for genetic polymorphisms and coagulative/chromogenic methods for othe coagulation factors.
Results Independently of genetic polymorphisms ETP was increased in patients with CRVO whereas sCD40L was higher in the whole cohort.
Conclusions Our data indicate an involvement of global coagulative activation in CRVO patients as suggested by ETP.

• 2663

Functional Expression of Toll-Like Receptors in Human Retinal and Choroidal Vascular Endothelial Cells

STEWART E , Wei R , Branch M , Sidney L , Amoaku W
University of Nottingham, Academic Ophthalmology, Nottingham, United Kingdom

Purpose Toll-like receptors (TLRs) are a family of proteins that initiate the innate immune response in reaction to invading microbes. Studies confirm the expression of TLRs in a variety of ocular tissues and cells, and it has also been suggested that selected TLRs may be associated with geographic atrophy and neovascularisation in age-related macular degeneration, diabetic retinopathy and other vascular and inflammatory diseases of the ocular posterior segment. However, TLR expression and localisation in the retinal and choroidal vasculature has not been defined.
Methods In this study the gene (mRNA) expression of TLRs 1-10 was investigated using RT-PCR and comparative qPCR and the protein expression and localisation of selected TLRs (3, 4, 6 and 9) were examined using western blotting, flow cytometry and immunofluorescent staining.
Results PCR showed gene expression of TLR1-6 and 9 in human choroidal endothelial cells (hCEC) and TLR2-6, 9 and 10 in human retinal endothelial cells (hREC). Western blotting detected TLR3, 4 and 9 proteins in both hCEC and hREC with higher levels in hCEC, whilst TLR6 protein was not detectable in either cell type. Flow cytometry detected all four TLRs (3, 4, 6 and 9) on the cell surface and intracellularly, TLR6 expression was detectable but low. The expression and localisation of TLR3, 4 and 9 were confirmed by immunofluorescent staining and TLR functionality tested by expression of IL-6 (ELISA) in response to TLR ligands.
Conclusions This study has, for the first time, identified the differential expression and localisation of TLRs in intraocular endothelial cells. This profiling will help inform our understanding of different retinal and choroidal vascular diseases, as well as the development of future treatments for intraocular vascular diseases.

Commercial interest

• 2664

Abnormal lymphatic-like differentiation and endothelial progenitor cell activation in hemi retinal vein occlusion

LOUKOVAARA S (1), Gucciardo E (2), Repo P (2), Lohi J (3), Salven P (3), Lehti K (2)
(1) *Helsinki University Central Hospital, Ophthalmology, Helsinki, Finland*
(2) *Biomedicum Helsinki- University of Helsinki, Research Programs Unit- Genome-Scale Biology, Helsinki, Finland*
(3) *Haartman Institute- University of Helsinki and Helsinki University Hospital-Helsinki- Finland, Pathology, Helsinki, Finland*

Purpose Pathological vascular differentiation in retinal vein occlusion-related neovessel formation remains poorly characterized. The role of the intraocular lymphatic-like differentiation or endothelial progenitor cell activity has not been studied in this disease.
Methods An eye with hemi retinal vein occlusion (RVO) underwent vitrectomy, neovessel membrane located at the optic nerve head was removed and subjected to immunohistochemistry. Characterization of the neovascular tissue was performed using hematoxylin and eosin, α-smooth muscle actin and pan-endothelial cell adhesion molecule (CD31). Expression of lymphatic endothelial cell (LEC) markers was studied by lymphatic vessel hyaluronan endothelial receptor-(LYVE)-1, podoplanin (PDPN), and prospero homeobox protein (Prox)-1. Potential vascular stem/progenitor cells were identified by active cellular proliferation (Ki67) and expression of the stem cell marker CD117.
Results Specimen contained blood vessels lined by ECs and surrounded by pericytes. Immunoreactivity for LYVE-1 and Prox-1 was detected, with Prox-1 being more widely expressed in the vessels. PDPN expression was found in the extravascular structures representing potentially monocyte- or bone-marrow derived cells. Expression of stem cell marker CD117 in actively proliferating Ki67-expressing ECs suggested for vascular endothelial stem cell activity.
Conclusions Intraocular lymphatic-like differentiation coupled with endothelial stem/progenitor cell activation may be involved in the pathology of neovessel formation in ischemia-induced human hemi-RVO.

• 2665

Two-year, Prospective, Multicenter Study of the Use of Dexamethasone Intravitreal Implant for Treatment of Macular Edema Secondary to Retinal Vein Occlusion in France

GUALINO V (1), Korobelnik J F (2), Kodjikian L (3), Delcourt C (4), Leaback R (5), Pinchinat S (6), Velard M E (7)
(1) Clinique Honoré Cave, Ophthalmology, Montauban, France
(2) Bordeaux University Hospital, Ophthalmology, Bordeaux, France
(3) La Croix-Rousse Hospital, Ophthalmology, Lyon, France
(4) Inserm- Centre INSERM U897-Epidemiologie-Biostatistiquede Recherche INSERM Bordeaux- Université de Bordeaux, Epidemiology and Biostatistics, Bordeaux, France
(5) Allergan- Ltd, Medical Affairs, Marlow, United Kingdom
(6) Biostatem, Biostatistics, Castries, France
(7) Allergan- Ltd, Affaires Économiques et des Relations Institutionnelles, Courbevoie, France

Purpose To characterize patterns of use, efficacy, and safety of dexamethasone intravitreal implant (DEX) in treatment of macular edema (ME) due to retinal vein occlusion (RVO) in the French clinical setting.
Methods A 24-month, observational, prospective, epidemiological study conducted at 48 randomly selected sites in France enrolled consecutive patients with ME due to RVO who were treated with DEX at baseline. DEX re-treatment and use of other RVO treatments was at the physician's discretion. The primary endpoint was change in best-corrected visual acuity (BCVA) from baseline to month 6. Secondary endpoints included BCVA change from baseline and adverse events through month 24.
Results Patients (n=375) received a mean of 2.6 DEX injections (range, 1–7) over 2 years; 167 received DEX only and 208 also received other types of RVO treatment. Mean (SD) change from baseline BCVA was +5.1 (19.0) ETDRS letters at month 6 (*P*<.001) and +4.6 (22.3) letters at month 24 (*P*<.001). For patients treated only with DEX during the study, mean (SD) change from baseline BCVA was +8.1 (20.9) letters (*P*<.001) at 24 months, compared with +2.5 (23.0) letters (*P*=.092) for patients moved to other treatments. BCVA improved significantly from baseline at 6 and 24 months in subgroups defined by diagnosis (branch RVO, central RVO), previous treatment, duration of ME, and pattern of DEX use. The most common adverse events were ocular hypertension and cataract.
Conclusions Patients with RVO-related ME treated with DEX in the French clinical setting had efficacy and safety outcomes similar to those seen in the phase 3 registration trials. BCVA gains were maintained over 2 years and largest in patients with recent onset (<3 months) ME, confirming the benefit of early treatment.

Commercial interest

• 2666

Visual Acuity (VA) Outcomes and Impact of Baseline (BL) Perfusion Status in VIBRANT

FELTGEN N (1), Asmus F (2)
(1) University, Ophthalmology, Goettingen, Germany
(2) Bayer Healthcare, Glabal Medical Affairs, Berlin, Germany

Purpose Report additional VA outcomes from VIBRANT.
Methods VIBRANT was a phase 3 study of intravitreal aflibercept (IVT-AFL) vs laser for macular edema (ME) due to branch retinal vein occlusion (BRVO). Patients received IVT-AFL 2 mg every 4 weeks to week 24 (W24) and every 8 weeks thereafter or macular grid laser at BL. Eligible laser patients received IVT-AFL rescue beginning at W24. Primary endpoint was the proportion of eyes gaining ≥15 letters in best corrected VA (BCVA) at W24. Retina was considered perfused for patients with ≤10 disc areas of capillary nonperfusion at baseline.
Results The proportion of eyes gaining ≥15 letters from BL to W24 and W52 was 52.7% vs 26.7% (*P*<0.001) and 57.1% vs 41.1% (*P*<0.03), for IVT-AFL vs laser; 36.3% and 49.5% of eyes receiving IVT-AFL gained ≥15 letters by W4 and W12. Overall mean BCVA gain from BL to W24 and W52 was 17.0 vs 6.9 letters (*P*<0.0001) and 17.1 vs 12.2 letters (*P*<0.004), for IVT-AFL vs laser. W52 results for laser group include patients who received IVT-AFL rescue. In the laser group, 80.7% received rescue IVT-AFL between W24 and W48. In perfused patients, mean BCVA gain from BL to W24 and W52 was 14.3 vs 5.7 and 13.7 vs 11.9 letters; in nonperfused patients, it was 19.1 vs 11.3 and 20.0 vs 15.6 letters. The most common ocular AE, conjunctival hemorrhage, occurred in 24.2% (IVT-AFL) and 15.2% (laser) of patients. Two APTC-ATEs occurred, both in the laser group.
Conclusions Here, IVT-AFL provided statistically and clinically significant VA benefits over laser at W24 that were maintained at W52. Benefits with AFL treatment were not dependent on baseline perfusion status.

Commercial interest

• 2667

Treatment of circumscribed choroidal haemangioma in 2015

MASCHI C (1), Thariat J (2), Baillif S (1), Caujolle J P (1)
(1) Hopital St Roch, Ophthalmology, Nice, France
(2) Centre Antoine Lacassagne, Radiotherapy, Nice, France

Purpose To assess local control and visual outcomes in patients treated for circumscribed choroidal hemangiomas either by photodynamic therapy (PDT) or proton beam therapy (PBRT) delivering 20 Gy(RBE) in 4 fractions after clip placement.
Methods this single institution series included all consecutive patients (pts) treated between 1994 and 2014. Before 2006, PBRT was the sole treatment available with PDT starting in 2006 and becoming the first option with PBRT for select cases or relapses. Descriptive statistics were performed.
Results There were 48 patients, 32 males, 16 females. Twenty and 208 patients were treated with PBRT and PDT respectively. Median follow up was 44 months, longer for PBRT pts. Initial visual acuity (VA) was no different between the 2 groups. More patients undergoing PDT as first option underwent retreatment (PDT 9/28 with 1 or 2 salvage PDT and/or PBRT, PBRT 1/20 with one salvage PDT) (p 0.023). There were more complications with PDT (macular atrophy 7, dsne 1, macular edema 2) than with PBRT (dep 5)(p 0.006). Post treatment visual acuity was not significantly different between the 2 groups (VA ≥ 4 in 84% of PBRT pts, and 59% of PDT pts, p 0.082). Post treatment thickness was better after PBRT (p 0.014).
Conclusions PDT more frequently required retreatments. PBRT is more invasive than PDT but yields better local control rates. VA was similar between PDT and PBRT with a trend for better results with PBRT. VA after PBRT might be improved with lower doses per fraction ; subsequently patients are now treated with 8 fractions up to 20 Gy(RBE).

• 2671

Introduction to the stem cell derived transplants

SKOTTMAN H
University of Tampere, BioMediTech, Tampere, Finland

Stem cell therapy is a potential approach for the replacement of degenerated cells of the eye. For retinal diseases such as age related macular degradation (AMD), the usability of human pluripotent stem cells (hPSC) are widely studied. Several groups have demonstrated that hPSC- derived retinal pigment epithelial cells (RPE) display typical RPE characteristics and the first clinical trials using human embryonic stem cell (hESC) derived RPE are ongoing.
For therapeutic use, the culture of transplantable cells needs to be performed in a culture environment fulfilling quality requirements. For example, the use of xeno-products in cell production should be avoided as this bears the danger of interspecies transfer of viruses and incorporation of immunogenic molecules. In addition, a supporting extracellular matrix or combined artificial scaffold promotes the stem cell differentiation and acquisition of the correct cell characteristics and function. This is especially important for highly polarized RPE cells possible improving cell survival and function after transplantations.

• 2672

Induced to cure: Engineering iPS cell derived RPE scaffolds to treat degenerative eye diseases

BHARTI K
United States

The recent success with embryonic stem (ES) cell derived retinal pigment epithelium (RPE) has provided hope for a cure for degenerative eye diseases. Induced pluripotent stem (iPS) cells are an autologous source of stem cells potentially with fewer immune-challenges as compared to ES cells. Using a developmentally guided differentiation protocol we have developed fully polarized RPE tissue from iPS cells. The RPE monolayer along with its secreted ECM and a degradable scaffold form a tissue that mimics the native tissue in structural and functional properties. This RPE tissue performs several key RPE functions like phagocytosis of photoreceptor outer segments, ability to transport water from apical to basal side, and the ability to secrete cytokines in a polarized fashion. Currently, we are testing the safety and the efficacy of this tissue in animal models. We have begun Phase I Investigational New Drug (IND) enabling studies with the goal to transplant autologous iPS cell derived RPE in patients in advanced Geographic Atrophy stage of age-related macular degeneration (AMD), one of the leading blinding diseases in the US. Our work will provide a potential personalized cell therapy for AMD patients.

• 2673

Subretinal implantation surgery and follow up in pig model

KIILGAARD J F
Rigshospitalet, Eye Dept., Copenhagen, Denmark

The dimension of the porcine eye is similar to the human eye. Combined with an almost identical anatomy to the human eye, the porcine eye makes an excellent model for surgical eye studies. Standard surgical instruments can be used in the pig model, and thereby can new surgical techniques be tested before they are introduced into the human.
Evaluation of the surgical outcome can be performed both in vivo, with fundus photo, OCT and mfERG, and ex vivo with histology, immunohistochemistry and molecular technologies.
Retinal pigment epithelium cells, biological membranes, artificial polymers and stem cells can be implanted in the pig, but the overall idea with subretinal implantation surgery is to regain function in diseased retina. There are transgenic porcine models of known retinal degenerative diseases and different iatrogenic traumas can simulate retinal disease, but there still need for development of new models.

For long time studies mini pigs are essential as modern pigs have been refined to gain weight quickly. Spontaneous regenerative potential and a remarkable resistance to retinal trauma can also invalidate interpretation of the surgical outcome.

• 2674

Subretinal implantation of human stem cell-derived RPE on ultrathin carriers in rabbits

STANZEL B V
(1) Dept. of Ophthalmology, University of Bonn, Bonn, Germany
(2) National Eye Institute, National Insitutes of Health, Bethesda/MD, USA

Transplantation of retinal pigment epithelium (RPE) is being developed as a cell replacement therapy for age-related macular degeneration (AMD). Human embryonic and adult human RPE stem cells (hESC and hRPESC, resp.) are known potential sources that are currently being pursued towards the clinic. Polarized monolayers of SC-derived RPE were shown to grow on biostable polyester (PET) membranes. They were found to be similar to fetal hRPE monolayers and to have near-native characteristics. Stamped pieces of RPE monolayers on the carrier were loaded into a custom-designed surgical instrument and transplanted subretinally in the rabbit, a large-eyed animal model. Compared to fetal and hRPESC derived RPE, hESC-RPE xenografts showed better preservation of the neural retina overlying the implant. Histology obtained 4 weeks after implantation confirmed a continuous polarized human RPE monolayer on PET. We demonstrate that the xeno-RPE monolayer implant survived well and retained its polarization. Moreover, our initial data suggest a distinctly advantageous tolerance of hESC derived RPE xenografts in rabbit subretinal space.

• 2675

Regulation of cell-based medicinal products

LODGE A
London, United Kingdom,

The regulation of cell-based medicinal products in the EU is governed by legislation for medicinal products in general plus dedicated regulations for advanced therapy medicinal products (ATMPs). In addition, the procurement and use of the tissues and cells used to manufacture these products are regulated by additional legislation. This presentation will focus on how a regulatory strategy for bringing a cell-based ATMP under development into clinical trials and ultimately to marketing authorisation should be formulated around all relevant legislation and the guidelines used to implement it. A regulatory strategy should address the quality, safety and efficacy aspects of a medicinal product intended for human use, through defined strategies around CMC (chemistry, manufacturing and controls), nonclinical studies and clinical trials. In addition, regulatory routes to clinical trials and market authorisation that are appropriate to the ATMP under development should also be considered from an early stage, for example including orphan designation, paediatric investigation plans and accelerated approval schemes. Building a regulatory and product development strategy around these elements for a cell-based ATMP will be outlined.

• 2711

New paradigms in Glaucome?

NORDMANN J P
Service d'Ophtalmologie, CHNO Des Quinze Vingts, Paris, France

Abstract not provided

• 2712

Can OCT be enough for glaucoma management?

NORDMANN J P
Service d'Ophtalmologie, CHNO Des Quinze Vingts, Paris, France

Abstract not provided

• 2713

Efficacy, Safety, Observance: What is the optimal balance ?

THYGESEN J
Ophthalmology 2061, Rigshospitalet, Copenhagen University Hospital

Abstract not provided

• 2714

Shall we wait Ocular surface disease to prescribe preservative free (PF) products in glaucoma ?

SHORTT A
NIHR Biomedical Research Centre, Moorfields Eye Hospital, London, United Kingdom

Abstract not provided

FRIDAY OCTOBER 9, 2015

• 3111

Epidemiology and genetic in degenerative myopia

LEVEZIEL N
Poitiers, France,

Abstract not provided

• 3112

Macular diseases in myopia

CREUZOT C
Department of Ophthalmology, Dijon, France

Pathologic myopia is a leading cause of blindness wordlwide with macular degeneration often related to a posterior ectasia named staphyloma. This degeneration leads to a progressive thinning of the retinal pigment epithelium and choroid. The main signs of macular diseases due to myopia can vary from yellow-white breaks in Bruch's membrane called lacquer cracks, subretinal hemorrhages and secondary neovascularisation that can be associated. The diagnosis can be made with visual acuity measurement, fundus exam, OCT, autofluorescence and angiography to differentiate isolated hemorhhages and choroidal neovascularisation. The prognosis of myopic choroidal neovascularisation has been greatly improved with antiangiogneic agents.

• 3113

Macular surgical diseases in myopia

POURNARAS J A C
Jules Gonin Eye Hospital, LAusanne, Switzerland

Macular surgical diseases in myopia are consecutive to vitreoretinal interface disorders associated to stretching forces due to staphyloma on the other side. OCT have largely contributed to the recognition and the understanding of vitreoretinal interface disorders occuring in myopic condition: epiretinal membrane alone or associated to foveoschisis, lamellar or full thickness macular hole and posterior retinal detachment. Surgical management by vitrectomy associated or not to ILM peeling will be discussed according to myopic disorders. Main surgical complications are macular hole formation and foveal atrophy. Fovea-sparing internal limiting membrane peeling for myopic traction maculopathy may represent an alternative option to avoid these complications. Scleral buckling surgery associated to vitrectomy may represent an other option under investigation.

• 3114

Retinal detachment

BERROD J P, Conart J B
CHU Nancy Brabois, Ophtalmologie, Vandoeuvre les Nancy, France

High myopia, defined as a refractive error of >– 6,00D or an axial length of > 26mm [2], is a growing condition in developed countries. These eyes candevelop myopic foveoschisis andretinal detachment (RD) secondary to macular hole (MH), posterior paravascular breaks that need the use of an internal tamponade. Other complications, such as rhegmatogenous RD due to peripheral retinal or giant tear, can also appear. The use of endotamponade agents such as gas or silicon oil plays a major role in the management of retinal detachment in high myopia. Anatomical and functional results inversely correlate with axial length.

• 3115

Clinical cases (all)

CREUZOT C
Department of Ophthalmology, Dijon, France

Clinical cases to illustrate diseases related to degenerative myopia will be discusses with the audience. Diagnosis, outcome and treatment will be considered.

• 3121
Ocular Autonomic Regulation

ROCHA DE SOUSA A (1), Barbosa-Breda J (2)
(1) Faculty of Medicine- University of Porto, Department Of Senses Organs, Porto, Portugal
(2) Centro Hospitalar de Sao Joao, Department of Ophthalmology, Porto, Portugal

The autonomic ocular regulation is described with focus on sympathetic and parasympathetic enervation. This is emphasized by the role of the alfa and b adrenergic system and by the muscarinic enervation mainly in the aqueous inflow and outflow systems and in ocular blood flow. Also the role of the non-adrenergic, non-cholinergic system in those pathways is described and discussed. Finally the neuro-humoral regulation, involving the cilliary epithelium role in the ocular regulation of ocular blood flow and aqueous humor kinetic.

• 3122
Ocular tests and interpretation

MARQUES-NEVES C
Faculty of Medicine of Lisbon University, Ophthalmology, Lisbon, Portugal

The eye is a richly enervated organ, with a dual supply from both the sympathetic and parasympathetic nervous system. The inputs from these two branches of the autonomic nervous system (ANS) are responsible for a vast number of ocular physiological responses, ranging from pupillary reflexes to accommodation and aqueous humor turnover. Accordingly, any dysfunction in one (or both) of these inputs can have a significant impact on the overall organ physiology and are likely involved in a number of diseases – such as glaucoma.
Accordingly, several ophthalmological tests using specific systemic and ocular stimuli have been developed to determine the integrity and relative contribution from each of these two ANS inputs. Validated normative databases allow for a proper diagnosis of an ANS dysfunction and can provide a valuable input in the diagnostic and treatment algorithm in a number of ocular conditions.
However, interpretation of these signals is usually complex and thus are not regularly used in the clinical setting. The purpose of this talk is to give an insight into the logistics and complexity of these ANS ocular tests and – more importantly – to provide the tools for its interpretation by a clinical researcher.

• 3123
Ocular autonomic dysfunction in glaucoma

VANDEWALLE E
UZ Leuven, Ophthalmology, Leuven, Belgium

The retina relies primarily upon autoregulation of the retinal vasculature in cases of increased metabolic demand or reduced ocular perfusion pressure. The choroidal blood vessels are highly innervated by the autonomic nervous system, but are separated too far from the retina to respond to the local accumulation of vaso-active metabolites. It could therefore be hypothesized that conditions interfering with either the autoregulation or the autonomic nervous regulation could render the retina at a higher risk of ischemic damage. Glaucoma has been associated with disturbances in both types of regulation. Retinal oximetry is capable of providing reproducible ***in vivo***, non-invasive measurements of the retinal vessel oxygen saturation and with the advent of enhanced depth imaging optical coherence tomography (EDI-OCT), allowing a detailed non-invasive evaluation of the choroid ***in-vivo***, renewed interest in the role of the choroid in the pathogenesis of glaucoma has grown.

• 3124
Systemic dysfunction in glaucoma

SCHMETTERER L
Medical University of Vienna, Medical Physics and Biomedical Engineering and Clinical Pharmacology, Vienna, Austria

The most important risk factors for the development of glaucoma is increased intraocular pressure. There is, however, evidence that systemic facts pay a role as well. As such it has been shown that patients with primary open angle glaucoma show signs of endothelial dysfunction as well as signs of systemic autonomic dysfunction. The latter is supported by data showing abnormal heart rate variability in glaucoma, particularly in normal tension glaucoma. In addition, studies have shown that glaucoma patients exhibit an abnormal systemic and ocular vascular response to warm-cold stimulation. The consequences of systemic autonomic dysfunction in glaucoma may be wide including abnormal diurnal fluctuations of intraocular pressure, blood pressure and ocular blood flow.

• 3125

Clinical relevance of ANS dysfunction in glaucoma management

ABEGAO PINTO L

Faculty of Medicine of Lisbon University, Department of Ophthalmology, Lisbon, Portugal

Research for autonomic nervous system dysfunctions (ANS) in glaucoma patients has a two-fold interest for the glaucoma specialist. On one hand, it provides the physician with a set of results that demonstrate the extent of the underlying systemic and ocular dysfunction. These data may provide clues as to why the disease is continuing to progress and may therefore help guide glaucoma management. While strategies towards correcting these imbalances have not been definitely proven to affect the outcome of glaucoma, there are an increasing number of anedoctal data that suggests they may have a positive impact in disease progression. Moreover, signalling the extent of the systemic dysregulation may help identify other, non-ocular related problems and thus be ultimately beneficial to the patients in the long term. More research is still needed to idenfity which patients are more likely to benefict from undergoing ANS function tests and - should any dysfunction be found - what would be the most consistent treatment strategy.

• 3131

DALK versus PK for keratokonus

BORDERIE V
Institut de la Vision- CHNO des XV-XX, Ophthalmology, Paris, France

Advanced keratoconus usually leads to keratoplasty in young adult patients who have a long life expectancy. Repeat keratoplasty is known to be associated with shorter graft survival compared with primary graft and increased risk of glaucoma that may result in progressive loss of vision. For these reasons, keratoplasty in keratoconus should aim not only to provide patients with good vision but also to permit long-term survival of the graft. Recent studies have raised controversies regarding survival of penetrating and deep anterior lamellar keratoplasties. In two large series of keratoplasties, graft survival was higher in PK than in DALK eyes. Conversely, a meta-analysis recently showed that DALK is associated with lower risk of rejection and lower risk of failure compared with PK. These findings make sense if we consider the absence of endothelial rejection and the high survival rate of the corneal endothelium observed in DALK eyes. DALK and PK appear to give similar visual recovery at least in the short and mid-term. It is not yet possible to determine which technique is associated with the highest chance of maintaining good vision in the long term. This issue depends not only on maintenance of graft transparency but also on corneal biomechanics. Progressive thinning of the peripheral inferior recipient cornea may result in severe irregular astigmatism after keratoplasty for keratoconus. This issue should be further addressed.

• 3132

Ultrathin DSAEK: The Present Status

BUSIN M
Dept. of Ophthalmology, Villa Serena Hospital, Forli, Italy

The lecture will present a complete review of Descemet Stripping Automated Endothelial Keratoplasty (DSEK), focussing in particular on the development of the technique for the dissection of ultrathin (UT) donor tissue. History as well as basic principles necessary to understand the mechanisms of UT DSAEK will be introduced to the attendees. In setting the indication to UT DSAEK, the author will discuss the role of recipient corneal status, type of endothelial disease, concomitant eye disease (i.e. glaucoma), presence of clear lens and other preoperative factors. The different techniques of conventional DSEK, UT DSAEK and Descemet membrane endothelial keratoplasty (DMEK) will be compared, pointing out the single steps, which are instrumental in facilitating surgery, while improving the final outcome. In case of multiple intervention, combined versus sequential procedures (e.g. phacoemulsification, IOL surgery, vitrectomy, etc.) will be discussed. The authors will highlight advantages and disadvantages of different surgical approaches. Possible implications for eye banking will also be addressed, with particular emphasis on preparation and storage of tissue for UT DSAEK and DMEK. Slides and videos of case studies will illustrate the most common complications (i.e. graft detachment, dislocation, failure, rejection etc.) as well as the appropriate solutions.

• 3133

Descemets membrane endothelial keratoplasty (DMEK)

KATAMISH T
Cairo University, Cairo, Egypt

Descemet's membrane endothelial keratoplasty (DMEK) has emerged as the superior technique for endothelial keratoplasty (EK) in routine cases to selectively replace diseased endothelium in patients with Fuchs endothelial dystrophy and pseudophakic bullous keratopathy. Despite all the advantages of DMEK the overall procedure is challenging for the surgeon. Crucial yet difficult steps of DMEK include: (1) Preparation of an intact donor lamella (D.M. and endothelium), (2) Transfer of the graft into the anterior chamber, (3) Unfolding and orientation of the graft, and (4) Final successful attachment after air filling. In my presentation I will demonstrate clearly how to perform these different steps safely and reproducibly.

• 3134

Pre-Descemets Endothelial Keratoplasty (PDEK)

DUA H S
Queens Medical Centre- Derby Road, Eye Ear Nose Throat Centre, Nottingham, United Kingdom

The most popular endothelial keratoplasty (EK) technique is Descemets stripping endothelial keratoplasty (DSEK). Descemets membrane endothelial keratoplasty (DMEK) has advantages but is technically challenging. In 2013 Dua et al reported a pre-Descemets layer (Dua's layer, DL) in the posterior cornea and suggested how this could be exploited for EK. This was later developed and performed as Pre-Descemets endothelial keratoplasty (PDEK).

PDEK tissue is harvested by injecting air into the donor cornea and creating a type-1 big bubble (BB). The posterior bubble wall composed of endothelial cells, DM and DL is excised and inserted in the recipient eye. This tissue rolls less than DMEK tissue and is more robust allowing easy handling and unrolling in the eye. It can also be physically centred in the anterior chamber. The limitations are that on occasions a type-2 BB may form requiring a DMEK procedure. The PDEK graft size is smaller being limited by the size of the BB (around 8.5mm). However, PDEK tissue can be taken form very young eyes with higher cell counts. Initial results, with regard to complications, visual acuity, refractive error and OCT changes are very encouraging making PDEK a viable option for EK.

Commercial interest

• 3135

There is still a place for Penetrating Keratoplasty (PK)

SAID D

Research institute of Ophthalmology, Ophalmology department, Maadi-Cairo, Egypt

With new emerging lamellar keratoplasty techniques, the number of penetrating keratoplasty has reduced, yet it is still the most commonly performed technique for corneal grafting.

For many indications penetrating keratoplasty (PKP) is the best option such as keratoconus with previous hydrops and central scarring, therapeutic corneal graft and long standing bullous keratopathy with stromal scarring. Other situations such as presence of peripheral anterior synaechia, aphakia, shallow phakic eyes, DSEK and DMEK have greater risk and more loss of tissue through wastage.

Advantages over other lamellar techniques are shorter learning curve, comparable or better visual outcome and in some centers better survival rate when performed for the same indication as lamellar grafts. Post-operative astigmatism and weak graft host junction remain to be major disadvantages of this technique.

Newer evolving cutting techniques of donor and recipient corneas using the femtosecond laser are being developed to address these issues, however, to date results do not justify the increase in cost.

• 3141

Benign or Malignant? Clinical features

LASUIDRY J

Ophthalmology, Hôpital Erasme, Université Libre de Bruxelles, Brussels

Despite the fact that the majority of eyelid tumours are benign, proper management in daily practice requires to detect the malignant ones. A few clinical behaviour criteria are usually examined to support the hypothesis of a malignancy, e.g. the rate of growth, associated inflammation or pigmentation, a cystic structure, ulceration, madarosis, etc. However most are of limited reliability. The course will review the most typical presentation scenarios of common eyelid tumours. In any case of doubt, biopsy is recommended, which is readily done in the outpatient setting, in order to reach a pathologic diagnosis, and draw the appropriate management plan.

• 3142

Clinico-pathologic correlations of unusual lesions of eyelid tumors

LOEFFLER K

Augenklinik, University Klinikum, Bonn, Germany

Management of eyelid lesions depends a lot on the presumptive diagnosis. By presenting some unusual tumours and their histopathologic correlate we would like to raise the awareness of specific features that will eventually help to better assess potentially benign or malignant neoplasms.

• 3143

Which margins for which tumors?

MOURIAUX F

Service d'ophtalmologie, CHU Pont Chaillou, Rennes, France

Traditional surgical treatment of non-melanoma skin cancer includes excision with subsequent surgical margins, the "security" margins leading to determine the theoretical level of recurrences. Thus, some authors favor a clinical excision margin of 4 mm for basal cell carcinoma and 6 mm for squamous cell carcinoma. However, such "security" margins could not be applied in all cases of eyelids tumors for anatomic and functional considerations because such recommendations may lead to severe ocular complications. Thus the best assurance of minimal excision with complete excision is obtained by extemporaneous examination of the resection margins by frozen section or by surgery in two times. The aim of this paper is to review these two techniques for eyelids (lid margins) and medial canthus. This article will discuss the concept of surgical margins in excisions of non-melanoma skin cancer and the role of frozen section of the margins for minimizing the amount of tissue that must be excised.

• 3144

Basis of eyelid reconstruction after tumor resection

BRISCOE D

Emek Medical Center, Ophthalmology, Savion, Israel

Eyelid reconstruction following tumour excision should be performed with two main goals in mind : the restoration of normal eyelid function, and a good cosmetic result. Strict observance of several surgical principles will ensure achieving those goals.These include, providing stable eyelid margins, reconstruction of the missing layers, including skin muscle and conjunctiva, and solid support between the outer and inner layer. The choice of which type of reconstruction to perform should be considered carefully bearingin mind the visual status of the contralateral eye, the extent of the defect, and the age, health and mobility of the patient. Surgery should be performed using operating loops, a good light source, and in conditions ofminimal bleeding. Good surgical reconstruction allows restoration of excellent visual function and a happy, comfortable patient

• 3151
Introduction and overview

SPALTON D
St Thomas' Hospital, London, United Kingdom

PCO remains the commonest complication of cataract surgery and is a particular problem with presbyopia correcting multifocal IOLs which are more sensitive to mild PCO and it remains the barrier to a truly accommodating IOL
This presentation reviews the current clinical status of PCO prevention and in particular the contribution of IOL material and design. Hydrophobic materials appear to induce less PCO than hydrophilic polymers and the reasons for this will be discussed.
Square edge profile IOLs have reduced the incidence of PCO but delay rather than cure the problem, edge profile quality is however is very variable and this has clinical implications. Haptic design also affects PCO performance. New 'open bag' IOL designs appear to offer a significant improvement in PCO prevention

Commercial interest

• 3152
TGF beta and fibrosis-ironing out the wrinkles

ELDRED J, Wormstone M
University of East Anglia, School of Biological Sciences, Norwich, United Kingdom

The fibrotic disorder Posterior Capsule Opacification (PCO) is the leading secondary ocular complication following cataract surgery. PCO causes a significant loss of vision for approximately 10-30% of patients, 2-5 years post cataract removal. The formation of PCO requires additional surgical treatment, presenting an additional and substantial burden on health care providers and affects the overall well-being of cataract patients. Fibrotic disorders affect many organs of the body and are associated with hyperproliferation, cell transdifferentiation, matrix modification and contraction. Identifying the major control of these features is essential to our understanding of PCO development. Transforming growth factor beta (TGFβ) has long been implicated in fibrotic disorders and is commonly defined as the "master switch" of fibrosis. However the actions governed by TGFβ can be complex and diverse involving multiple signalling pathways and cross-talk between many signalling cascades. Significant understanding of the key pathways regulating TGFβ induced modifications in PCO has been identified using human cell and tissue culture models. These important findings and how they may be used as therapeutic targets will be presented.

• 3153
Migration of lens epithelial cells and IOL drug soaking

WERTHEIMER C, Kueres A , Mayer W , Liegl R , Eibl-Lindner K
University Eyeclinic Munich, Ophthalmology, Munich, Germany

Purpose: To assess the effect of EGFR Inhibitor Erlotinib and the downstream Inhibitor Erufosin (PI3K) soaked into intraocular lenses (IOLs) on human lensepithelialcell (LEC) proliferation in vitro.
Methods: addition Foldable IOLs were incubated with Erufosin or Erlotinib. Intraocular lenses of the same lot served as uncoated controls. Each IOL was placed into cell cultre containing proliferating human LECs. Cell survival was tested by the XTT-dye reduction assay 5 days later. Furthermore IOLs were put into the Gotoh anterior chamber model. In addition, soaked IOLs were implanted into the human capsular bags and braught to cell-culture. The time until full cell-coverage of the capsular bag was measured.
Results: Erufosin ($P<0.05$) and Erlotinib ($P<0.05$) coated IOLs attenuated human LEC proliferation in all above described models. For both substances soaked hydrophilic acrylic IOLs were more effective inhibitors of human LEC proliferation than coated hydrophobic acrylic.
Conclusions: Results show that both substances are suitable agents for IOL-soaking without linker molecules. Soaked IOLs can inhibit human LEC proliferation in our models and might become of clinical relevance in future.

• 3154
Sealed-capsule irrigation with distilled deionized water to prevent posterior capsule opacification

REKAS M, Kluś A , Kosatka M
Military Institute of Medicine, Department of Ophtalmology, Warsaw, Poland

Purpose: To evaluate efficacy and safety of sealed-capsule irrigation (SCI) using distilled water (DW). Materials and methods: Phacoemulsification was performed in 60 patients. In the control the capsular bag was mechanically cleaned (MC), in the DW group DW for 3' in SCI was additionally applied. SN60WF IOL was implanted in all eyes. Examinations were performed before and 1, 30, 180 days, 1 and 2 years after surgery. UDVA, CDVA, IOP, K_2-SIA, SEQ, endothelial cell and the complications were examined. Total PCO score in the area of 1, 3 mm and capsulorhexis (CAPS) were determined using EPCO 2000. Results: As far as safety parameters are concerned, no differences were observed between groups ($P>0.05$). However, in the DW group the endothelial cell loss was higher ($P<0.05$). Total PCO score differences were observed in both groups between the areas ($P<0.05$). In CAPS area both, Total PCO score and PCO area were decreased in DW group ($P<0.05$). PCO was also lower within 3 mm zone in the DW group ($P<0.05$).Conclusions: SCI is a safe procedure and the endothelial cells loss can be associated with the Perfect Capsule™ device in the anterior chamber insertion. DW irrigated for 3' reduces PCO in long-term follow-up.

• 3155

Capsular opacification and accommodative lens refilling

KOOPMANS S
University of Groningen, Ophthalmology, Groningen, The Netherlands

After lens refilling with a silicone polymer, accommodation has been demonstrated in rhesus monkeys. However, coinciding with the development of capsular opacification the accommodative amplitude decreases to zero. Several strategies may be followed to prevent the development of capsular opacification. A straight forward strategy is the attempt to destroy remaining lens epithelial cells in the lens capsule by cytotoxic drugs. By isolating the lens capsular bag from the rest of the anterior chamber the lens capsule may be selectively treated with drugs. Our experiments in various animal models have shown that lens epithelial cells are very resistant to these treatments. This suggests that better strategies are needed. In further experiments we found that the choice of a proper biomaterial in the capsular bag may also significantly influence the capsular opacification response. Results of lens refilling with Hyaluronan and functionalized nanogels will be discussed.

Commercial interest

• 3161

Understanding and perceptions of inherited eye diseases and attitudes to genetic testing and gene therapy in a primary eye care setting

GANNE P , Votruba M , Garrioch R
School of Optometry & Vision Sciences- Cardiff University, Ophthalmology, Cardiff, United Kingdom

Purpose To explore the level of understanding and perceptions of inherited eye diseases and attitudes to genetic testing and gene therapy in a primary eye care setting
Methods This study was undertaken as a part of an EVER foundation fellowship at the School of Optometry and Vision Sciences, Cardiff University, UK in 2014. Participant groups were surveyed by questionnaire. The groups were: undergraduate students of optometry, primary eye care professionals and the members of general public attending the optometry practice to have a routine eye test or a routine annual follow-up. Four focus groups were conducted to design the questionnaire. A preliminary study aimed to understand perceptions and to explore the level of knowledge about genetics, inherited eye diseases and gene therapy. A second questionnaire was designed to explore attitudes to genetic testing and gene therapy
Results The majority of participants (82%) perceived genetics as an important science. However, the level of understanding of genetics and inherited eye diseases was relatively low among all groups of participants. Undergraduate students and primary eye care professionals were better informed about inherited eye diseases than the general public (p=0.001). The majority (80%) across all three groups had a positive attitude to genetic testing and gene therapy. There was a lack of knowledge about the genetic services available among all groups of participants
Conclusions This study shows a broadly supportive attitude to genomic medicine among the public albeit a poor level of knowledge of genetics and genetic eye diseases. Improving public awareness and education in inherited eye diseases can improve the utility of genetic testing and therapy

• 3162

Genetic variants in the TNFA are associated with Korean Dry Eye Disease

YANG S (1), Na K S (2), Mok J W (3), Ju H J (3), Joo C K (1)
(1) *Catholic Institutes of Visual Science- Department of Ophthalmology & Visual Science- College of Medicine- The Catholic University of Korea- Seoul St. Mary's Hospital Eye Institute SSEI, Ophthalmology, Seoul, South-Korea*
(2) *Yeouido St.Mary's Hospital- Catholic Institutes of Visual Science- Department of Ophthalmology & Visual Science- College of Medicine- The Catholic University of Korea, Ophthalmology, Seoul, South-Korea*
(3) *Catholic Institutes of Visual Science, Ophthalmology, Seoul, South-Korea*

Purpose To determine whether variations altering the function or expression of TNFA, contribute to the pathogenesis of dry eye disease.
Methods Genomic DNA was extracted from blood samples of unrelated dry eye disease patients (non-Sjogren's syndrome patients (n=200) and Sjogren's syndrome patients (n=100). Polymerase chain reaction and direct sequencing were used to screen variations in promoter region of TNFA gene. One hundred fifty control individuals without corneal disease were selected from the general population.
Results We investigated 6 SNPs of TNFA; -1196 C>T, -1031 T>C, -863 C>A, -857C>T, -308 G>A (rs1800629) and -238 A>G (rs361525) in promoter. Among them, -1196 C>T, -857 C>T, rs1800629 and rs361525 were different between patient groups and control groups. The *A allele frequency of rs361525 in dry eye patients (2.6%) and Sjogrens' patients (2.5%) were decreased compared with control subjects (5.1%). The *A allele frequency of rs1800629 was lower in Sjogrens' patients (2.5%) than in the controls (4.8%). In -1196C>T variation, *T allele of both patient groups was decreased compared with control subjects. Whereas, the * T Allele frequency of -857 C>T was higher in the Sjogrens' patients (30.0%) than in the controls (16.8%). The genotype distributions of all polymorphisms of TNFA among the control subjects and the affected individuals were in Hardy-Weinberg equilibrium.
Conclusions Our results suggested that the genetic variations of TNFA gene seem to be associated with dry eye predisposition in a Korean.

• 3163

Investigation of genotype-phenotype correlation of TGFBI mutations reveals c.1868G>A; p.(Gly623Asp) is associated with a variable clinical phenotype, including epithelial basement membrane dystrophy

EVANS C (1), Davidson A (1), Carnt N (2), Veli N (2), Tuft S J (2), Hardcastle A (1)
(1) *UCL, Institute of Ophthalmology, London, United Kingdom*
(2) *Moorfields Eye Hospital, Cornea and External Disease, London, United Kingdom*

Purpose Autosomal dominant mutations in TGFBI cause a range of clinically distinct corneal dystrophies. We investigated the TGFBI mutation spectrum in our cohort and correlated genotype with phenotype.
Methods TGFBI exons 4, 11, 12, 13, 14 and 16 were Sanger sequenced in 59 unrelated probands attending Moorfields Eye Hospital with a diagnosis of a potential TGBFI-associated corneal dystrophy.
Results The majority of individuals, 86%, carried a mutation at one of the two known hotspot residues for TGFBI-associated corneal dystrophies: Arg-124 and Arg-555. Mutations affecting either of these residues demonstrated genotype-phenotype correlation. A c.1868G>A; p.(Gly623Asp) mutation was identified in five unrelated probands; one with a clinical diagnosis of lattice corneal dystrophy, two with a Bowman's layer dystrophy (Reis-Bücklers or Thiel-Behnke corneal dystrophy) and two with epithelial basement membrane dystrophy (EBMD). The clinical variability associated with this mutation indicates that other genetic or environmental factors can influence phenotypic expression.
Conclusions This is the first time the c.1868G>A; p.(Gly623Asp) mutation has been associated with EBMD, although other mutations in TGFBI have previously been identified in a small number of EBMD patients. These results demonstrate that the c.1868G>A; p.(Gly623Asp) mutation is responsible for a significant proportion of the disease burden for TGFBI-associated corneal dystrophies in the UK and highlights the need for patients with EBMD to be screened for mutations in TGFBI.

• 3164

Target region sequencing in sporadic congenital cataracts reveals a new genotype-phenotype relation for the GALK1 gene

LI D (1), Yang J (2), Ye H (2), Tang Y (2), Luo Y (2), Lu Y (2)
(1) *Eye & ENT Hospital of Fudan University, Research Center of Ophthalmology, Shanghai, China*
(2) *Eye & ENT Hospital of Fudan University, Ophthalmology, Shanghai, China*

Purpose The purpose of this study was to investigate the genetic effects underlying sporadic congenital cataracts (SCC).
Methods We collected DNA samples from 74 SCC patients and 20 traumatic cataract (TC) patients in the same age group as normal controls and performed genomic sequencing of 61 cataract-related genes (including introns, exons and 10 bases from the 3' and 5' ends) by target region capture and next generation sequencing. We chose previously reported cataract-related genes and also included other lens disease-related genes, including microphthalmia (SOX2, PAX6, OTX2, RAX, FOXE3 and CRYBA4); aniridia (FOXC1, PITX2 and PITX3); Marfan syndrome (FBN1); ectopia lentis (ADAMTSL4 and ADAMTS17) and Alport syndrome (COL4A5).
Results By filtering the SNPs that were previously deposited in the NCBI SNP database (dbSNP) or were associated with TC cases, we identified 72 novel variants in 40 genes from 49 patients. The mutation frequency of the GALK1 gene was much higher than the other tested genes, with mutations detected 10 times in 7 patients; followed by CRYBB3 and FBN1 the mutation of which were detected 4 times. Moreover, we observed a posterior polar-cataract phenotype in 86% (6 out of 7) of SCC patients with mutations in GALK1.
Conclusions We conclude that genetic mutations could be important contributing factors to non-hereditary congenital cataract; for example, GALK1, the most frequently mutated gene in this group of patients, was related to the posterior polar subtype of cataract.

• 3165

Ocular fundus changes in patients with Down syndrome and pulmonary hypertension

LEYS A (1), Delcroix M (2), Willems A (1), Wirix M (3), Nijs I (3)
(1) KULeuven and ZOL, Ophthalmology, Leuven and Genk, Belgium
(2) UZLeuven, Pneumology, Leuven, Belgium
(3) ZOL, Ophthalmology, Genk, Belgium

Purpose The ocular and visual problems in Down syndrome are due to refractive errors, poor accomodation, strabismus, keratoconus, cataract, optic disc and retinal structural anomalies and brain changes. Pulmonary hypertension (PH) is associated with high mortality and morbidity and ocular complications may occur.
PH associated central serous choroidopathy-like maculopathy, venous thrombosis and neovascular glaucoma have been described in case reports but no large studies of ocular complications are available. Improved non-invasive imaging with optical coherence tomography (OCT), enhanced depth OCT and OCT angiography without dye allow a detailed study of the retinal and optic disc changes.
Methods A cross sectional study of 180 adult patients with PH included 9 Down patients with congenital heart disease. Age of the Down patients was 25-44 years. The fundus changes included PH associated and Down associated anomalies.
Results PH associated mild changes included episcleral and retinal vein dilation and a thick choroid. None of the Down patients had severe complications of PH. The Down associated fundus changes included absence of optic disc cup, supranumerary optic cisc vessels,and structura lmacular anomalies with small capillary free zone. Two eyes were functionally lost due to complications of hydrops keratoconus.
Conclusions Non-invasive imaging with OCT allows a detailed analysis of fundus changes in Down patients with or without PH.

• 3166

Two Sisters with Congenital Blindness caused by Osteoporosis-pseudoglioma Syndrome due to new Mutations in the LPR5 Gene

WELINDER L (1), Robitaille J M (2), Boerkoel C F (3), Rupps R (3), Lyons C (4)
(1) Aalborg University Hospital, Ophthalmology, Aalborg, Denmark
(2) Dalhousie University and IWK Health Centre, Department of Ophthalmology and Visual Sciences, Halifax, Canada
(3) University of British Columbia- BC childrens Hospital, Genetics, Vancouver, Canada
(4) University of British Columbia- BC childrens Hospital, Pediatric Ophthalmology, Vancouver, Canada

Purpose To discover the reason behind two sisters being born blind with retinal detachment and microphthalmia with later findings of severe osteoporosis with low impact fractures
Methods Molecular testing identified biallelic lipoprotein receptor-related protein 5 (LRP5) mutations (NM_002335.3:c. [889dupA]; [2827 + 1G4A]) confirming a diagnosis of osteoporosis–pseudoglioma (OPPG) syndrome.
Results Two new mutations in the LPR5 gene were each found in the unrelated parents of the girls and were found heterozygote in the girls. Both parents were then discovered to have osteopenia, as did several relatives, who all started preventive treatment.
Conclusions OPPG is a autosomal recessive disease almost uniformly causing blindness from very early age with severe osteoporosis and low impact fractures, which was also the case of our two sisters. The diagnosis of OPPG was confirmed by sequencing the LPR5 gene, where two new mutations were found.

• 3171

Allergic mediators in tears: what's new?

LEONARDI A
University of Padua, Department of Ophthalmology, Padova, Italy

The identification of inflammatory mediators in tear fluid have been used in ocular allergy:
a) to identify a 'disease marker';
b) to understand the immune mechanisms involved;
c) to correlate the severity of the disease;
d) to identify potential targets for therapeutic interventions;
e) as an indicator of treatment outcomes.
Limitations of these findings are the lack of extensive validation of candidate biomarkers and the lack of determination of the specificity of the candidate markers. The increased concentrations of mast cell derived mediators in tears, such as tryptase and histamine, have been considered biomarkers of allergic IgE-mediated response, while ECP levels is considered a specific biomarker of both allergic IgE- and non-IgE-mediated allergic conjunctivitis. The increased production and activation of cytokines, growth factors, imbalance between MMPs and TIMPs, are all involved in the pathogenesis of conjunctival inflammation, remodeling and corneal changes typical of chronic severe allergies. It is possible that patients with diseases can have a different protein profile and, therefore, protein or peptide analysis can be used as a possible fingerprint for disease biomarkers and pathological molecule identification.

• 3172

Healing and corneal ulcers

GABISON E
Fondation A. de Rothschild, Paris, France

Abstract not provided

• 3173

Immuno modulation

CALDER V
UCL Institute of Ophthalmology, London, United Kingdom

Abstract not provided

• 3211

Adaptive Optics

PAQUES M
Quinze-Vingts Hospital, Paris, France

During dry age-related macular degeneration (ARMD), adaptive optics (AO) en face flood imaging improves the resolution of drusens and of pigmentary changes and hence of the progression of atrophic lesions. In addition, AO revealed the presence of numerous migrating hyporeflective clumps, which are most likely melanin-loaded cells (MLCs). Time-lapse imaging demonstrates a high kinetic activity of these MLCs, that appear to migrate subretinally because the photoreceptors are visible over them. The linear velocity of MLCs peakee at ~ 1µm/day, hence they can be tracked only if there is a short ionterval of time between imaging sessions. As many adjacent MLCs are seen to migrate in opposite direction, there appears to be no migrating scheme. Such subretinal migration of MLCs occurs throughout the posterior pole, in atrophic as well as in nonatrophic areas. It is likely that these MLCs correspond to the hyperreflective dots reported by optical coherence tomography. The nature of these cells and their role in the process of ARMD remains to be clarified. Nevertheless, we believe that this finding may have important consequences for the understanding and monitoring of dry ARMD, as well as for the validation of experimental models of ARMD.

Commercial interest

• 3212

Lessons talk by imaging about atrophy in retinal disease: Fundus autofluorescence

LOIS N
Queen's University, Belfast, Northern Ireland, UK

Fundus autofluorescence (AF) and near-infrared autofluorescence (NIA) have been used for many years to assess clinically, in a non-invasive manner, the status of the retinal pigment epithelium (RPE). Their value in the evaluation of patients with posterior segment disorders has expanded; both are currently used in ophthalmic clinics throughout the world for the assessment of patients with degenerative, inflammatory and neoplastic disorders, among others. This talk will provide an overview on how AF and NIA have contributed to the characterisation of atrophy in retinal diseases, from lessons learnt using these imaging technologies on the understanding of mechanisms underlying this pathology, to identification of people at risk of visual loss as well as providing enhanced disease phenotyping and assessment of potential, unwanted, treatment effects. Recent advances, such as wide angle autofluorescence imaging, will likely contribute furthering the understanding of atrophy in retinal disease.

• 3213

ICG

STAURENGHI G
University Eye Clinic, Department of Biomedical and Clinical Science "Luigi Sacco", Milan, Italy

Abstract not provided

• 3214

En face OCT

SCEMAMA TIMSIT C *(1), Mauget-Faÿsse M (2), Wolff B (3)*
(1) Fondation ophtalmologique Adolphe de Rotschild, service du Pr Sahel, PARIS 19 eme, France
(2) Fondation Rothschild, service du Pr Sahel, Paris, France
(3) Strasbourg, rétine, Strasbourg, France

« En face » OCT (Spectral Domain and Swept Source) realizes frontal section of the retina or C-scans. "En face" OCT software informs immediately the layer of the cuts; it joins viewing images "en face" and B-scan with the graphical representation of their different scans. Normal retinal layers have their specific reflectivity.
Atrophy can occur at different stages of many retinal diseases, and at different retinal layers. On "en face" OCT, there are 2 main areas to consider in case of atrophy in retinal diseases:
- the inner nuclear layer which may presents pseudocystic lesions that reflect a damage inducing optic nerve atrophy,
- the outer retinal layers in degenerative retinal diseases such as age related macular degeneration (AMD), genetic diseases such as Stargardt's macular dystrophy, retinitis pigmentosa, MacTel type 2 and in inflammatory diseases such as Serpiginous and Birdshot retino choroidopathies
The pseudocystic lesions might represent a mitochondrial dysfunction inducing degeneration of Muller cells.
The outer retinal damage can be related to material resorption (drusen , pseudodrusen, PED), disappearance of choriocapillaris , ellipsoid disruptions ."En face" has increased the understanding of atrophy in retinal disease

• 3215

OCT angiography of the choriocapillaris and choroid

COSCAS G (1), LUPIDI M (2), COSCAS F (1)

(1) Universitè Paris XII, Hôpital Intercommunal de Créteil - Service d'Ophtalmologie, Creteil, France

(2) University of Perugia, Department of Biomedical and Surgical Sciences- Section of Ophthalmology, Perugia, Italy

Age-related macular degeneration (AMD) is a degenerative disease of the retina, in which the macula is most affected.In dry AMD, loss of vision occurs gradually and progresses to Geographic Atrophy (GA), a degeneration of the RPE and death of photoreceptor cells, leading to irreversible vision loss.Although the introduction of OCT allowed an additional step forward in understanding the major diseases of the macular region, the origin of the GA is almost unclear.

The OCT Angiography (OCT-A) enables distinct, depth resolved, three-dimensional visualization of the retinal and choroidal microvasculature. The concept underlying OCT-A is that in a static eye, the only moving structure in the fundus is blood, flowing in the vessels. The utilization of motion contrast differentiates OCT-A from fluorescence angiography, which requires administration of intravenous markers such as fluorescein or indocyanine-green.

All this, is taking a leading role in the identification of perfusion abnormalities, of ischemic areas and retinal or choroidal neovascular lesions. Moreover it might also provide useful information on morphological and functional aspects of choroidal perfusion in GA, that could be partially responsible of such a severe disease.

• 3221
Ocular lubrication

SCHMETTERER L
Medical University of Vienna, Clinical Pharmacology and Medical Physics and Biomedical Engineering, Vienna, Austria

Lubricants are the mainstay of dry eye treatment. Whereas they do not target the disease itself they relief from the symptoms associated with both tear-deficient and hyper-evaporative dry eye. The duration of action of lubricants critically depends on the residence time at the ocular surface. This is influenced by the viscosity of the eyedrops, their charge, but also by their ability to bind to mucins. Residence time of drugs at the ocular surface has traditionally been investigated using radio-active labelling of the drugs. This does, however, have several drawbacks. Labelling changes the molecule thereby potentially changing the residence time. In addition, experiments are costly and require significant experimental effort. We have developed a technique that is capable of measuring tear film thickness using a custom-built OCT. With this device it is possible to get insight into the residence time of topically administered lubricants. Data for hyaluronic acid, osmoprotective substances and chitosan thiomer are presented.

• 3222
New and old drug delivery systems

WILSON C
SIBS, University of Strathclyde, Glasgow, United Kingdom

Effective, prolonged and safe drug delivery to the eye in the treatment of ocular disease is a complex issue for clinical management. The approach to date has largely been adaptive: taking existing potent molecules which are active in reducing VEGF action and repurposing in new vehicles. From the point of view of a device, such materials may not be ideally druggable, the period of treatment too short or the true target involve more than one receptor. The dispersion of the dosage form is also an issue. Outside the eye, the drug may be lost by dilution and vascular/lymphatic clearance and inside, formulation debris at the back of the eye is a risk factor and may alter vision. The next generation of systems must address these concerns and utilize every tool at our disposal to improve efficacy. This includes the selection of better molecules, the use of modeling to better predict the disposition in the aged eye and perhaps the adoption of surgical procedures to increase drug flux more reliably. Up to now, we have relied on a singular approach – the drug- to solve the problem and now we realize that drug, vehicle and procedure must be integrated.

• 3223
Recent advances in drug delivery to the retina

DAVIS B
London, United Kingdom,

Drug delivery to the retina is presently one of the greatest challenges in ophthalmology due to the inherent limitations of ocular barriers. This therapeutic impediment affects many promising treatments including; anti-VEGFs, which have revolutionised the management of age-related macular degeneration, and have increasing indications for use as sight-saving therapies in diabetes and retinal vascular disease. However, large molecular weight anti-VEGF therapies such as ranibizumab and bevacizumab currently require invasive intravitreal (IVT) injections to bypass ocular barriers, and thus carry a risk of significant side effects. Despite this, the success of anti-VEGF therapies has led to a dramatic increase in the number of IVT procedures, placing a high burden on healthcare resources. For these reasons, the development of non-invasive ocular drug delivery systems has received considerable interest in recent years. This talk outlines the current understanding of anatomical barriers to ocular drug delivery and recent developments in overcoming these barriers for delivery of large drug cargo to posterior ocular tissues. Particular focus will be paid to the role of nanotechnology and annexin A5, which we recently reported to enhance the delivery of topically applied bevacizumab to the rabbit retina.

• 3224
Development pathway

CORDEIRO M F
Glaucoma & Retinal Neurodegeneration Research Group, UCL Institute of Ophthalmology, London, United Kingdom

One of the biggest hurdles in ophthalmology, particularly glaucoma, in recent years has been the successful translation of laboratory advances to the clinic. This is not unique to glaucoma - such a problem has been well-described in different spheres of medicine. In fact, a search in PubMed on this subject reveals over 1000 references . A major identifiable bottleneck is the developmental pathway and the adherence to regulatory requirements. Regulatory issues and common problems will be provided, using examples that are well-documented in the field of glaucoma

• 3231
Limbal stem cell niche - New insights into structural and molecular composition

SCHLOTZER-SCHREHARDT U
Department of Ophthalmology, University of Erlangen-Nürnberg, Erlangen, Germany

Maintenance and regeneration of the corneal epithelium relies on unipotent progenitor cells at the corneoscleral limbus, which are regulated by extrinsic factors from their local microenvironment, the stem cell niche. The postulated limbal niche is an anatomically protected site of intimate epithelial-mesenchymal interaction and is highly vascularised, innervated, pigmented due to intraepithelial melanocytes, infiltrated with immune cells, and supported by a specialized extracellular matrix as well as subepithelial mesenchymal cells emitting soluble signals. For ex vivo expansion and transplantation, limbal stem cells are unfavourably removed from their niche. This lecture outlines our current understanding and novel findings regarding the structural and molecular composition of the limbal niche including specific matrix components, cell-matrix- and cell-cell adhesion molecules, and niche cell populations, which are involved in stem cell regulation through multiple signalling pathways including the Hedgehog pathway. This lecture also provides an overview of current tissue-engineering approaches for corneal surface regeneration that aim at incorporating specific niche components, such as matrix proteins, growth and signalling factors, or putative niche cells, into the culture systems in order to support maintenance of stemness and to improve the therapeutic use of limbal stem cell transplantation.

• 3232
The epithelial-stromal TGFBI corneal dystrophies

LISCH W
Germany

Purpose: To correct the IC3D classification system from 2008.
Methods: To examine the corneal specimens of 54 patients with lattice, granular 1 and 2, Reis-Bücklers, and Thiel-Behnke who underwent unilateral penetrating keratoplasty.
Results: All specimens showed epithelial and stromal pathological deposits by staining with HE and Congo red, and distinct alterations of Bowman`s layer.
Discussion: The 5 TGFBI dystrophies are to classify from the clinical, genetic, but also from the histopathological aspect as "Epithelial-stromal TGFBI corneal dystrophies."

• 3233
Mechanisms of Stromal Fibrosis

BEUERMAN R
Singapore Eye Research Institute, Singapore,

Purpose: This study was designed to uncover new drug targets to deal with the problems of fibrosis of the corneal stroma which can occur following an injury or infection, preventing the normal recovery of vision. Although, TGF-β is clearly involved the detailed intracellular mechanisms necessary for a practical drug target are not available. The cellular target is the transition of the sessile keratocyte to a myofibroblast. Methods: Corneas of 8 week old C57BL6 mice underwent either an anterior keratectomy (AK) wound or infection with Pseudomonas aeruginosa (PA), and animals were sacrificed at 2 and 7 days, as well as 2 and 4 weeks after the procedures. The isolated stroma was used to monitor the expression and location of moesin, phospho-moesin, TGF-β1 and α-SMA. Results: TGF-β1 and phospho-moesin were not detected in normal corneal stromas. However, after either treatment, TGF-β1 expression increased, along with phospho-moesin and moesin in the wounded corneal stroma from day 2 to 7, and decreased after 2 weeks. No expression of TGF-β1 and phospho-moesin was found at PO week 4. Myofibroblasts positive for α-SMA associated with either treatment were detected from day 2 to week 4 and peaked at week 2. Conclusion: These studies show that moesin interactions with actin fiber growth may be a focus drug development in fibrosis decreases; however, it remains to determine the exact details of that interaction.

• 3234
Limbal stem cells and their application in ocular surface reconstruction

MELLER D
Universität Essen, Essen, Germany

Various ocular surface diseases are caused by loss of corneal epithelial stem cells or dysfunction of limbal niche. Besides conventional transplantation of autologous or allogeneic limbal tissue recent advances in tissue-engineering have led to the development of new culture and expansion techniques of human limbal stem and progenitor cells as a new strategy to treat successfully limbal stem cell deficiency (LSCD). From a small limbal biopsy with a limited amount of LSPC an epithelium ready for transplantation is achieved. Autologous grafting of cultured limbal epithelium led in most of the treated cases to a successful reconstruction of the corneal surface. However, allogeneic grafts of cultivated limbal epithelium show a higher graft failure. The etiology of the disease causing LSCD seems to influence the outcome of the procedure. In this presentation challenges and limitations associated with stem cell culture techniques for ocular surface reconstruction are reviewed.

• 3235

Biomaterials for ocular surface reconstruction and lamellar keratoplasty

FUCHSLUGER T

Dept. of Ophthalmology, University Hospital Erlangen, Erlangen, Germany

This presentation present strategies to engineer a biomatrix through nanofibers. Different characteristics of the fibers and the matri, f.ex. biocompatibility, degradability, wetability are displayed. Future possibilities of use in ocular surface reconstruction are discussed.

• 3241

The Initial Consultation – when and how to suspect non-organic visual loss

SPILEERS W
UZ St. Rafael, Leuven, Belgium

Purpose When a patient reports visual loss and the doctor can not immediately find the etiology, a non-organic visual loss has to be excluded.
Methods Different testing methods can be of value in deciding on organic versus non-organic visual loss: visual acuity and visual field measurements, pupillary reflexes, electrophysiologic testing, imaging techniques, ...
Results The value of these different methods will be discussed and illustrated
Conclusion The investigation of possible non-organic visual loss is a complex task

• 3242

Potential retinal causes: when and how to investigate

LEROY B P (1,2,3,4)
(1) Department of Ophthalmology, Ghent University Hospital, Ghent, Belgium
(2) Center for Medical Genetics, Ghent University Hospital, Ghent, Belgium
(3) Division of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia
(4) Center for Cellular & Molecular Therapeutics, Children's Hospital of Philadelphia, Philadelphia

Purpose: To describe the retinal conditions that need to be excluded when non-organic visual loss is suspected, and the investigations required to either confirm or exclude them. Methods: A case presentation format will be used to illustrate those conditions which can be discovered using psychophysical and electrophysiological tests as well as special imaging including blue and near-infrared autofluorescence and reflectance imaging and spectral-domain optical coherence tomography, in patients in whom a non-organic origin for visual loss is initially suspected. Results: Inherited retinal diseases such as Stargardt macular dystrophy, X-linked retinoschisis and cone dystrophy as well as Batten disease in their early stages all need to be excluded when visual loss is thought to be non-organic. In addition, several acquired retinal conditions such as acute acular neuroretinopathy need to be taken into account. Visual field testing, ISCEV-standard full-field flash electroretinography, pattern electroretinography and visual evoked potentials and specialised imaging techniques contribute significantly to making the correct diagnosis. Conclusions: Visual loss in a list of organic conditions may mimic non-organic visual loss. Functional testing as well as specialised imaging techniques are essential in differentiating true organic from non-organic visual loss.

• 3243

Neuro-ophthalmic considerations and investigations

KAWASAKI A
Hopital Ophtalmique Jules Gonin, Lausanne, Switzerland

Unexplained visual loss is a challenging clinical situation. It is important to distinguish underlying occult pathology from visual loss without organic basis . Even trickier are patients in whom concurrent organic disease does exist but the degree of visual dysfunction is exaggerated, leading to the false notion of malingering. This lecture examines some objectives techniques for discerning visual function in the patient with medically unexplained visual loss .

Commercial interest

• 3244

The role of electrophysiology

HOLDER G
Electrophysiology, Moorfields Eye Hospital, London, United Kingdom

Abstract not provided

• 3251

αB-Crystallin Phosphorylation as a Precursor to Cataractogenesis

THORNELL E, Ecroyd H, Aquilina A
University of Wollongong, Illawarra Health and Medical Research Institute and School of Biological Sciences, Wollongong, Australia

Purpose The molecular mechanism behind age-related cataract formation is yet to be elucidated, although phosphorylation induced hyperactivity of αB-crystallin (αB) and its subsequent association with fibre cell membranes has been implicated. This study evaluates the effect phosphorylation of αB at three well characterised sites (S19, S45 and S59) has on its chaperone activity and aims to characterise αB's membrane association with a focus on its role in cataractogenesis.
Methods The chaperone activity of αB phosphomimics (S D) were measured via aggregation assays using creatine phosphokinase (CPK) as a substrate. In vivo association of αB phosphoisotypes with two abundant membrane proteins, connexin 46 (cx46) and aquaporin 0 (AQP0) in aged human lenses was visualised using Duolink proximity assays and confocal microscopy.
Results The chaperone activity of αB increased with an increase in modification sites. Modification at the S19 and S59 residues activated αB to a greater extent than at S45. In the lens, phosphorylated αB was found to interact with Cx46 and AQP0 at cell membranes.
Conclusions This study confirms that multiple phosphorylation events of αB cause a cumulative increase in activity, and that membrane association, at least in part, is mediated by interactions with membrane pore proteins. The proposed mechanism of cataractogenesis is that phosphorylation induced increases in substrate affinity of αB may lead to increased association with membrane pore proteins, leading to the obstruction of the diffusion of small molecules into inner regions of the lens, contributing to cataract formation.

• 3252

Endothelial cell loss after phacoemulsification according to different anterior chamber depths measured by IOL master

HWANG H, Lyu B, Yim H, Lee N
Incheon St. Mary's Hospital- The Catholic University of Korea, Department of Ophthalmology, Incheon, South-Korea

Purpose To compare the loss of corneal endothelial cells after phacoemulsification according to different anterior chamber depths (ACDs), as measured with the IOL Master.
Methods We conducted a prospective, randomized clinical study on 135 eyes of 135 patients with senile cataracts. Eyes with nuclear density grades of 2 to 4 were divided into three groups according to ACD: ACD I, 1.5 < ACD ≤ 2.5 mm; ACD II, 2.5 < ACD ≤ 3.5 mm; or ACD III, 3.5 < ACD ≤ 4.5 mm. Intraoperative ultrasound time (UST), mean cumulative dissipated energy (CDE), and balanced salt solution (BSS) use were measured. Clinical examinations included central corneal thickness (CCT), endothelial cell count (ECC), and corrected distance visual acuity (CDVA) preoperatively, and 1 day, 1 month, and 2 months postoperatively.
Results There were no significant differences in CDE among the ACD groups ($P > 0.05$). The percentage of endothelial cell loss was significantly higher in ACD I than ACD III in the grade 3 and 4 cataract density groups 2 months after phacoemulsification ($P < 0.05$). There were also more changes in CCT in all of the cataract density groups in the ACD I group compared to the ACD II and III groups 2 months postoperatively, but the difference was not statistically significant.
Conclusions Eyes with shallow ACDs, especially those with relatively hard cataract densities, can be vulnerable to more corneal endothelial cell loss in phacoemulsification surgery. Thus, more attention is needed to avoid corneal decompensation in cataract surgery on patients with shallow ACDs and hard nucleus densities.

• 3253

Changes of intraocular pressure and cornea biomechanical properties after cataract phacoemulsification.

YUGAY M, Ryabtzeva A
Moscow Region Research Clinical Institute, ophthalmology, Moscow, Russia

Purpose Cataract phacoemulsification is accompanied by changes in intraocular pressure and biomechanical parameters of the eye. Corneal hysteresis characterizies the visco-elastic properties of the cornea. Our purpose was to analyse the changes of intraocular pressure and corneal hysteresis during 3 months after phaco.
Methods The study included 80 eyes of 80 patients who underwent uncomplicated phacoemulsification throught clear corneal incision with IOL implantation. Preoperative examination included standard techniques and measurement of corneal hysteresis, central corneal thickness (CCT), corneal compensated intraocular pressure (IOP) and Goldman IOP by Ocular Response Analyzer, repeated before surgery, 1 day, 2 weeks, 1 and 3 months after surgery.
Results Corneal hysteresis decreased on the first day after cataract phacoemulsification from 9,90±0,24 mm Hg to 8,88±0,26mm Hg and after 2 weeks to 7,91±1,13 mm Hg ($p<0,05$). Then corneal hysteresis increased and after 3 months after surgery returned to preoperative values (9,78±0,29mm Hg). Intraocular pressure raised after surgery by 3 mm Hg, decreased to preoperative values by 1 month after phaco, and continued to decrease by 1,5-2mm Hg up to 3 months after phacoemulsification. Central corneal thickness increased after phaco from 539±21 mcm to 559±33mcm the first day after surgery and 659±28 mcm in 2 weeks. It decreased to 552±26mcm in 1 month and returned to preoperative values in 3 months.
Conclusions Corneal hysteresis decreased in the early postoperative period after phaco, dropping to a minimum 2 weeks after surgery. Then corneal hysteresis gradually increased, reaching preoperative values at 3 months after surgery. Changes of intraocular pressure are opposite to changes of corneal hysteresis. CCT increased after phaco, reached maximum in 2 weeks and returned to preoperative values in 3 months.

• 3254

Increased Uptake of Intracameral Antibiotic Prophylaxis in Europe

BARRY P
St Vincent's University Hospital Group, Ophthalmology, Dublin, Ireland

Purpose To determine the use of intracameral cefuroxime at the end of cataract surgery across Europe since the beneficial results were first reported by the ESCRS Endophthalmitis Study Group in 2007 and examine the reasons for the different practice patterns identified.
Methods The ESCRS conducted a survey of 250 ophthalmic surgeons across Europe regarding their awareness of the ESCRS study and seeking the reasons for their current use or non-use of i/c antibiotics in their cataract surgery. Simultaneously, data on practice patterns for prophylaxis were searched in the main European countries concentrating on the uptake of the i/c route and the reasons for the switch.
Results In the ESCRS survey, 74% always/usually use i/c antibiotics and 82% of these use cefuroxime. Lack of need, protocol, or concerns re adverse events related to the absence of an approved product, accounted for non-use. Only 8% would not use i/c cefuroxime whether commercially available or not. Germany has the lowest use and the highest cataract volume whilst France has the next highest volume and the most rapid conversion due to Government guidelines introduced in 2011. The approval of a product of i/c cefuroxime for use in cataract surgery by the EMA (European Medicines Agency) in 2012 eliminated the risks of errors of dilution, diluent, contamination or TASS and is largely responsible for the major shift to the i/c route.
Conclusions The landmark ESCRS Study results of 2007 heralded a worldwide increase in the use of i/c antibiotic for the prevention of postoperative endophthalmitis following cataract surgery. Subsequent studies all over the world have validated these results - where the rate was high it got much lower, where it was low it got even lower with almost no adverse events.

Commercial interest

• 3255

Impact of intracamerular Cefuroxime on post-operative endophthalmitis in Languedoc Roussillon, France from 2010 to 2014

DAIEN V (1), Papinaud L (2), Lacombe S (3), Daures J P (3), Villain M (1)
(1) CHU Montpellier-Hospital Gui Chauliac, Ophthalmology, Montpellier, France
(2) Echelon Régional de l'Assurance Maladie du Languedoc Roussillon, Biostatistics department, Montpellier, France
(3) University Institute of Clinical Research- University of Montpellier I, Laboratory of Biostatistics, Montpellier, France

Purpose Post-operative endophthalmitis remains the most severe complication of cataract surgery. The purpose of this study was to determine the incidence of post-operative endophthalmitis in Languedoc Roussillon between 2010 and 2014. Secondary objective was to assess the correlation between the use of intracamerular injection of cefuroxime and post-operative endophthalmitis incidence.
Methods All patients > 40 years old who underwent a primary cataract surgery in Languedoc Roussillon (France) between January 2010 and December 2014 were collected from the regional administrative database of medical care. Incidence rate of post-operative endophthalmitis was estimated. Spearman coefficient was used to assess the correlation between the incidence of post-operative endophthalmitis and the use of intracamerular cefuroxime at the end of cataract surgery.
Results In 5 years, 179,515 eyes underwent a cataract surgery in Languedoc Roussillon. A total of 182 patients had a post-operative endophthalmitis owing to a 1 year incidence of 0.10% after cataract surgery. The incidence of endophthalmitis decreased over the study: 0.16%, 0.12%, 0.11%, 0.07% and 0.05% in 2010, 2011, 2012, 2013 and 2014, respectively. The use of cefuroxime prophylactic injection at the end of cataract surgery increased over the study: 3.27%, 7.65%, 32.04%, 75.67% and 85.36% in 2010, 2011, 2012, 2013 and 2014, respectively. The incidence of post-operative endophthalmitis was negatively correlated with the use of intracamerular injection of cefuroxime ($r=-0.96$, $p = 0.008$).
Conclusions This study provides information on the decrease of post-operative endophthalmitis incidence and its correlation with the increased use of cefuroxime intracamerular injection to prevent the risk of infection in the real world. This observational study confirms the promising results of the ESCRS study.

• 3256

Anterior chamber and refractive parameters in diabetic patients according to metabolic status

COSTA L , Cardigos J , Vicente A , Borges B , Ferreira J , Cunha J P , Amado D
Centro Hospitalar de Lisboa Central, Ophthalmology, Lisbon, Portugal

Purpose Diabetes Mellitus is associated with changes in refractive parameters. Some aspects already studied were the corneal biomechanics and lens thickness. Although, the discussion about anterior chamber angle and depth is still open. The author objective was to analyze and correlate the anterior chamber depth, lens vault and lens thickness with disease duration and metabolic status.
Methods Prospective case-control study. The anterior chamber and refractive parameters were studied using the Visante OCT and the differences between diabetic patients with metabolic control and disease stability were determined (group 1), without (group 2) and group-control (3). The metabolic control is based on HbA1c levels. The cut-off considered was 7%.
Results A total of 64 patients were evaluated (group 1 – n = 21; group 2 – n = 20; group 3 – n = 23). The mean age was 64.32 ± 7.55 years and approximately 5 years of disease duration. In both groups of diabetic patients we found thicker lens, narrow anterior chamber and higher lens vault compared to control group. There was a difference between diabetic groups exists, but it was not statistically significant.
Conclusions The anterior chamber angle and lens vault are influenced by the serum glucose levels. Further studies will be necessary to clarify the physiopathology mechanism responsible for the anterior segment modifications.

• 3261
Radiation-induced cataracts: governmental safety aspects

AINSBURY E
Public Health England, CRCE- Radiation Effects, Oxford, United Kingdom

Despite relative ease of treatment, radiation induced cataracts are still the most frequent cause of blindness worldwide. Recent advances have demonstrated that the lens is more radiosensitive than was previously thought and that occupational radiation exposure leads to a small but genuine increase in the risk of radiation cataract for workers, for instance hospital based interventional radiologists and cardiologists. As a result of this and other work, the ICRP recommended to reduce the dose limit from 150 mSv/yr to 20 mSv/year (averaged over 5 years with no single year exceeding 50 mSv). This recommendation has recently been incorporated in the EU Basic Safety Standards in full, with member states required to comply from February 2018. This presentation will outline the epidemiological and mechanistic research upon which the new limits are based; consider the implications for radiation protection in terms of who will be affected, what will need to be measured and how individuals can be protected and, finally, discuss the specific scientific gaps and research needs in order for the relevant authorities to ensure individual radiation workers and members of the public are adequately protected against radiation induced cataracts.

• 3262
Scheimpflug analysis in an epidemiological study

WEGENER A
Dept. of Ophthalmology, University Clinics, Bonn, Germany

Radiation cataract enhances age-related scattering increase. Radiation induces formation of subcapsular and cortical cataracts. Light scattering changes in lens layers evidences radiation damage to lens proteins. Scheimpflug imaging today offers standardized recording procedures minimizing the operator influence. The initial disadvantage of Scheimpflug imaging of only a few optical sections, has been overcome by the number of images recorded by the Pentacam® (25/50 images/eye). Densitometric and biometric image analysis needs a 3D data localization in the lens. This type of image analysis has been proven suitable for nuclear and cortical cataracts. Subcapsular cataracts pose more problems because of their 2D extension. Scheimpflug imaging with 50 images per eye partly compensates this, but retroillumination imaging can be superior in this case. OCT has been developed for imaging of the retina, but is now also used for the anterior eye segment. However, in radiation cataract and epidemiological studies, this technique is not useful, because optical coherence tomography detects coherence shifts at interfaces not particle related light scattering. It detects clearly shaped cataracts, but not changes in lens light scattering.

• 3263
The EURALOC Project

STRUELENS L
Belgian Nuclear Research Centre SCK-CEN, Environment- Health and Safety, Mol, Belgium

For radiation protection purposes, it has generally been assumed that there is a threshold of dose below which no non-cancer effects arise. Early dose threshold estimates for detectable lens opacities were defined at 0.5 to 2 Gy after acute or 5 to 6 Gy after protracted exposures. Due to the heterogeneity of ophthalmological data and too short observation periods, the thresholds were reconsidered in the ICRP report 118 (2012) and reduced to 0.5 Gy. An overview will be given of epidemiological studies that prompted the change in ICRP recommendations. These studies reported excess risks of lens opacities, but could not provide statistical significant evidence of a dose threshold. The results from all these studies are difficult to compare or combine. Moreover, another point of concern is the dosimetry which was often poor. These issues limit the possibility of a quantitative synthesis of evidence for a dose-response analysis in the low dose region to confirm this new dose threshold and urged the need of a harmonised European initiative. The EURALOC project, initiated in December 2014, aims at quantifying this dose-response relationship between ionising radiation and cataract among a cohort of European interventional cardiologists.

• 3264
Lifetime study in mice for radiation-induced cataracts

DALKE C (1), Rößler U (2), Neff F (3), Greiter M (4), Gomolka M (2), Hornhardt S (2), Unger K (5), Garrett L (1), Rosemann M (6), Kempf S (6), Azimzadeh O (6), Wurst W (1), Aubele M (3), Zitzelsberger H (5), Hölter S (1), Tapio S (6), Hoeschen C (4), Kulka U (2), Atkinson M (6), Graw J (1)
(1) *Helmholtz Zentrum München, Institute of Developmental Genetics, Neuherberg, Germany*
(2) *Federal Office for Radiation Protection, Department of Radiation Protection and Health SG1.1, Oberschleißheim, Germany*
(3) *Helmholtz Zentrum München, Institute of Pathology, Neuherberg, Germany*
(4) *Helmholtz Zentrum München, Research Unit Medical Radiation Physics and Diagnostics, Neuherberg, Germany*
(5) *Helmholtz Zentrum München, Research Unit of Radiation Cytogenetics, Neuherberg, Germany*
(6) *Helmholtz Zentrum München, Institute of Radiation Biology, Neuherberg, Germany*

We initiated a lifetime study in mice focusing on non-cancer effects after exposure to middle and low doses of ionizing radiation, particularly radiation-induced cataracts and retinal disorders.
Mice (males and females) were irradiated (0, 0.063, 0.125 and 0.5 Gy) and received ***in vivo*** examinations for lens opacities by Scheimpflug imaging monthly and for retinal effects by OCT every four months. To investigate the underlying mechanisms of radiation-induced effects mice are sacrificed at different time points (4 and 24 hours, 12, 18 and 24 months after irradiation) for pathological and histological examinations.
Beside wild-type mice, heterozygous ***Ercc2/Xpd*** mutants are included in the study to estimate the risk of genetic susceptibility in virtually healthy mutant mice, while homozygous ***Ercc2*** mutants develop cortical cataracts at early age. The ERCC2 protein has DNA helicase activity and is involved in general transcription and DNA repair.
First analyses of the Scheimpflug examinations did not show significant changes within the groups up to 20 months after irradiation with 0 and 0.5 Gy, while OCT data showed a reduction of the retinal thickness in irradiated heterozygous mutants. This study is still in progress.

• 3271

The obsession of the eyes in Luis Buñuel's work (Spain, 1900-Mexico, 1983)

ASCASO F (1,2,3)
(1) Hospital Clínico Universitario "Lozano Blesa", Department of Ophthalmology, Zaragoza, Spain
(2) Instituto de Investigación Sanitaria de Aragón, IIS Aragón, Zaragoza, Spain
(3) School of Medicine- University of Zaragoza, Department of Surgery, Zaragoza, Spain

Luis Buñuel was a highly regarded Spanish film director particularly famous for his silent surrealist short movie he made with the famous Spanish painter Salvador Dalí: *"An Andalusian Dog"*. Released in 1929, it is considered as the first film produced purely from within the Surrealist movement, and a landmark in the history of cinema. Based on an exchange of dreams between Dalí and acclaimed director Luis Buñuel, this tale of unfulfilled desire opens innocently with the words *"Once upon a time."* What follows is one of the most shocking and celebrated sequences in movie history: a razor slashing a woman's eye in extreme close up, along with the prolapsing vitreous. Buñuel's violent aggressions against sight actually force us back to his particular way of seeing. His world is seen first as a grey, hazy, distant jumble of undetermined things; no other director shoots a scene from quite that neutral, passive distance. Then the eye of the camera suddenly picks out an object that has been there all the time, or a revealing gesture, zooms into them, makes them come violently alive before again retiring to the indifferent point of view. This particular way of seeing also appears in: "*This Strange Passion*", *"Belle de jour"* and *"Viridiana"*.

• 3272

The history of the description of retinopathy in onchocerciasis

KESTELYN P
UZ Gent, Ophthalmology, Gent, Belgium

Up until 1930 the scientific community considered African onchocerciasis to be a pure skin disease and not the blinding disease encountered in America. Jean Hissette, a belgian general practitioner with a special interest in eye pathology, was the first to document onchocerciasis in Africa as a blinding disease. Between 1931 and 1938, he published a series of articles on the subject, based on the experience he gained from several expeditions in the endemic Babindi country (Belgian Congo). His discussions with J Bryant in 1932 stimulated the latter to publish an article in 1935 on the posible relationship between ***Onchocerca volvulus*** and endemic choroiditis in Sudan. As the result of his collaboration with R Strong, an expert from Harvard on the Central American form of the disease, Hissette wrote a paper that appeared in 1938 as a supplement to the American Journal of Tropical Medicine. In this landmark paper he describes with great precision the chorioretinitis of the posterior pole typical of onchocerciasis, later to be known as the Hissette-Ridley fundus. Although the names of the two men are linked, Hissette's work preceded Harold Ridley's publication in the BJO on ocular onchocerciasis in Ghana by more than a decade.

• 3273

Military ophthalmia and the Napoleonic campaign in Egypt.

DE LAEY J J
UZ Gent, Ophthalmology, Gent, Belgium

In 1798 the French armies landed in Egypt. During this campaign both the French and the British troops were confronted with eye infections. When they returned home the disease spread all over Europe. The Dutch army was also affected. When Belgium became independent in 1830, there were major discussions as what caused the disease. Some called "compressionist" considered it neither to be contagious nor Egyptian, but the consequence of the pressure of the leather collar on the jugulars and of the heavy shako on the forehead. For the others the "contagionists" the disease was highly contagious and spread directly from patients to healthy soldiers although there was also a possibility of "miasma." The uniform was adapted and hygienic measures were taken. Unfortunately one decision with dramatic repercussions was sending home diseased soldiers. As a result the disease spread within the civilian population and became a major health issue.
The very first international congress of ophthalmology was held in Brussels in 1857 and one of the major topics was the "military ophthalmia."
With strict measures the disease was eventually controlled although some regions were still affected up to the end of the 19th Century.

• 3274

Wegener's granulomatosis – should we change the name of the disease?

GRZYBOWSKI A
Poznan City Hospital, Department of Ophthalmology, Poznan, Poland

It was proposed that the eponym "Wegener's granulomatosis" should not be used any more due to the fact that Friedrich Wegener (1907-1990) was the member of the National Socialist German Workers Party and because it was suggested that had been involved during the WWII in human experiments and genocide. Based on this accusations the American College of Rheumatology, The American Society of Nephrology and the European League Against Rheumatism decided that all medical scientists should no longer use the term Wegener's granulomatosis. However, the real value of these accusations were questioned. It was confirmed that Wegener joined Sturmabteilung (SA "brownshirts"), the German State Party NSDAP and the National Socialist German Physicians' Federation (NSDÄB). It was also showed that the main accusations against him, namely human experiments and genocide during WWII had no foundation, and were based on speculations. The life of Wegener between 1933-1945 has been also presented in the historical perspective of situation in Germany in 30ties. There are no proofs that Wegener was ever involved in genocide and human experiments during the WWII, thus the term "Wegener's granulomatosis" should be considered as still appropriate.

Introducing a rare breakthrough in mitochondrial medicine

Abstract not provided

Optic neurodegeneration – the time to act is now

GUIEVEN N
Australia

Abstract not provided

Reaching key milestones in LHON – the idebenone clinical development program

METZ G.
Switzerland

Abstract not provided

Changing the patient journey in LHON: the evidence

KLOPSTOCK T
Germany

Abstract not provided

Q&A with panel

Abstract not provided

Blocking VEGF and PlGF : what is the interest in clinical practice?

DOT C
France

Abstract not provided

Systemic exposure to anti-VEGF : what is the reality ?

LEVY B
France

Abstract not provided

From basics to clinical evidences : Overview of efficacy & safety across macular edema indications (RVO & DME)

ZAMBROWSKI O
France

Abstract not provided

• 3421

Autophagy in neurodegeneration and inflammation and novel modulators of macroautophagy

BEHL C
University Medical Center Mainz, Mainz, Germany

Deregulated autophagy leads to protein accumulation and has been linked to aging, inflammation and neurodegenerative disease. While studying cell aging we found an expression switch between co-chaperones BAG1 and BAG3 during aging and acute stress triggering BAG3-mediated autophagic degradation of aggregated proteins (e.g. mtSOD1) ***in vitro*** and ***in vivo***. ***BAG3-mediated selective macroautophagy*** is an important adaptation of the PQC to pro-oxidant and aggregation-prone conditions. Recently, we performed a RNAi screen in ***C.elegans*** and identified ***rbg-1*** as modifier of protein aggregation and autophagy. The mammalian ortholog RAB3GAP1/2, components of the TBC domain-free RAB3GAP complex, affect autophagy at basal and rapamycin-induced conditions also in human fibroblasts. RAB GTPase activating proteins (RABGAPs) are important factors for vesicle transport. Correlating the activity of RAB3GAP1/2 with ATG3 and ATG16L1 and analyzing ATG5 punctate structures, we found that the RAB3GAPs actually modulate autophagosomal biogenesis: RAB3GAP1/2 colocalizes with lipid droplets, and their autophagy modulatory activity depends on GTPase activating activity of RAB3GAP1.

• 3422

Innate immunity in age-related retinal degeneration

LUHMANN U (1,2)
(1) *UCL Institute of Ophthalmology, Genetics, London, United Kingdom*
(2) *Current/new address: Roche Innovation Center Basel, Molecular Pharmacology & Biomarkers- Ophthalmology, Basel, Switzerland*

Purpose: Ageing is a major risk factor for the development of multifactorial ocular conditions like glaucoma, diabetic retinopathy and age-related macular degeneration. We aim to understand how its influence on the innate immune system may contribute to increased morbidity of retinal degenerations with age.
Methods: Changes in expression of cytokines, chemokines and complement genes in response to ageing, laser-injury or light were determined in young (2-4 months) and aged (18-24 months) wildtype, chemokine (***Ccl2-/-***) and complement regulator (***CD59a-/-***) deficient mice and correlated with myeloid cell populations and histology of the retina and the RPE-choroid.
Results: Ageing promotes pro-inflammatory ***Ccl2-Ccr2*** signalling and up-regulation of complement genes in particular in the choroid. Genetic ablation of ***Ccl2*** attenuates these age-related inflammatory changes and is associated with reduced recruitment of pro-inflammatory myeloid cells and a reduced CNV response. Deficiency of ***CD59a*** enhances complement activation but not pathology.
Conclusion Age-related innate immune activation by Ccl2 or by complement can promote ocular pathology, and may represent common mechanisms for enhanced pathology in age-related inflammatory diseases.

Commercial interest

• 3423

Heterogeneity of retina Müller glia and their possible role neuroprotecting retinal ganglion cells

VECINO E
Cell Biology, University of the Basque Country, Vizcaya, Spain

The retinal Müller glia, provide structural and trophic support to retinal ganglion cells (RGCs) in the healthy retina and may also have a function in promoting cell survival after injury. Defining and understanding glial heterogeneity is an important goal since it would enable to better understand the fundamental role of these cells during retinal pathologies and could even open novel therapeutic avenues, such as targeted manipulations of sub-populations in order to quench pro-inflammatory destructive processes and/or stimulate regeneration of neurons in retinal degenerative diseases. Muller glia primary cell cultures in combination with RGCs have been studied. The heterogeneity of the glial cultures was characterized and their effect on RGC survival and neurite elongation. We found that cultured adult RGCs in close contact with adult Müller cells exhibit improved cell viability and significant neurite elongation. Not all Müller cells express their molecular markers with the same intensity. These results suggest that Müller glia support RGC regeneration not only by direct interaction, but also releasing soluble trophic factors. Further understanding of the relationship between retinal glia and RGCs is important in order to identify potential therapeutic targets to encourage retinal neuroregeneration.

• 3424

Retinal innate immune activation in health and disease

XU H
Queen's University Belfast, Center for Experimental Medicine, Belfast, United Kingdom

Retina is considered as an immune privileged tissue, yet many inflammatory retinal diseases occur. Circulating immune cells are not able to freely migrate into the healthy retina due to the blood retina barrier. Retina is protected by its own innate immune system, including microglia, perivascular macrophages, a small number of dendritic cells and the complement system. When retina suffers from exogenous/endogenous insults, a well-controlled innate immune response is initiated to maintain homeostasis and restore functionality, such response is therefore beneficial. Dysregulation or malfunction of the innate immune response may result in excessive production of inflammatory mediators that may contribute to retinal pathology. The presentation will discuss how innate immune response is controlled in the retina, and the potential contribution of uncontrolled or dysregulated innate immune activation to retinal lesion development in common sight-threatening diseases such as age-related retinal degeneration.

• 3425

Beta II tubulin as molecular marker of intraocular pressure in endothelial cells

PROKOSCH-WILLING V
Münster, Germany,

The human CNS - like the adult mammalian CNS in general- lacks the capability to regenerate axons and restore neuronal tissue. After injury or in degenerative diseases like e.g. in glaucoma, neurons fail to regrow and reconnect with their target cells, frequently underlay apoptosis and are abnormally replaced. This regenerative failure in CNS remains an enormous scientific and clinical challenge. However under certain conditions neurons may regain the ability to regenerate in vivo and in vitro. One interesting group which shows enormous regenerative potential on retinal ganglion cells are the crystallins. We present our data on the regenerative potential of crystallins in experimental models.

• 3441

Improving the overall diagnosis of eyelid margin tumours with in vivo reflectance confocal microscopy

GRIVET D (1,2), Singer A (1), Forest F (3), Cinotti E (4), Douchet C (3), Labeille B (4), Perrot J L (4), Cambazard F (4), Dumollard J M (3), Peoc'h M (3), Gain P (2), Thuret G (5)
(1) University Hospital, Ophthalmology department, Saint-Etienne, France
(2) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint-Etienne, France
(3) University Hospital, Pathology department, Saint-Etienne, France
(4) University Hospital, Dermatology department, Saint-Etienne, France
(5) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine and Institut Universitaire de France, Saint-Etienne, France

Purpose The clinical diagnosis of eyelid margin tumours is often challenging and surgical excision in this area may have both functional and aesthetic consequences. Aim: to assess the role of handheld in vivo reflectance confocal microscopy (IVCM) in the diagnosis of eyelid margin tumours
Methods We prospectively evaluated and characterized 130 eyelid margin lesions using a handheld dermatology IVCM (Vivascope 3000, Mavig/Lcid, NY). Patients were referred to our multidisciplinary consultation from may 2013 to april 2015. All lesions were first clinically characterized as benign or malignant and then evaluated under IVCM by 3 skilled Dermatologists. Surgical excision was decided for 79 of them, based on both clinical and IVCM features. The 51 remaining lesions with no signs of malignancy were under followed up for at least 6 months. Clinical, IVCM, and histopathology diagnoses were compared
Results Considering the 79 excised lesions: IVCM showed a sensitivity (Se) of 90% and a specificity (Sp) of 57% for malignant tumours (basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma) as compared to the histopathology. Clinical evaluation had Se of 81% and Sp of 50%. IVCM showed Se and Sp of respectively 89% and 62% for BCC; 60% and 100% for SCC; 100% and 45% for melanoma. None of the non-excised lesions had clinical progression at 6 months and all these lesions were considered as benign
Conclusions IVCM is an important tool in the management of eyelid margin tumours by improving the global sensitivity and specificity of the clinical diagnosis
GRANT: AP jeune chercheur GIRCI RAA

• 3442

New management of peri-ocular basal cell carcinoma using in vivo and ex vivo confocal microscopes

ESPINASSE M (1), Grivet D (2), Perrot J L (3), Cinotti E (3), Labeille B (3), Forest F (4), Gain P (5), Thuret G (6)
(1) University Jean Monnet- Faculty of Medicine, Laboratory Biology- engineering and imaging of Corneal Graft- EA2521, Saint-Etienne, France
(2) University Hospital, Ophthalmology, Saint-Etienne, France
(3) University Hospital, Dermatology, Saint-Etienne, France
(4) Hospital University, Pathology, Saint-Etienne, France
(5) University Hospital, Ophtalmology, Saint-Etienne, France
(6) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine and Institut Universitaire de France- Bd St Michel- Paris- France, Saint

Purpose We have been using a handheld dermatology in vivo reflectance confocal microscopy (IVCM) for the imaging of the whole ocular surface and ocular adnexa for more than two year (JAmAcadDermatol2014;71:912, AJO2015;159:324), mainly for noninvasive diagnosis before surgery. Ex vivo confocal microscopy (EVCM) is a new device that allows pseudo histology in freshly excised tissue. Aim: to assess a new management strategy for eyelids lesions suspected to be basal cell carcinoma (BCC) using these two complementary confocal microscopes (CM).
Methods IVCM and EVCM, both using vivascope CM (Lucid Inc, NY) were performed by 3 skilled dermatologists having more than 500 CM diagnoses each with pathology confirmation. Forty consecutive peri-ocular BCC were diagnosed by IVCM. Two millimetre-margin incisions were made during surgery. Freshly excised tissues were mounted, unstained, between two glass slides and analysed « en face » with EVCM to delimitated the tumour and the clearance of margins. Diagnosis and margins were confirmed by standard pathology and immunolabeling on fixed tissues.
Results We obtained the first « en face » EVCM to delimitated the tumour. The acquisition of the whole tumour took less than 3 minutes. Tissues were not damaged by flat mount nor by exposure to laser beam. Histology confirmed all IVCM diagnosis of BCC and all clear margins.
Conclusions Association of IVCM and EVCM allowed accurate management of peri ocular BCC, using micrographic surgery to reduced surgical margins.
GRANT: project INNOVEYE GIRCI RAA

• 3443

Cyclin kinase inhibitor p27 is downregulated in conjunctival melanoma

MOULIN A , Schalenbourg A , Zografos L , Nicolas M
Jules-Gonin Eye Hospital, Ophthalmology, Lausanne, Switzerland

Purpose As loss of cyclin dependent kinase inhibitors p27 and p21 have been identified in cutaneous melanoma and associated with a poorer prognosis, we decided to assess the expression of p27 and p21 in benign and malignant conjunctival melanocytic proliferations.
Methods The expression of p27 and p21 was assessed by immunohistochemistry in 35 conjunctival naevi and 32 conjunctival melanomas. Statistical analysis was performed with JUMP 8,0 software. Immunohistochemistry was evaluated independently by two observers.
Results There was a concordance in 94.02 % and 92.54% of the cases in the evaluation of the expression of p27 and p21, respectively. Discrepant cases were simultaneously reviewed to achieve complete agreement. There were 13 subepithelial nevi and 22 compound nevi. There were 14 females and 21 males with a mean age was 36.9 ± 3.6 yo (SEM). Nuclear expression of p27 was found in all the nevi. p21 was identified in only 4 nevi (11.4%). The melanoma group was composed of 18 females and 14 males with a mean age of 65.9 ± 3.38 yo (SEM). p27 and p21 were respectively lost in 18 cases (56.25%) and in 24 cases (75%). There was a significant downregulation of p27 in conjunctival melanoma compared to benign conjunctival nevi ($p>0.0001$). In the melanomas, there was a correlation between loss of p27 expression and depth of invasion ($p=0.0141$) as well as non-bulbar tumor localization ($p=0.0279$). Although the proliferation index was more elevated in melanomas with p27 loss, this was not significant.
Conclusions The downregulation of p21 in benign melanocytic proliferations identified in the skin appears also to occur in the conjunctiva. Our results also demonstrate in vivo a significant downregulation of p27 in conjunctival melanoma. Restauration of p27 function in conjunctival melanoma might represent a potential therapeutical option for this tumor.

• 3444

Looking for the best mouse model to study retinoblastoma

LEMAITRE S (1), Poyer F (1), Cassoux N (2), Fréneaux P (3), Thomas C (1)
(1) Institut Curie, U1197-UMR9187, Orsay, France
(2) Institut Curie, Ophtalmologie, Paris, France
(3) Institut Curie, Pathologie, Paris, France

Purpose Retinoblastoma is the most common primary intraocular tumor in children. Current therapies have many adverse effects. New approaches must therefore be developed and evaluated on animal models. Retinoblastoma mouse models include transgenic mice and patient-derived xenografts. We report our experience with orthotopic xenograft models of retinoblastoma using different mice strains.
Methods Human retinoblastoma tumors were established and maintained by xenografted cells from enucleated eyes on immunodeficient mice. The orthotopic model was obtained by subretinal injection of cells in suspension in the right eye of immunodeficient (nude, SCID) and immunocompetent mice (C57BL6N, B6ALB). Tumor growth was monitored by SD-OCT imaging and histology was also performed.
Results Tumor growth was observed both in immunocompetent and in immunodeficient mice. Chronic retinal detachment may occur after the subretinal injection. Retinal, subretinal and vitreal tumor growth were achieved in four different strains. Retinal anatomy (thickness and number of layers) is different in nude mice. Mouse strains include immunocompetent and immunodeficient mice, albino and pigmented mice. Albino mice suffer from light-induced retinal degeneration and a retinal degeneration mutation is present in the C57Bl6 strain. Consequently, visual function after treatment can be difficult to interpret in these mice. Retinal anatomy in nude mice may be responsible for chronic retinal detachment after the subretinal injection.
Conclusions The genetic background of a given mouse can influence on its visual properties but it does not seem to influence the establishment of a xenograft model.

• 3445

Orbital T-cell lymphoblastic lymphoma

HEEGAARD S, Stenman L
Ojenpatologisk Institut, Glostrup/RH Eye Department, Copenhagen, Denmark

Purpose To present the clinical, pathological and genetic characteristics of a case of primary T-cell lymphoblastic lymphoma of the orbit.
Methods Clinical work-up and morphological - and immunohistochemical study. Genetic analyses using FISH, DNA sequencing and arrayCGH analysis.
Results A 22-year-old man presented with a 3-week period of headache, reduced visual acuity and restricted eye movements of the left eye, unresponsive to antibiotic treatment. MRI scan showed large thickening of the extraocular muscles. Biopsies showed infiltration of lymphoma cells in the medial and superior rectus muscle as well as the superior oblique muscle of the left eye. Morphological and immunohistochemical studies of the biopsies showed T-cell lymphoblastic lymphoma. No major genomic imbalances were detected by high-resolution arrayCGH. FISH analysis revealed no evidence of chromosomal translocation involving the *ETV6* and *MLL* genes.
The patient received chemotherapy according to the high-risk NOPHO-protocol as well as a myeloablative allogenic bone marrow transplantation. The patient remains free of lymphoma nine months after the diagnosis, but with loss of visual acuity on his left eye.
Conclusions Primary T-cell lymphoblastic lymphoma in the eye region is very rare. It is important to recognize these patients early and think of lymphoma as a differential diagnosis in patients with involvement of the extraocular muscles. This is the first reported case of a T-cell lymphoblastic lymphoma in the orbit.

• 3446

The effect of PAXgene fixation on preservation of morphology and nucleic acids in microdissected retinal tissue

EDWARD D, Liu Y
Wilmer Eye Institute, Ophthalmology, Baltimore, United States

Purpose To compare the effect of the 2 fixatives on tissue morphology and to obtain good quality nucleic acids for molecular analysis from micro-dissected retinal samples
Methods Enucleated specimens from NZ white rabbits were fixed in formalin or PAXgene fixative using standard protocols, and then processed and embedded in paraffin for sectioning. H&E stained were used to assess the structural integrity of the retina. Retinal tissue on slides was micro dissected using a 27 gauge needle under a dissection microscope. DNA/RNA were extracted and assessed for preservation of quality and quantity of the retinal tissue.
Results The retinal morphology was well preserved with both PAXgene and formalin fixation. The RNA yield from both fixation methods was similar, but RNA from PAXgene fixed samples had a better purity than that extracted from formalin fixed paraffin embedded samples (FFPE). For DNA, there was a twofold greater yield in PAXgene fixed samples (PFPE) compared to FFPE but with similar purity. Quantitative reverse transcription polymerase chain reaction analyses from two assays showed that the mean Cycle threshold values for beta-actin, beta-microglobin, Opsin 1-sw, Rhodopsin and 18S RNA of PFPE group was significantly lower than those of FFPE group (suggesting better RNA integrity) ($p < 0.01$ for all groups). A greater than 10-fold level of gene expression was detected in PFPE relative to FFPE for the above genes in both assays. Furthermore, the number of tissue sections required for these studies suggested that this technique could be applied to study retinal macular molecular pathology.
Conclusions PAXgene fixed tissue retinal morphology is comparable to FFPE tissue. PAXgene may be a good alternative to formalin, providing good tissue morphology and ability to isolate high quality nucleic acids from micro-dissected paraffin embedded retinal samples.

• 3451

Optic coherence tomography in analyzes of optic nerve and macula in neuro-ophthalmological patients

COSTA L , Vicente A , Anjos R , Santos A , Ferreira J , Amado D , Cunha J P
Centro Hospitalar de Lisboa Central, Oftalmologia, Lisboa, Portugal

Purpose Historically, is made the distinction between optic neuropathies and macular diseases. Although, in our practical experience we believe that optic nerve (ON) damage, such as nerve edema or atrophy, at certain point will affect the macula. We have analyzed the scientific/structural impact of this clinical impression. The authors studied the correlation between Retinal Nerve Fiber Layer (RNFL) thickness and total macular/ganglionic cell layer (GCL) thicknesses using Optic Coherence Tomography (Heidelberg Spectralis®).
Methods This retrospective study, evaluate 114 patients with the initial diagnose of optic neuropathy. First, was measured the average thickness of RNFL in 4 quadrants and the central macula and GCL thicknesses in 1º, 2º and 3º mm in fovea. We studied it in 3 groups: ON pathology (1º - n: 68), chiasmal compressive lesions (2º – n: 8) and retro-chiasmal pathology (3º – n: 38). The layer's thickness was correlated in 3 groups.
Results The 1º and 3º group had a significant impairment in all measures (RNFL, total central macula and GCL). There is a moderate correlation between RNFL and total central macular thicknesses (r: 0,354 and r: 0,314) and the correlation is strong comparing RNFL and GCL in 2º mm (r: 0,653 and r: 0.775) and 3º mm (r: 0,674 and r: 0, 839) thicknesses. Although, we didn't find any correlation between the RNFL and GCL thicknesses in 1º mm of fovea. In 2º group the results wasn't statistically significant, possible because the sample is short (n: 8).
Conclusions In both groups, there is a correlation between the RNFL and total macula thicknesses. The impairment of total macula thickness is strongly correlated with the decreased thickness in GCL of foveae's 2º and 3º mm. This study shows in that pré-chiasmal and retrochiasmal lesions, the impairment RNFL co-exists with affection of macula thickness.

• 3452

Optic nerve Drüsens in black patients : a case series of 16 patients

SUSTRONCK P , Jean-Charles A , Benzekri R , Merle H
University Hospital of Martinique, ophthalmology, Fort de France, France

Purpose Optic nerve Drüsens are rare among black patients. The goal of our study was to describe the characteristics of ophthalmological findings in this population.
Methods We carried out a descriptive prospective study from June 2006 to October 2014 on 19 eyes of Afro-Caribbean patients from Martinique with optic nerve Drüsens diagnosed by fundoscopy and B-Scan ultrasonography. Patients underwent clinical exam, Optical coherence tomography (OCT), colour vision, and visual field. Three eyes were excluded from visual acuity and paraclinic analysis due to an anterior optic ischemic neuropathy (AOIN), a penetrating eye injury and an epimacular membrane.
Results 11 Afro-Caribeean patients were included: four men and seven women with age ranking from 11 to 68 years with a mean age of 41. Nine of the 11 patients (69%) had bilateral optic nerve Drüsens. Only 2 patients (12%) were symptomatic including the AOIN. Mean ETDRS visual acuity was 56 at 4 meters (min 31, max 68, sd 7.0). Three of 16 eyes (19%) had an ETDRS vision loss. Four of 16 (25%) had a Pellirobson contrast vision loss due to cataracts. Four patients (25%) had a dyschromatopsy. The average OCT RNFL was 94µm (min 57, max 150, sd 18.7). Mean foveal threshold was 34 db (min 22, max 39; sd 2.8). 11 of 16 eyes (69%) showed a visual field defect: Nine had an enlarged blind spot and nine had an arcuate scotoma. None of the patients had a pathology associated with optic nerve Drüsens such as pigmentary retinopathy or angioïd streaks.
Conclusions This study is the largest case series carried out on optic nerve Drüsens in black patients. It shows that the majority of them is asymptomatic but campimetric defects are common. Some rare but severe complications can occur such as AION.

• 3453

Treatment of Leber's hereditary optic neuropathy with EPI-743: the Brazilian experience

KARANJIA R (1), Ganti A (2), Chu E (2), Wagschal T (3), Belfort- Jr. R (4), Moraes- Filho M (4), Salomao S (4), Chicani F (4), Guy M (5), Sadun A (1)
(1) Doheny Eye Centers UCLA, Ophthalmology, Pasadena, United States
(2) University of Southern California, Ophthalmology, Los Angeles, United States
(3) University of Iowa, Visual Field Reading Center, Coralville, United States
(4) Universidade Federal de Sao Paulo, Ophthalmology, Sao Paolo, Brazil
(5) Edison Pharmaceuticals, Research and Development, Mountain View, United States

Purpose To determine the degree of visual improvement in a homogeneous Brazilian cohort of Leber's Hereditary Optic Neuropathy (LHON) 11778 receiving 18-24 months of therapy with the quinone EPI-743.
Methods Six patients with severe vision loss from LHON were enrolled in an open label clinical trial. Each patient received 400 mg TID of EPI-743. Two patients were treated at the time of conversion, while 4 patients had chronic disease (>5 years). Outcome measures included best corrected visual acuity (BCVA), retinal nerve fiber layer (RNFL) thickness as measured by Optical Coherence Tomography and Humphrey Visual Fields (HVF) mean deviations. Mean deviations were calculated using the HVF algorithm (Stim III) or
University of Iowa Visual Field Reading Center Algorithm (Stim V).
Results VA declined or stabilized in the first 6 months, then improved gradually for all 6 patients and remained stable for 18-24 months with EPI-743. VF increased marginally in one chronic and both acute patients, while 3 chronic patients remained at baseline. The acute patients showed continued bilateral progression for the first 6 months, consistent with the natural history of LHON. As expected, all eyes showed a decline in RNFL that stabilized after treatment.
Conclusions VA improvements continued beyond the initial 1 year period to 18-24 months of treatment, including 4 patients who had lost vision over 5 years prior to start of EPI-743. This data is consistent with data from the United States where an EPI-743

Commercial interest

• 3454

The influence of lingering fusional adaptation on the Bielschowsky head tilt test in superior oblique paresis

IRSCH K (1,2), Guyton D (1), Ying H (1)
(1) The Johns Hopkins University School of Medicine, The Wilmer Eye Institute, Baltimore, United States
(2) Clinical Investigation Center – CIC 1423 INSERM, Quinze-Vingts National Eye Hospital, Paris, France

Purpose To investigate how fusion influences the Bielschowsky head tilt test (BHTT) in unilateral superior oblique paresis (SOP).
Methods In eight fusing patients, we correlated haploscopic-determined fusion mechanisms with BHTT differences (BHTTD).
Results Five patients used the vertical recti for vertical fusional vergence and had a mean±SD BHTTD of 22±8PD. After a 30-minute patch test one of those, in whom the test was performed, showed a decrease of 10PD. Two patients used the "paretic" superior oblique muscle (SOM) and the contralateral superior rectus muscle (SRM) to fuse, and had a mean±SD BHTTD of 6±8PD. The BHTTD of one, in whom a patch test was performed, increased by 11PD. The remaining patient used the "paretic" SOM and contralateral inferior oblique muscle (IOM) to fuse, and had a BHTTD of only 3PD, increasing to 21PD after patching. One explanation for this behavior in the last patient involves lingering vergence adaptation of the "paretic" SOM and contralateral IOM, which makes these muscles more effective when activated on ipsilateral head tilt, lessening the expected increase in hyperdeviation. Similarly, in our patients with oblique/rectus-mediated fusion, the vergence-adapted "paretic" SOM and contralateral SRM are activated on ipsilateral and contralateral tilt respectively, lessening the hyperdeviation in both directions. In the other five patients, however, the vergence-adapted ipsilateral IRM and contralateral SRM are activated on contralateral tilt, accentuating the BHTTD.
Conclusions Fusion influences the BHTTD, either decreasing or increasing it depending on the particular muscles used for fusion. The absence of a positive BHTT should not be relied upon to rule out the diagnosis of SOP. In suspected SOP patients with fusion, performing the BHTT after a patch test may be necessary to bring out the BHTTD supporting the diagnosis.

• 3455

Optic disc swelling : Prospective study of sixty-seven patients

SITBON C , Fel A , Bodaghi B , Le Hoang P , TOUITOU V
La Pitié Salpétrière, Ophthalmology- DHU Vision et Handicaps, Paris, France

Purpose To assess the clinical features and etiologic work-up of patients presenting with optic disc swelling (ODS) in the emergency room.
Methods Patients seen in the ophthalmology emergency department of a single tertiary center between november 2014 and october 2015 were prospectively included. Each patient underwent an etiologic work-up including a brain-MRI, blood work, fluorescein angiography, and visual evoked potential.
Results 67 patients (39 female and 28 male) were included in this study. Average age was 46 years (17-86 years). ODS was unilateral in 45% of cases and bilateral in 55% of cases. The average time between the onset of symptoms and diagnosis of papillary edema was 80 days (3 days to 8 months). The mean initial visual acuity was 0.2 logMAR, and the mean final VA was 0.1 logMAR. Final diagnosis was intracranial idiopathic hypertension (43%), anterior ischemic optic neuropathy (25%), inflammatory or infectious papillitis (22%), compressive optic neuropathy (2%) and unknown in 3 cases (8%). The etiologic work-up was contributive for the final diagnosis in 10% of cases for fluorescein angiography; 35% for MRI of the optical nerve; 32% for laboratory tests; 67% for visual evoked potentials; 90% for the visual field of Goldman. Findings of Goldman's visual field included central or caecocentral scotoma (32%), exclusion or enlarged blind spot (41%), inferior altitudinal scotoma (19%), and bitemporal quadrantanopia (5 %).
Conclusions Our results demonstrate that causes of ODS could be identified in 92% of patients presenting with ODS. According to the clinical features at presentation, the etiologic work-up can be further adjusted but a standard minimal etiologic work-up is usually efficient to state the diagnosis.

• 3456

Nonarteritic anterior ischemic optic neuropathy (NAION): A misnomer. A non-ischemic papillopathy caused by vitreous separation

PARSA C (1), Hoyt W (2)
(1) *Quinze-Vingts National Eye Hospital / UPMC-Sorbonne Universités, Ophthalmology, Paris, France*
(2) *UCSF School of Medicine, Ophthalmology, San Francisco, United States*

Purpose Vascular abnormalities such as disc hemorrhages and swelling present at the time of visual loss in NAION, followed by peripapillary vascular narrowing and ensuing disc pallor is enticing, but not etiologically conclusive for ischemia. Optic disc as well as retinal findings of whiteness with disc swelling is indicative of axoplasmic stasis that may also occur simply from anatomic distortion of axons rather than occlusion of vessels. It may also occur from mechanical stretching with fracture of the axonal cytoskeleton.
Methods Review of the literature regarding 1) vitreous attachments and effects of separation from the optic disc, 2) dynamic shear force stretch injury to axons.
Results Within the normal population and in the age-goup in which NAION occurs, 10% have complete PVD, 70% partial PVD, and 20% no PVD. In those with acute NAION, however, either total vitreous separation from the disc, or complete parapapillary detachment, is always present. Any teleangectatic vessels on the disc surface correspond to areas of visual field sparing and encompass areas of unseparated vitreous still under tension.
Conclusions Where internal limiting membrane is absent over the disc and peripapillary retina, most notably in cupless discs where epipapillary membrane adhesions are strongest, vitreous separation may momentarily stretch and elongate axons, breaking the cytoskeleton in more aged and less distensible axons, leading to immediate axoplasmic accumulation and atrophy in the prelaminar sites of separation. Vitreous synchysis occurs more precociously in diabetics. Ischemic pathophysiology need not be invoked in so-called NAION, better termed papillary vitreous detachment, or *PVD-N*. In those at risk, the timely and controlled release of vitreous connections to the optic disc may prevent such optic disc injury.

• 3457

Ophthalmic insert for pupillary mydriasis in neonates

BREMOND-GIGNAC D (1,2), Jacqz-Aigrain E (3), Abdoul H (3), Beresniak A (4), Baud O (3), Alberti C (3)
(1) *APHP- Hôpital Universitaire Necker Enfants Malades, Pediatric Ophthalmology, Paris, France*
(2) *CNRS Unit FR3636, Binocular vision, Paris V University, France*
(3) *APHP- Hôpital Universitaire Robert Debre, 75019, Paris, France*
(4) *Data Mining International, Geneva, Geneva, Switzerland*

Purpose To study efficacy and tolerance of ophthalmic insert Mydriasert® versus standard treatment phenylephrine and tropicamide eye drops for fundus examination in neonates.
Methods Prospective, randomised, single-blinded non-inferiority study of 80 premature and full-term babies and infants treated for fundus examination. Mydriasis was obtained with two groups randomly assigned. The eye drop group received three instillations of 2.5% phenylephrine and 0.5% tropicamide and the insert group received Mydriasert® containing phenylephrine and tropicamide. the mydriasis was evaluated 75 minutes after the introduction of the mydriatic agents.
Results The mydriasis was successfully achieved in both eyes in 97.5% of infants in the insert group and 90% in the eye drop group at 75 minutes after dispensation. The efficacy of the insert was non-inferior compared to the eye drops. To reach effective mydriasis, the insert group required fewer nursing interventions for one patient comparing to the eye drop group. Good general and local tolerance was observed in the two groups. However two patients reported an adverse event as bradycardia and gastro-oesophageal reflux that could be related to neonate pathology.
Conclusions Mydriasis obtained with the ophthalmic insert Mydriasert® was not inferior compared to standard eye drop treatment. Insert reduced the number of nursing interventions to obtain mydriasis for a fundus examination.

• 3458

Homonymous hemimacular thinning in retrochiasmal lesions

CUNHA J P , Proença R , Dias-Santos A , Vicente A , Anjos R , Costa L , Cardigos J , Ferreira J , Amado D
Centro Hospitalar de Lisboa Central, Oftalmologia, Lisboa, Portugal

Purpose To evaluate the thickness of macular retina and determine which retinal layers are most affected by retrochiasmal visual pathways lesions.
Methods mean retinal thickness utilizing automated intraretinal layer segmentation of spectral domain optical coherence tomography scans was performed in 40 eyes of 40 patients with retrochiasmal visual pathways lesions and compared with 60 eyes of control subjects. Multiple linear regression analysis was used to determine the relationship between retinal thickness and follow-up, age and gender.
Results Ganglion cell and inner plexiform layer was thinner in the temporal hemiretina ipsilateral and in the nasal hemiretina contralateral than in healthy controls. The mean thickness was significantly reduced in lesions over 6 months of duration, with no differences in correlations with age or gender.
Conclusions This study demonstrate ganglion cell and inner plexiform thinning in the hemimacular area. These results support the concept that transneuronal retrograde degeneration of the retinal ganglion cells can be detected by OCT in humans with retrochiasmal visual pathways lesions.
This homonymous hemimacular thinning in OCT represents an imaging biomarker that can be of valu in diagnosis, prognosis and clinical trials of neuroprotectives therapies.

• 3461

Mutations in Connexin-encoding genes

BEYER E, Berthoud V
University of Chicago, Pediatrics, Chicago- IL, United States

Gap junctions formed of connexin46 (Cx46) and connexin50 (Cx50) facilitate lens function and survival. Mutations of the connexin-encoding genes (***GJA3*** and ***GJA8***) have been linked to inherited cataracts. We expressed these mutants ***in vitro*** to elucidate abnormalities that contribute to cataractogenesis. Most of the mutants reduce intercellular communication due to alterations of channel function or impaired connexin synthesis/assembly/stability. One unusual mutant (Cx50P88S) forms cytoplasmic accumulations that may act as light scattering particles. Another unusual mutant (Cx50G46V) exhibits increased hemichannel function that may cause cell injury and death. We have studied mice expressing two different connexin mutants (Cx50D47A and Cx46fs380) that mimic cataract-linked human mutations. Both mouse lines develop cataracts (although with different time courses) and have reduced connexin levels (mutant and co-expressed wild type) likely due to protein degradation. Our studies suggest that reduction of intercellular communication is a common feature that contributes to connexin mutant-linked cataractogenesis, but individual mutants cause additional abnormalities that contribute to differences in phenotypes.

• 3462

Mutation in the Ercc2 gene of the mouse causes cataracts

GRAW J (1), Kunze S (1), Dalke C (1), Fuchs H (2), Klaften M (2), Sabrautzki S (2), Hrabe de Angelis M (2)
(1) Helmholtz Center Munich, Institute of Developmental Genetics, Neuherberg, Germany
(2) Helmholtz Center Munich, Institute of Experimental Genetics, Neuherberg, Germany

Cataracts have been associated with many mutations. In a large-scale high-throughput ENU mutagenesis screen we analyzed the offspring of paternally treated C3HeB/FeJ mice for obvious ocular dysmorphologies.
We identified a mutant suffering from rough coat and small eyes only in homozygotes; homozygous females turned out to be sterile. The mutation was mapped to chromosome 7 between the markers ***116J6.1*** and ***D7Mit294***. The critical interval (8.6 Mb) contains 3 candidate genes (***Apoe***, ***Six5***, ***Opa3***); none of them showed a mutation. Using exome sequencing, we identified a c.2209T>C mutation in the ***Xpd/Ercc2*** gene leading to a Ser737Pro exchange.
During embryonic development, the mutant eyes did not show major changes. Postnatal histological analyses demonstrated small cortical vacuoles; later, cortical cataracts developed. Since XPD/ERCC2 is involved in DNA repair, we checked also for the presence of the repair-associated histone γH2AX in the lens. During the time, when primary lens fiber cell nuclei are degraded, γH2AX was strongly expressed in the cell nuclei; later, it demarcates clearly the border of the lens cortex to the organelle-free zone. These findings demonstrate the importance of XPD/ERCC2 for lens fiber cell differentiation.

• 3463

Whole exome sequencing in patients with congenital cataracts

LIŠKOVA P
Charles University, Prague, Czech Republic

Next-generation sequencing (NGS) represents one of the most significant technological advances in the biological sciences of the past decade. NGS is now being introduced by many laboratories for routine diagnostic use. For genetically heterogeneous disorders approaches include custom-designed target enrichment permitting analysis of disease-associated gene panels and whole exome sequencing (WES). The sensitivity, speed and cost per sample makes WES a valuable tool and it is increasingly being used to identify the molecular genetic causes of inherited cataracts. The detection rate of disease-causing mutations is high and the results enhance clinical diagnosis and genetic counselling of the affected families.

• 3464

Gene panels and genomic testing for childhood cataract and lens dislocation disorders

BLACK G C (1), Hall G (2), Ramsden S (2), Lloyd I C (3)
(1) St. Mary's Hospital- Children's University Hospitals NHS Trust, Manchester, United Kingdom
(2) Central Manchester University Hospitals NHS Foundation Trust, Centre for Genomic Medicine, Manchester, United Kingdom
(3) Central Manchester University Hospitals NHS Foundation Trust, Royal Eye Hospital, Manchester, United Kingdom

Congenital cataract (CC) affects 3-5 individuals per 10,000 and is a significant cause of lifelong visual disability worldwide. Highly heterogeneous, CC may be isolated or may form one manifestation of a multisystemic condition. It is estimated that around 50% of bilateral CC cases have a genetic basis, with well over 100 genes implicated in their underlying etiology. Consequently, the identification and characterisation of CC is not equivalent to making a clinical diagnosis on which is based care planning, genetic counselling and non-ocular management. Until recently, clinical investigation of patients with CC has been based upon an iterative, clinically-driven process that is expensive, time-consuming and inefficient. The advent of Next Generation Sequencing promises to provide a platform upon which can be built a unified approach to diagnosis. We, and others, have shown that such an approach can identify the molecular basis of CC and other lens-related disorders such as lens subluxation in the majority (over 70% in our series) of cases. When applied early in the diagnostic pathway this can direct ongoing management, improve outcomes for pathents, and direct genetic counselling for families with CC.

• 3471

Light-Induced Retinopathy in neonatal rats: A new retinal degeneration slow model

LACHAPELLE P, Polosa A , Ait Igrine W , Chevrolat L A , Bessaklia B
McGill University-Montreal Children's Hospital Research Institute, Ophthalmology, Montreal Quebec, Canada

Purpose We showed that compared to adult rats (AR), the retina of neonatal rats (NR) is significantly more resistant to light damage. The purpose of this study was to determine the minimum exposure time that the neonatal retina requires to cause an adult-like retinopathy at long term.
Methods Starting at postnatal age 14 days (P14), NR were exposed to 10,000 lux for various lengths of time [1, 2, 3, 6, 9, 12 and 16 consecutive days (d)]. ERGs and retinal histology were performed at predetermined time points.
Results Maximal effect was obtained after 3 days of exposure [50% control ONL thickness ($p<.05$) compared to 97% and 75% for 1 and 2 days] beyond which no further significant ($p>0.05$) thinning of the ONL was observed. In contrast, a significant ($p<0.05$) dose-dependent decrease of all ERG components is observed immediately following the cessation of light exposure. Athough non-significant structural damage could be documented immediately following 1 day of exposure, when re-examined at P70, the photoreceptor loss was almost identical ($p>0.05$) to the damage produced following a 14 day long exposure.
Conclusions Our findings suggest that in NR, a one day long light exposure is sufficient to produce, at long term, a significant retinal degeneration that will significantly impact the retinal structure and function and that in spite of the fact that no measurable structural and functional retinal anomalies could be demonstrated immediately following this 1-day exposure (i.e. at P15). Our light-induced slow retinal degeneration model thus represents an attractive (especially its dose-dependent nature) alternative (to other more genetic models) to study the pathophysiology of photoreceptor-induced retinal degeneration and therapeutic strategies to counteract it. Funding: CIHR and FRQ-S, under the frame of E-Rare-2, the ERA-Net for Research on Rare Diseases.

• 3472

Clinical evaluation of video imaging technology during visual field exams

CHARLIER J (1), Zanlonghi X (2), Defoort-Dhellemmes S (3)
(1) Metrovision, France,
(2) Clinique Sourdille, Visual function evaluation, Nantes, France
(3) CHU Lille, Sevice d'exploration des fonctions visuelles, Lille, France

Purpose Video imaging consists in recording the entire visual field process in synchrony with the video of the patient's head. Several clinical applications have been investigated to evaluate the clinical usefulness of this new technology.
Methods The study included results from 48 visual field exams performed on a MonCvONE full field projection perimeter with synchronized video recording.The video from a large viewing field camera was recorded in synchrony with the position of the visual stimulus, with other test parameters such as luminance and size and with the patient's response obtained from the patient's press button or from the operator judgment. The study included patients who were unable to perform automated perimetry due to young age or handicap, patients with abnormal eye movements, head posture or ptosis and controls performed after automated perimetry.
Results Video recording was extremely useful in the majority of clinical cases. 24 exams were performed on young children (age between 2 and 5 years) using attraction perimetry. The eye orientation responses could be interpreted and validated after the exam. In other cases, the video recording facilitated the interpretation and documentation of visual field results with the inclusion of video snapshots in the examination report. Additional applications included the recording of cardinal eye gaze positions and of the fusion visual field.
Conclusions Synchronized video imaging performed during visual field exams is a clinically useful tool for the examination of patients who cannot perform automated perimetry and for the documentation of artefacts and situations such as ptosis, abnormal eye movements, abnormal head posture and incorrect position of refraction.

Commercial interest

• 3473

Using reaction time in visual search and decision making task to measure visual field thresholds in multifixation perimetry

LEINONEN M , Mäntysalo T , Sampinen K , Ojala M
Ocuspecto Ltd, Research, Turku, Finland

Purpose The ability to make eye movements to point the fovea toward object perceived in peripheral visual field is a fundamental feature of human visual system. We studied if reaction time (RT) in visual search task can be used for deciding if a peripheral visual field stimulus is visible when measuring visual field thresholds.
Methods Ocusweep™ ambient light perimeter was programmed to display peripheral 0.2° stimulus of 100 ms duration for triggering a reflex saccade to point the fovea towards the location of the stimulus which was replaced with a faint arrow figure for reporting its direction with a button press and thus confirming foveal fixation. Next peripheral stimulus followed by a new arrow was then displayed. RT between button presses were recorded. Thresholds of the right eye of eight experienced healthy persons (mean age 43, range 22 - 58 years) using Humphrey 30–2 grid were measured with a staircase algorithm adjusting the intensity of the stimulus in response to the RT. Measurement reliability was estimated with catch trials, viewing distance controlled using ultrasonic rangers and variation in ambient room lighting (94 - 240 cd/m^2) compensated using ambient light sensors of Ocusweep™.
Results Thresholds measured with RT perimetry were close to normal age corrected values of Octopus perimeter: mean MD was 0.7 dB and mean sLV 2.5 dB. The RT difference between positive (no stimulus, pure visual search, mean RT 1980 ms) and negative catch trials (suprathreshold stimulus, reflex saccade, mean RT 649 ms) was 1331 ms (SD 369 ms).
Conclusions Reaction time perimetry can be used to measure visual field thresholds and also to assess reflex saccades.

Commercial interest

• 3474

Electrophysiological ON and OFF responses in Autosomal Dominant Optic Atrophy

MORNY E (1), Margrain T (1), Binns A (1,2), Votruba M (1,3)
(1) Cardiff University, School of Optometry and Vision Sciences, Cardiff, United Kingdom
(2) City University, Division of Optometry and Visual Science, London, United Kingdom
(3) University Hospital of Wales, Cardiff Eye Unit, Cardiff, United Kingdom

Purpose To assess the effect of ADOA on the ON and OFF components of the photopic negative response (PhNR).
Methods Twelve participants from 6 families with OPA1 ADOA and 16 age matched controls were recruited. Electrophysiological assessment involved long flash focal (20o) and full field ERGs using red flash (664nm, 250msec, 55 cd/m2, 2Hz) on a rod saturating blue background (454nm, 100 scot cd/m2); and brief xenon flash ERGs using red filter (Lee Filter "Terry Red", max 300 µs flash duration, 1.69 cd.s.m-2, 4Hz) over a continuous rod saturating blue background (Schott Glass Filter BG28, 206 scot cd/m2). Amplitudes (from peak and baseline to fixed time point) and implicit times of the ERG components were analysed.
Results Mean amplitude (peak to fixed time) of the focal PhNR-ON were significantly ($p<0.05$) reduced by 40% while the focal PhNR-OFF was completely eliminated. In the long duration full field ERG, the PhNR-ON and –OFF were reduced by 21% and 57% respectively. Subtraction of the grand averaged ERG of ADOA participants from that of the controls produced a difference plot with a nearly symmetrical loss in the PhNR-ON and OFF components of the focal ERG. ROC curve analysis showed focal PhNR-ON and OFF amplitudes performed better than their full field counterparts.
Conclusions We show that OFF components of the photopic ERG were more severely affected in ADOA than ON components. Additionally, the focal PhNR-ON and –OFF components were more effective in assessing ADOA than their full field components.

• 3475

Apparent Contradictions in Pupillomotor, Sensory Visual and Electrodiagnostic Findings in Chiasmal Compression

KRASTEL H (1), Landauer M (2), Diehm T (3), Kubarko A (4), Schlichtenbrede F (2)
(1) Mannheim Medical Faculty- University of Heidelberg, Dept. of Ophthalmology, Neckargemünd, Germany
(2) University Medical Center Mannheim- Germany, Dept. of Ophthalmology, Mannheim, Germany
(3) University Medical Center Mannheim- Germany, Dept. of Radiology, Mannheim, Germany
(4) University of Minsk, Dept. of Physiology, Minsk, Belarus

Purpose To improve the understanding of pupillomotor and electrodiagnostic findings in correlation to visual sensory defects in chiasmal compression.
Methods Full and half field VEPs were recorded by the Roland Retiport system. Stato-kinetic dissociation in visual field findings was demonstrated by Goldmann kinetic and Twinfield static perimetry. Low luminance conditions are applied with both kinetic and static perimetry. In addition, the he swinging flashlight pupil test was applied in different variants, to solve apparent contradictions in functional findings. Analyzed are two cases of chiasmal compression by aneurysms of the internal carotid artery and one case of a tuberculum sellae meningeoma, in which visual symptoms were the presenting ones.
Results Despite sensory symptoms may be confined to one eye, contralateral involvement due to chiasmal compression may show up in perimetry - more early by static than by kinetic examination. Low luminance perimetry produces more significant field defects in chiasmal lesins than standard perimetry. The swinging flash comparison of pupil responses may miss the unilateral relative afferent defect, depending on the direction of the light stimulus. Comparing not only responses to OD and to OS stimulation but also pupil responses to upper and lower half field stimulation helps to not overlook relative afferent pupil defects. Comparing, on the other hand, upper and lower half field VEPs has to consider physiological differences in these responses.
Conclusions In chiasmal compression, apparent contradictions in results of functional examinations may lead to false diagnostic conclusions or even to doubts concerning the somatic origin of visual complaints. The above mentioned extended toolbox of functional exams improves the diagnostic reliability.

• 3476

Choroidal thickness changes in response to defocus in emmetropia and in myopia

WEBER M (1), Esmaeelpour M (2), Drexler W (2), Findl O (1)
(1) VIROS - Vienna Institute for Research in Ocular Surgery- a Karl Landsteiner Inst, Department of Ophthalmology- Hanusch Hospital, Vienna, Austria
(2) Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria

Purpose This prospective study aimed to investigate the effect of myopic defocus on choroidal thickness in emmetropic, in moderately myopic and in highly myopic subjects.
Methods A 3-dimensional spectral domain-optical coherence tomography (SD-OCT) system that operates at a wavelength of 1060 nm was used to measure choroidal thickness in the 9 sections according to the "early treatment diabetic retinopathy study" (ETDRS) grid before and after a period of 60 minutes of defocus with a +3.00 Dioptre (D) lens in one eye of 15 emmetropic (spherical equivalent-SE: -0.75 to +0.75D; group A), 15 moderately myopic (SE: -6.00 to -2.50D; group B) and 15 highly myopic subjects (SE: ≤ -6.25D; group C).
Results Choroidal thickness was in all ETDRS fields significantly thicker in emmetropic than in moderately and in highly myopic subjects. Central field choroidal thickness before and after defocus was in group A 322±59µm and 321±57µm, in group B 259±71µm and 258±65µm and in group C 237±64µm and 237±65µm. Choroidal thickness did not differ from before to after defocus in the central ETDRS field (group A: -1±12µm, p=0.710; group B: -1±8µm, p=0.660; group C: 0±6µm; p=0.995; paired t-test) and these differences did not differ significantly between the groups (p=0.940, ANOVA). In the peripheral ETDRS fields choroidal thickness changes from before to after defocus were neither found to be significant within the groups (p>0.05, paired t-test) nor between the groups (p>0.05, ANOVA).
Conclusions Myopic defocus does not influence the choroidal thickness in emmetropic, moderately myopic and in highly myopic subjects.

• 3511

Evaluation of the vitreoretinal interface

GUALINO V
Clinique Honoré Cave, Ophthalmology, Montauban, France

Abstract not provided

• 3512

Vitreoretinal traction syndrome

LE MER Y
Fondation Ophtalmologique A. de Rothschild, Service Pr Sahel, Paris, France

Individualized from the other vitreoretinal interface diseases in the 80, the vitreoretinal traction syndrome has really been thoroughly described with the advances in OCT imaging.
We'll present the proposed new international classification. By evaluating physiologic and pathological features, it allows to choose between different therapeutic options : watchful waiting, vitreolysis and vitrectomy
The new treatment using vitreolysis may in some cases avoid surgery in selected cases highlighted by this classification. We'll show some real life cases illustrating what we may really achieve with this non surgical therapy..

Commercial interest

• 3513

Diabetic maculopathy

POURNARAS J A C
Jules Gonin Eye Hospital, Ophthalmology, Lausanne, Switzerland

Vitreoretinal macular interface plays an important role in the formation and progression of diabetic macular edema. Main vitreoretinal diseases as epiretinal membrane, vitreous traction and macular holes may occur in this condition. They are due to abnormal mechanical and biochemical interactions between posterior hyaloid and retinal surface. OCT has changed our understanding of the contribution of vitreoretinal interface disorders on the course of macular edema. Tractional elements contribution seems to be more obvious compared to untractional elements as epiretinal membranes. The management of vitreoretinal retinal disorders associated to diabetic macular edema will be discussed. Specific surgical approach will be detailled and compared to same conditions occuring in non diabetic patients.

• 3514

Venous occlusions

PAQUES M
Quinze-Vingts Hospital, Paris, France

The retinovitreal interface may be altered during retinal vein occlusions, either through vitreal traction participating to macular edema or the development of an epiretinal membrane. Surgical treatment of these may reduce macular thickness, although the severity of the underlying retinal damage may impair visual results. Epiretinal membrane peeling may also be useful to prevent multirecidivant macular edema. An emerging concern is surgical damage to the nerve fiber layer. Beside these well-known entities, the role of a normal inner limiting membrane in the maintenance of macular edema is debated.

• 3515

High myopia

STANGOS A (1,2)
(1) Centre Ophtalmologique de Florissant, Geneva, Switzerland
(2) Eye Research Unit, Rothschild Foundation, Geneva, Switzerland

Urbanisation and increasing of education of modern societies is influencing normal homeostasis of eye growth, which in turn is causing an important myopic shift. Myopia is associated with increased vitreous liquefaction and premature synchisis and syneresis of the vitreous body. Syneresis can be anomalous in high myopes owing to stronger vitreoretinal adhesions. Foveoschisis, macular hole with or without retinal detachment, premacular membranes and paravascular retinal microholes are the most frequent myopic-related vitreomacular intrface disorders. In this course we will explore the pathogenesis of those vitreomacular disorders and will discuss the therapeutic approaches.

• 3521

Healthcare delivery, not just about the doctor and the patient

MAZY R
Cliniques UCL, St. Luc, Brussels, Belgium

In this paper we explore the evolution of a classic hospital in a static building to a patient-focused "concept" of healthcare delivery system where the healthcare provider can exercises high quality medicine with the necessary structural and organizational support. An organizational support for each individual(ist) healthcare provider who wants to perform "independently" the excellence in his work and be patronage and protected by its organization. As Wegener described "doctors are not manageable" but they should be supported and encouraged. Lean implementation, teamwork, promoting healthcare pathways, enriching the resources for all professionals to prevent Burn-out are some of the aspect of a modern supportive organization to improve the quality of care AND the quality of life for the healthcare provider. Promoting the excellence and the professionals in order to increase the financial resources is one of the "jobs" of the manager of the hospital in his extensive list of To Do's.

• 3522

The evolving role of nurses and allied health professionals in the management of age-related macula degeneration

HAMILTON R , Mapani A , DaCosta J , Pavesio C , Flanagan D
Moorfields Eye Hospital, Medical Retina, London, United Kingdom

One of the major developments within the medical retinal (MR) over the last five years has been the introduction of an intravitreal injection of anti-vascular endothelial growth factor medications (Anti-VEGFs) for patients with AMD and other macular disease. As a consequence of this development, outpatient attendances within the MR Service have increased significantly.
The Royal College of Ophthalmologists acknowledges challenges related to staffing levels. A document produced by the Royal College of Ophthalmologists in 2009 stated that training nurses or technicians to perform intravitreal injections may offer a potential solution to increased pressure in the retinal therapies clinics despite the label recommending that intravitreal injections be given by trained ophthalmologists. Nursing staff at Moorfields Eye Hospital have given over 15,000 injections now and are currently giving over 60% of all injections. Enabling nurses to be trained to perform intravitreal injections has improved the efficient delivery and capacity of the injection service and enabled national guidelines and service delivery targets to be met, whilst maintaining high standards of care with an excellent safety record.

• 3523

Optometrists and the management of glaucoma; the Rotterdam experience

LEMIJ H
Rotterdam Eye Hospital, Rotterdam, The Netherlands

Shared glaucoma care is performed in 2 different ways in the Rotterdam area: 1) through telemedicine connecting optometrists and a glaucoma specialist and 2) by technicians following a strict working protocol in a separate department of the Rotterdam Eye Hospital. In the Telemedicine project, extensive information is provided via a secured internet connection, including a detailed history, pachymetry, applanation tonometry, slit lamp examination, gonioscopy, fundus photographs and sophisticated imaging (OCT or GDx). It primarily serves the detection of glaucoma and the monitoring of those at risk. In the hospital based follow-up, strict criteria are observed that require referral to the glaucoma clinic; these criteria relate to the history, visual acuity, applanation tonometry, target IOP and any progression in structural or functional measurements. Eligible patients are those deemed stable. Both projects function well. In the Telemedicine project, initially 32% of patients were referred to a glaucoma specialist, but, as the provided information improved, later only approx. 10%. The hospital based follow-up unit was preferred slightly by the patients to the regular visits to their glaucoma specialists.

• 3524

Can ophthalmic technicians be used to deliver glaucoma care?

KOTECHA A
UCL Institute of Ophthalmology, BRC for Ophthalmology, London, United Kingdom

The presentation will describe the development of a technician-delivered glaucoma screening and monitoring service introduced to help improve capacity and the patient experience within glaucoma outpatient clinics in a London hospital. The service involves the use of ophthalmic technicians to collect clinical data from patients, with a specialist reviewing these data remotely; thus, it removes the face-to-face doctor consultation. The nature of glaucoma detection and monitoring lends itself to a 'remote review' care model. The patient journey time in this clinic averages at around 50 minutes, compared with 163 minutes in the glaucoma outpatients department. The overall first visit discharge rate for the new patient screening service is 58%; the proportion of patients attending the Stable Monitoring Service who have been rebooked into the service is now 83%. Patient satisfaction with the new service is high. Early analysis suggests that there exists a discrepancy between consultant reviewer management decisions for stable patients, suggesting some may be more risk-averse than others when managing patients seen within this model.

• 3525

Patient-focused glaucoma care delivery, maintaing quality despite cost limitation

POURJAVAN S

Cliniques Universitaires St. Luc, Ophthalmology, Brussels, Belgium

To assess the degree of patient satisfaction in a Glaucoma Outpatient centre and its correlation with the subjective scoring of the Ophthalmologist for the quality of provided care using a short not-validated questionnaire. The practice of medicine has evolved in the latest decade. Disruptive innovation in healthcare causes a shift away from traditional health care venues like hospitals into clinic settings and outpatient's facility. There is also transference of skills from highly trained sub-specialist to more accessible specialist. The outpatient offices, especially in Belgium provide accessible and fast services in a convenient location. In order to remain competitive the outpatient offices have to provide high level of healthcare quality. In the published report Crossing the Quality Chasm, the Institute of Medicine (IOM) set forth six aims for a quality health care system: safe, equitable, evidence based, timely, efficient and patient centered. The latter three factors directly influence patient satisfaction. The patient satisfaction on the other hand has been commonly used as an indicator for measuring the quality of care given by the health professionals. In this lecture we explain patient's motivations for their satisfaction degree during an outpatient Glaucoma clinic.

• 3531

Corneal nerves maintain the immune privilege of the cornea

HAMRAH P (1,2), ()
(1) Schepens Eye Research Institute, Boston, MA, USA
(2) Cornea Service, Massachusetts Eye & Ear Infirmary, Department of Ophthalmology ()and 2, ,

The aim of the current study is to investigate if neuronal dysfunction leads to the loss of corneal immune privilege. After trigeminal axotomy, corneal cytokines were measured by multiplex bead assay. Corneal hem- (HG) and lymph-angiogenesis (LG), as well as immune cell infiltration and phenotype were assessed by immunohistochemistry staining. Trigeminal axotomy was performed in recipient mice one week prior to corneal transplantation and allospecific delayed-type hypersensitivity (DTH) was used to compare results between groups. Axotomy resulted in significant increase of CD45+ cells and up-regulation of MHC-2. Pro-inflammatory cytokines in the cornea were significantly increased. The area of corneal HG and LG were significantly increased by 6.3 fold and 5.7 fold respectively. Axotomy before corneal transplantation resulted in rejection of all grafts, and donor-specific DTH response in these mice was positive at 2 weeks, as compared to transplanted mice without prior axotomy.Neurogenic immune homeostasis is a critical process, whereby the peripheral nervous system directly maintains corneal immune privilege.

3532

Immune Responses at the Ocular Surface

SABAN D R (1,2)
(1) Departments of Ophthalmology, Duke University School of Medicine, Durham
(2) Departments of Immunologys, Duke University School of Medicine, Durham

Immune-mediated diseases of the ocular surface are relatively broad in their respective etiologies, which can involve infection, autoimmunity, or allergy. Despite this range, immune responses often converge upstream at the level of the dendritic cell (DC)—a highly specialized group of antigen presenting cells required in the activation of naïve T cells. Our lab has established a novel mouse model of allergic eye disease (AED), which leads to severe clinical manifestations, sustained ocular inflammation, and eosinophilic infiltration at levels seen in patients with atopic keratoconjunctivitis. Use of the AED model has led to identification of classical CD11b+ DCs as the key subset responsible for activating allergen reactive T cells. In addition, the AED model has uncovered the importance of CCR7 as the master chemokine receptor in homing of ocular surface DCs to the regional lymph nodes. Additionally, CCR7 has recently been shown to contribute to activation of Th17 cells in the mouse model of dry eye disease. Likewise, similar to the dry eye disease model, AED involves corneal lymphangiogenesis—potentially suggesting a role for corneal DCs in allergic immune responses. Thus, efforts to progress the current understanding of DC biology holds tremendous promise for advancement of novel and effective medicines in immune mediated diseases of the ocular surface.

• 3533

Immunomodulation in allergic eye disease

CALDER V
UCL Institute of Ophthalmology, London, United Kingdom

Abstract not provided

• 3534

Tregs in corneal health and disease

DANA R
Harvard Medical School, Schepens Eye Research Institute- Massachusetts Eye & Ear Infirmary, Boston MA, United States

This symposium will focus on the complex network of cells and molecular mechanisms that regulate immunity in the cornea and ocular surface. Talks will focus on the phenotype and function of corneal and ocular surface antigen-presenting cells in heath and disease; the immunopathogenesis and regulation of allergic eye disease; the myriad functions of nerves in maintaining immune homeostasis in the ocular surface; and T cell regulatory mechanisms that maintain immune privilege and how they be subverted in chronic inflammation and autoimmunity. Those attending the symposium should achieve a greater in-depth understanding of how immune cells, epithelial cells, and nerves interface to regulate immunity in the anterior segment of the eye.

Commercial interest

• 3535

The Role of Antigen Presenting Cells in the Pathophysiology of Dry Eye

STERN M E

Biological Sciences, Allergan Inc, Irvine CA, United States

Purpose Dry eye (DE) disease is perpetuated by self-antigen driven autoimmune-based inflammation. During the initiation of desiccating stress (DS)-induced DE acute cytokine production and dendritic cell activation precedes autoreactive CD4+ T cell activation, and CD4+ T cells isolated from these DE mice are sufficient to mediate disease following adoptive transfer to T cell-deficient nude recipient mice.

Methods Flow cytometry, IHC, ELISA and ocular surface antigen presenting cell (APC)-depletion were used to phenotype expression and function of dendritic cells and cytokines during DS-DE (induced in C57BL/6 female mice exposed to sc scopolamine (0.5 mg/0.2ml) TID, humidity <40%, and sustained airflow).

Results In response to DS-induced DE there is a significant increase ($p \leq 0.05$) in the expression of CD11cloPDCA+ plasmacytoid dendritic cells (pDCs) and secretion of type I interferons (IFNa/b) in draining cervical lymph nodes (CLN) and ocular surface tissues compared to naïve controls. The higher frequency of pDCs within the CLN correlated with enhanced IFNa levels in both CLN and ocular surface tears ($p \leq 0.05$). Furthermore, CD4+ T cells isolated from APC-depleted mice exposed to DS are not pathogenic; CD4+ T cell infiltration was markedly ($p < 0.05$) reduced relative to controls, which was associated with an attenuated proinflammatory cytokine/chemokine response.

Conclusions Collectively, these data further support the concept that DE is a localized self-antigen-driven autoimmune disease.

• 3541
Update on lymphoma diagnostic

COUPLAND S
Dept. of Pathology, University of Liverpool, United Kingdom

Lymphomas are classified according to the current WHO classification, which emphasizes an approach whereby the clinical characteristics are correlated with distinct morphological, immunophenotypical, and genotypical features of each neoplasm. The classification of lymphoid malignancies recognizes three major categories: B-cell neoplasms, T-/NK-cell neoplasms, and Hodgkin lymphomas. B- and T-cell lymphomas are further classified into precursor- and mature neoplasms, the latter being subdivided again according to their clinical manifestation: i.e. into disseminated/leukemic, extranodal and nodal malignancies. Hodgkin's disease, now more appropriately termed Hodgkin lymphoma, comprises nodular lymphocyte-predominant Hodgkin lymphoma and classical Hodgkin lymphomas of nodular sclerosis, mixed cellularity, lymphocyte-depleted and lymphocyte-rich subtype. This talk will provide a of the major lymphoid malignancies affecting the eye, and an overview of the techniques used to diagnose them.

• 3542
Vitreoretinal Lymphomas

CASSOUX N
Institut Curie, Ophtalmology Oncology, Paris, France

Abstract not provided

• 3543
Orbital and palpebral lymphomas

ROBERT P Y (1), Flausse R (2)
(1) CHRU Dupuytren, Ophtalmologie, Limoges, France
(2) CHU, Ophthalmology, Poitiers, France

Extra nodal lymphomas may involve the ocular adnexae in 8% of cases. The mean age of onset is basically in the sixth decade. Lymphomas may present as a palpebral mass (39%), conjonctival infiltrate (39%) or proptosis (31%). It may involve orbital fat (47%), orbital muscles (26%), lacrymal gland (19%), preseptal tissues of eyelids (10%), or conjonctiva (60%). However, no specific location has been statistically associated to a better prognosis.

Although MALT lymphoma (low grade with good prognosis) is the most common type (46%), other types such as follicular (20%), DLCB (11%), Mantel (5%), or other (17%) may occur. Lymphoma of ocular adnexae represent around 12% of all MALT lymphomas.

The incidence of ***Chlamydia Psittaci*** infection in lymphoma patients may vary according to the geographic area, for instance 0% in Florida and 80% in Italy.

The incidence of amyloïdosis in lymphoma patients arises from 0.85% to 7,5%. However amyloïd deposits are often not systematically looked for, and therefore may remain misdiagnosed.

The handling of orbito-palpebral lymphomas requires the collaboration of a multidisciplinary team involving pathologists, biological and clinical haematologists, microbiologists and orbital surgeons.

• 3544
Imaging and Biopsies

VAN GINDERDEUREN R
UZ St. Rafael, Ophthalmology, Leuven, Belgium

Imaging is necessary before taking a biopsy for diagnostic purposes, to delineate the extension, find the correct location and plan the most adequate procedure for the biopsy. In case of suspicion for conjunctival/palpebral lymphoma a CT scan is performed to exclude bilaterality and delineate the exact proportions. For orbital/lachrymal gland tumors with differential diagnosis of lymphoma a CT/MRI shows the exact location and dimensions of the tumor. In case of a tumor with easy access a large biopsy is preferred over fine needle aspiration biopsies. Special precaution is necessary not to crush the specimen to prevent artefacts of the fragile lymphoma cells The biopsy is divided in a fresh portion for frozen sections and for genetic analysis; the bulk of the tumor is fixed in formalin for the standard stainings Retinal/choroidal lymphomas can be diagnosed by fundus examination, OCT, ultrasound and fluoangiography. Biopsies require special surgical skills and adapted laboratory techniques because of the paucity of cells. Steroids must be discontinued for at least 10 days. A vitreal above a scleral approach is preferred because of the possibility to obtain also a retinal sample.

• 3545

Medical treatment of Lymphoma in 2015

BORDESSOULE D
Limoges, France,

Abstract not provided

• 3551

Apoptosis in the lens after oxidative stress induced by in vivo exposure to UVR

GALICHANIN K
Ophthalmology, Karolinska Institute/Uppsala University, Stockholm, Sweden

Abstract not provided

• 3552

Active caspase-3 in the lens and its response to oxidative stress induced by in vivo exposure to UVR

TALEBIZADEH N
Ophthalmology, Neuroscience, Uppsala, Sweden

Purpose: To determine the time evolution of active caspase-3 protein expression after exposure to low dose UVR-300nm
Methods: Forty rats were unilaterally exposed in vivo to 1 kJ/m2 UVR-300nm for 15 min. All lenses were processed for immunohistochemistry. Time evolution of active caspase-3 expression was determined based on the differences in the probability of active caspase-3 expression at 0.5, 8, 16, and 24 hrs after the UVR exposure. A logistic model was introduced for the expression of active caspase-3.
Results: Active caspase-3 expression was higher in the exposed lenses. The mean differences between the exposed and non-exposed lenses were 0.17±0.02, 0.20±0.03, 0.21±0.03, and 0.11±0.04 (95%CI) for the 0.5, 8, 16, and 24 hr time groups, respectively. There was a difference when comparing the 0.5 and 24 hrs groups to the 8 and 16 hrs groups (95%CI = 0.06±0.03). Exposure to UVR-300nm impacted on the parameters of the logistic model by time.
Conclusions: Expression of active caspase-3 in the lens epithelium increased after UVR exposure. The peak of expression was around 16 hrs after the exposure. The logistic model predicts the impact of exposure to UVR on the spatial distribution of active caspase-3 expression, depending on time.

• 3553

The immunoproteasome in human lens epithelial cells during oxidative stress

PETERSEN A (1), Zetterberg M (2)
(1) *University of Gothenburg - Institute of Neuroscience and Physiology, Department of Clinical Neuroscience and Rehabilitation, Gothenburg, Sweden*
(2) *University of Gothenburg- Institute of Neuroscience and Physiology, Department of Clinical Neuroscience and Rehabilitation, Gothenburg, Sweden*

The immunoproteasome has been detected not only in immune-tissue, but also in non-immune tissues like the immune-privileged eye. The aim of this study was to investigate if the immunoproteasome is present in cultured human lens epithelial cells and in human lenses with cataract, as well as to measure expression and activity of immunoproteasome subunits in response to oxidative stress.
Expression of the immunoproteasome and constitutive proteasome subunits b1*i*/ b1, b2*i*/ b2 and b5*i*/ b5 were studied by western blot in lens fibre extracts from phacoemulsification surgery, in fresh lens capsule pieces with adherent cells obtained during cataract surgery as well as in oxidatively stressed native human lens epithelial cells (HLECs) in culture.
The present study shows that the immunoproteasome is present in native HLECs and in human cataractous lenses. Furthermore, in native HLECs, oxidative stress upregulates immunoproteasome expression in contrast to the constitutive proteasome. The increased expression of the immunoproteasome is not accompanied by increased chymotrypsin-like activity.

Invited SIS speaker at Oxidation and defense in the ocular lens (SIS organizers, Per Söderberg and Madeleine Zetterberg)

• 3554

Estrogen as an antioxdant in the lens

ZETTERBERG M
Dept. of Ophthalmology, Institute of Clinical Neuroscience, Mölndal, Sweden

Female gender is a known risk factor for age-related cataract, although the explanation for this is still largely unknown. We have demonstrated that physiologic concentrations of 17b-estradiol (E2) protect cultured human lens epithelial cells (HLECs) from oxidative stress induced by H2O2, as evident by decreased production of reactive oxygen species (ROS) and a stabilization of the mitochondrial membrane potential. Total superoxide dismutase (SOD) activity was increased by these concentrations of E2 but no change in gene or protein expression of SOD was seen. In cataract patients and controls, a significant correlation between higher age and decreasing serum levels of E2 was found but no correlation between serum levels of E2 and SOD was demonstrated. Men exhibited higher E2 levels compared to postmenopausal women. To conclude, estrogen seems to exert antioxidative effects on human lens cells, possibly by affecting SOD activity, which may explain the difference in risk of cataract between genders. The finding that men have higher levels of E2 than postmenopausal women further supports the hypothesis that it is the decline in estrogen at menopause that causes the higher risk of cataract in women.

• 3555

Caffeine, an in vivo oxidation protectant in the lens

KRONSCHLAGER M , Yu Z , Talebizadeh N , Söderberg P
Uppsala University, Ophthalmology, Uppsala, Sweden

The major avoidable cause of cataract is ultraviolet radiation (UVR). We aimed at investigating topical caffeine in UVR-induced cataract.
Topical caffeine and a placebo were applied to the eyes of separate groups of Sprague Dawley rats that were exposed to sub-doses of UVR and protective effect was evaluated. Penetration of topical caffeine in the rats to lens and blood was analysed by HPLC. Influence of topical caffeine on pupil diameter was measured in ketamine/xylazine anesthetized rats.
Topically administered caffeine protected against UVR-induced cataract development with a Protection Factor, an objective relative measure of protective properties, of 1.23 and inhibited UVR-induced apoptosis. Topical caffeine peaked at 30 min in the lens, increased up to 120 min in the blood and antagonized ketamine/xylazine-induced mydriasis. Eyes treated with caffeine reacted with quick dilatation after tropicamide application.
In conclusion, topically applied caffeine protects against ultraviolet radiation cataract, reducing lens sensitivity 1.23 times. Considering that caffeine is a powerful antioxidant that is easily available and well tolerated our finding implicates that caffeine may be a clinically useful anticataract agent.

• 3561

Novel mouse phenotypes identified in the eye screen of the German Mouse Clinic

AMARIE O V (1), Fuchs H (2), Gailus-Durner V (2), Hrabě de Angelis M (2), Graw J (1)
(1) Helmholtz Center Munich- German Research Center for Environment and Health, Institute of Developmental Genetics, Munich-Neuherberg, Germany
(2) Helmholtz Center Munich- German Research Center for Environment and Health, German Mouse Clinic- Institute of Experimental Genetics, Munich-Neuherberg, Germany

The German Mouse Clinic (GMC) is a large-scale mouse phenotyping facility that provides systematic analysis of all organ systems using a standardized workflow. The tests for the eye phenotyping include Scheimpflug imaging, Optical coherence tomography, Laser interference biometry, Virtual drum, ERG, and histology. It allows the identification of novel genetic models for human eye diseases. One example is the ***Meis1*** mutant line, which have retinal and eye size deficits, and impaired visual acuity. Importantly, our results reveal that a single mutant ***Meis1*** allele in the mouse is sufficient to elicit multiple phenotypic abnormalities, consistent with a dominant mode of inheritance in human patients being characterized by microphthalmia (and leukemia). These data provide a starting point for further investigation of several organ systems to dissect the underlying pathogenic mechanisms and to identify reliable phenotypic endpoints for therapeutic testing. Another example is the ***Ap4e1*** mice that show retinal deficits, revealing a new phenotype for a mutation of this gene. The eye screen along with the GMC identifies new (and frequently pleiotropic) traits that bring progress in understanding the molecular mechanism in human eye diseases.

• 3562

Eye diseases identified in the ENU-Ageing Screen

JACKSON I (1), Starbuck B (2), McKie L (1), Banks G (2), Blease A (2), Simon M (2), Wisby L (2), Cross S (1), Nolan P (2), Brown S (2), Potter P (2)
(1) University of Edinburgh, MRC Human Genetics Unit, Edinburgh, United Kingdom
(2) MRC Harwell, MRC Mammalian Genetics Unit, Harwell, United Kingdom

MRC Harwell is generating cohorts of mutagenized mice, bred to reveal recessive mutations. Cohorts are repeatedly screened for a range of phenotypes at different ages up to 18 months. Included among the screens is optokinetic response to test visual acuity, pupillometry and examination by slit lamp and indirect ophthalmoscopy. We identify both early and late onset disease models, and document disease progression over the lifetime of the mouse. The genetic design of the screen means that the mutant gene can be rapidly identified by mapping and next-generation sequencing To date we have identified early onset phenotypes including retinal degeneration due to mutation of ***Rpgrip1***, a model for Leber congenital amaurosis-6, and abnormal pupil response due to mutation in ***Chrm3***. Late onset phenotypes include corneal opacity, caused by mutation of ***Ikzf2***, and progressive vision loss with retinal degeneration. We have identified a missense mutation in ***Idh3a*** that results in reduced visual acuity and retinal degeneration from 12 months. ***Idh3a*** encodes the α subunit of the mitochondrial enzyme, isocitrate dehydrogenase. This mouse is a model for retinitis pigmentosa 46, due to mutation in the β subunit of human mitochondrial IDH enzyme.

• 3563

The eye screen design in Czech Centre for Phenogenomics and selected models for eye diseases

ANTOSOVA B, Smolikova J, Zilova L, Lachova J, Bendova M, Machon O, Kozmik Z
Institute of Molecular Genetics of the ASCR- v. v. i., Laboratory of Transcriptional Regulation, Praha 4, Czech Republic

The eye screen will be part of emerging Czech Centre for Phenogenomics (CCP) in proximity to Prague. The purpose of our eye screen will be the detection of various eye abnormalities in eye morphology and eye physiology. We would like to examine retina structure abnormalities using optical coherence tomography, or anterior segment abnormalities using Scheimpflug imaging. In addition, we plan to perform functional analysis of the visual system using virtual optomotor system. Finally, retinal function will be tested by electroretinography.
Based on our previous work, we have expertise especially in the field of transcriptional regulation of eye development. Specifically, our interest is transcriptional regulation of ***Pax6*** that is crucial for eye development in various species. ***Pax6*** haploinsufficiency is characterized by aniridia in human and by ***small eye*** phenotype in mouse. Therefore, here we describe our results using transgenic mouse models to reveal requirement of upstream regulators of Pax6 for lens induction.

• 3564

Angiography reveals novel features of the retinal vasculature in mice

RUBERTE J
Center for Animal Biotechnology and Gene Therapy, Autonomous University of Barcelona, Ceradanyola del Valles, Spain

Here, we present a comprehensive characterization of the mouse retinal vasculature by SLO-OCT fluorescein angiography. Using this clinical imaging technique, we report previously unrecognized variations in C57BL/6J vascular anatomy. All layers of the mouse retinal vasculature could be readily visualized during fluorescein angiography by SLO-OCT. Blood vessel density was increased in the deep vascular plexus (DVP) compared with the superficial vascular plexus (SVP). When we examined different regions of the SVP and DVP, no differences in capillary density were observed between the inferior and superior hemispheres, or between different regions of the SVP. However, a small, but significant increase in capillary density was detected in the temporal hemisphere of the DVP compared with the nasal hemisphere of the DVP. Arteriolar and venular typologies were established and structural differences were observed between venular types. Unexpectedly, the hyaloid artery was found to persist in 15% of C57BL/6 mice, forming anastomoses with peripheral retinal capillaries.

• 3571

The Effect of Hypertension on Intraocular Pressure and Apoptosis of Retinal Ganglion Cell Through ET-1 Signaling Pathway Activation in Trabecular Meshwork of Hypertension Rat Model

PRAYITNANINGSIH S (1), Sujuti H (2), Abdullah Hamid A (1), Permatasari N (3), Aris Widodo M (3)
(1) Brawijaya University, Ophthalmology, Malang, Indonesia
(2) Brawijaya University, Biochemistry, Malang, Indonesia
(3) Brawijaya University, Pharmacology, Malang, Indonesia

Purpose To evaluate the effect of Deoxycorticoacetate (DOCA)-salt Hypertension model on IOP,retinal ganglion cell (RGC) apoptosis, ratio of endothelin (ET-1)/ endothelial Nitric Oxide Synthase (eNOS), ETA and ETB Receptor (ETRA and ETRB), Myosin Light Chain Kinase (MLCK), and Caldesmon (CaD) in endothelial cells of Trabecular Meshwork (TM).
Methods Experimental study was performed on 20 male Spraque Dawley rats divided into control group(1), hypertension group (2-4): DOCA subcutaneous 10 mg/kg BW twice a week+ NaCl 0.9% daily for 2, 6, and 10 weeks respectively. Blood pressure were measured by BP analyzer with animal tail-cuff method and IOP measured by handheld tonometry before study and before enucleation. ET-1 signaling pathway and RGC apoptosis were evaluated by immunofluorescent staining, then observed by laser scanning confocal microscopy. Data were analyzed by one way Anova.
Results Peak of IOP elevation occurred on 2 weeks of hypertension (7.78 ± 4.14 mmHg). The average ratio of ET-1/eNOS was highest on 2 weeks (1.31 ± 0.025 au). The ETRA were significantly increased in 2 and 6 weeks (1476.3 ± 20.9 au and 1209.7 ± 6.1 au), while ETRB only in 2 weeks (1160.5 ± 18.2 au).The highest average of MLCK (1916.68 ± 6.41 au), CaD (1676.37 ± 7.72 au), and RGC apoptosis (576.15 ± 33.28 au) were found in 2 weeks hypertension.
Conclusions Hypertension induced by DOCA-salt stimulated significant activation of ET-1 signaling pathway on TM, elevation of IOP, and RGC apoptosis. The peak of activation was achieved at 2 weeks of hypertension.

• 3572

TrkB signaling in Müller glia stimulates neuroprotection after optic nerve injury

HARADA T, Namekata K, Guo X, Kimura A, Harada C
Tokyo Metropolitan Institute of Medical Science, Visual Research Project, Tokyo, Japan

Purpose Brain-derived neurotrophic factor (BDNF) is a neurotrophic factor that regulates neural cell survival mainly by activating TrkB receptors. Several lines of evidence support a key role for BDNF-TrkB signaling in survival of adult retinal ganglion cells (RGCs) in acute and chronic models of optic nerve damage. On the other hand, glial cells have recently attracted considerable attention as mediators of neural cell survival. To further elucidate the role of glial cells in BDNF-mediated neuroprotection, we examined the effect of optic nerve injury (ONI) on TrkBGFAP KO mice, in which TrkB is deleted in retinal glial cells.
Methods We examined the effect of ONI in WT and TrkBGFAP KO mice at day (d) 7 and 14 after ONI by spectral-domain optical coherence tomography (SD-OCT), retrograde labeling of RGCs, immunohistochemistry and quantitative real-time PCR analyses.
Results ONI-induced RGC loss and retinal degeneration occurred quickly in TrkBGFAP KO mice at d7 after ONI, but the severity was comparable with WT mice at d14. We next examined the effects of ONI on the production of trophic factors in the retina. ONI markedly increased mRNA expression levels of basic fibroblast growth factor (bFGF) in WT mice at d3, but not in TrkBGFAP KO mice. Immunohistochemical analysis at d7 revealed that ONI induced bFGF upregulation mainly in Müller glia. On the other hand, glial cell line-derived neurotrophic factor (GDNF) expression level was slightly decreased in TrkBGFAP KO mice compared with WT mice at d3, but not at d10.
Conclusions These results demonstrate that BDNF signaling in retinal glia plays important roles in the early stage of neural protection after traumatic injury. Additionally, our genetic models provide a system in which glia-specific gene functions can be examined in central nervous system tissues *in vivo*.

• 3573

Downregulating the Myocardin-related transcription factor/ Serum response factor (MRTF/ SRF) pathway is a novel therapeutic approach to prevent post-surgical fibrosis in glaucoma.

YU-WAI-MAN C (1), Treisman R (2), Khaw P T (1), Bailly M (1)
(1) NIHR BRC at Moorfields Eye Hospital and UCL Institute of Ophthalmology, Cell Biology & Ocular Biology and Therapeutics, London, United Kingdom
(2) Francis Crick Institute, Transcription Lab, London, United Kingdom

Purpose Glaucoma is the first leading cause of irreversible blindness worldwide and fibrosis is the main cause of failure of glaucoma surgery. There are currently no available anti-fibrotic treatments in the eye. We have previously described how the MRTF/ SRF transcription pathway is intricately linked to all the key pathways in ocular fibrosis. We thus hypothesised that inhibiting the MRTF/ SRF pathway would be a good therapeutic target to prevent fibrosis in the eye.
Methods MRTF and SRF expression were knocked down in human Tenon's fibroblasts using small interfering RNAs, and three-dimensional fibroblast-populated collagen gels were used to measure contraction in vitro. Cytotoxicity was assessed using the live-dead assay. Live cell imaging was used to study the cell protrusive behaviour during contraction and quantification was performed using a custom parameter, the dynamic index. Reflection confocal microscopy and DQ collagen were also used to measure matrix degradation. Real-time qPCR was used to compare the gene expression of key matrix metalloproteinases in contracting gels.
Results MRTF and SRF silencing significantly decreased collagen matrix contraction by 80% and 87% respectively. MRTF silencing did not impair cell viability compared to controls. Knocking down MRTF markedly reduced the protrusive behaviour of human Tenon's fibroblasts (dynamic index = 0.19 as compared to 0.66 for controls). MRTF silencing also significantly decreased matrix degradation and the expression of MMP-1, MMP-2, MMP-9, and MMP-14 genes.
Conclusions Our study is the first to show that inhibiting the MRTF/ SRF pathway significantly decreases collagen matrix contraction, cell protrusive behaviour of fibroblasts, and matrix degradation in the conjunctiva, and thus represents a promising new therapeutic approach to prevent post-surgical fibrosis in glaucoma.

• 3574

In vivo modified peripheral glia enhance regenerative capacity in a rat retina

SMEDOWSKI A (1,2,3), Pietrucha-Dutczak M (1), Kaarniranta K (3,4), Lewin-Kowalik J (1)
(1) Medical University of Silesia, Physiology, Katowice, Poland
(2) Medical University of Silesia, Ophthalmology, Katowice, Poland
(3) University of Eastern Finland, Ophthalmology, Kuopio, Finland
(4) Kuopio University Hospital, Ophthalmology, Kuopio, Finland

Purpose To investigate impact of transplanted peripheral glia on neurites outgrowth and synaptogenesis in adult rat retina associated with ongoing optic neuropathy.
Methods In this study we used two models of retinal neurodegeneration – degeneration of denervation represented by retinal explants culture and glaucomatous degeneration represented by rat model of ocular hypertension. Retinal explants were cultured in standard supplemented Neurobasal A medium (n=48). Ocular hypertension has been induced using beads occlusive model (n=10). In both ex vivo and in vivo approaches we applied transplantation of peripheral glia, prepared as previously described (Marcol et al. 2015), of density 10^4/5µl for ex vivo and 10^6/5µl for in vivo. PBS treatment was used as a control. After proper follow-up time (10 days for retinal explants and 6 weeks for glaucoma model), tissue was fixed and processed for immunostaining (GAP43, synaptophysin, mGlu2/3R) and stereological analyses.
Results There were visible differences in GAP43, synaptophysin and mGlu2/3R staining between experimental groups. Treatment with peripheral glia increased expression of above proteins both ex vivo and in vivo. Synaptic proteins expression was increased in glial cells treated glaucomatous retinas with mostly within inner plexiform layer, however punctate staining appeared also in ganglion cells layer and retinal nerve fiber layer that might be associated with synaptic plasticity induced by our treatment. Retinal explants analyzed in stereology revealed significant differences expressed in parameters of neurites outgrowth (U-Mann Whitney test, $p<0.05$).
Conclusions Transplantation of in vivo modified peripheral glia support regeneration and might have impact on synaptogenesis and synaptic plasticity within inner rat retina.

• 3575

MMP-9 null mice display elevated IOP due to reduced aqueous humor drainage from the trabecular meshwork

DE GROEF L (1), Siwakoti A (2), Geeraerts E (1), Billen J (3), Stalmans I (4), West-Mays J (1), Moons L (1)

(1) K.U.Leuven, Laboratory of Neural Circuit Development and Regeneration, Leuven, Belgium
(2) McMaster University, Department of Pathology and Molecular Medicine, Hamilton, Canada
(3) K.U.Leuven, Laboratory of Socioecology and Social Evolution, Leuven, Belgium
(4) K.U.Leuven, Laboratory of Ophthalmology, Leuven, Belgium

Purpose Aqueous humor outflow resistance depends on a complex equilibrium of extracellular matrix biosynthesis ***versus*** proteolysis in the trabecular meshwork. Several members of the MMP family, including MMP-9, are essential to the regulation of aqueous humor outflow resistance, ***i.e.*** to intraocular pressure (IOP) homeostasis. Here, we characterized the baseline ocular phenotype of MMP-9 null mice, with emphasis on the dysregulation of IOP homeostasis.

Methods MMP-9 null and wild type mice, from 3 to 13 months of age, were studied. IOP and central corneal thickness were measured via rebound tonometry and pachymetry, resp. Anterior chamber morphology and trabecular meshwork organization were studied (1) ***in vivo*** with OCT, (2) via light microscopy and (3) by means of transmission electron microscopy (TEM), and its collagen composition was studied using Sirius Red and immunostainings. Integrity of the retina and optic nerve were evaluated with OCT and histological stainings on tissue sections and retinal flatmounts.

Results MMP-9 null mice present with early-onset ocular hypertension, and fluorophotometric measurements of aqueous humor turnover revealed a reduced aqueous humor drainage. While OCT, light microscopy and TEM analysis did not disclose any abnormalities in the cellular organization of the trabecular meshwork, collagen staining indicated that there is an aberrant extracellular matrix composition in MMP-9 null mice. Remarkably, the observed IOP elevation in MMP-9 null mice did not result in a glaucomatous phenotype at the level of the retina and optic nerve at the ages studied.

Conclusions Our observations corroborate the role of MMP-9 as an important remodeler of the trabecular meshwork, and evidence for a causal link between MMP-9 deficiency, trabecular meshwork composition and IOP elevation is revealed.

• 3576

Neuroprotective modifications in retinal Müller cells due to oxidative stress and energy restriction

TOFT-KEHLER A K (1), Gurunbaram R (1), Brændstrup C (1), Desler C (2), Rasmussen L (2), Skytt D (1), Kolko M (1)

(1) The Panum Institute, Department of Neuroscience and Pharmacology, Copenhagen, Denmark
(2) The Panum Institute, Department of Cellular and Molecular Medicine, Copenhagen, Denmark

Purpose The viability of retinal ganglion cells (RGCs) is essential to maintain the neuronal function of the retina. Müller cells (MCs) are assumed to be vital in neuroprotection of the RGCs. In this study, we evaluated modifications in retinal MCs due to oxidative stress and energy restrictions.

Methods The human Müller glial cell line, MIO-M1, was used in all experiments. Changes in glutamate uptake were evaluated in oxidative stressed and energy restricted MCs. The cell viability was evaluated by LDH and MTT assays. Regulations in gene and protein expression were evaluated by qPCR and western blot. The ATP production was measured as well as the mitochondrial activity.

Results Glutamate uptake was significantly in energy-restricted MCs. Simultaneous energy restriction and oxidative stress significantly decreased glutamate uptake. The mitochondrial activity was reduced after exposure to energy restriction and further reduced during simultaneous exposure to energy restriction and oxidative stress. The intracellular ATP levels were decreased in the latter condition.

Conclusions Oxidative stress and energy restriction alter the neuroprotective characteristics of MCs by increasing the glutamate uptake during energy restriction and by decreasing the uptake during simultaneous exposure to energy restriction ***and*** oxidative stress. The impaired mitochondrial activity and reduction of intracellular ATP levels may affect the ability of MCs to maintain a cellular homeostasis in such way that their ability to protect RGCs may to suffer.

SATURDAY OCTOBER 10, 2015

• 4111

Introduction: DME in vitrectomized eyes

XIROU T
Red Cross Hospital, Glyfada, Greece

INDRODUCTION: DME IN VITRECTOMIZED EYES
Diabetic Macular Edema (DME) is the most frequent cause of vision loss related to diabetes.
The etiology of DME is multifactorial, and different treatment modalities are targeting to different triggering factors.
The spectrum of treatment options include corticosteroids, anti-vascular endothelial growth factor agents, laser treatment, combined therapy, pars plana vitrectomy, even if no epiretinal membrane is present.
The beneficial effect of vitrectomy on diabetic macular edema is attributed to improved oxygenation of the retina. However many patients may require drug therapy following the surgical procedure. The widespread distribution and increased circulation of intra-vitreally administered drugs in vitrectomized eyes might be rensposible for rapid clearance and reduced effectiveness of drug therapy. In vitrectomized eyes, sustained-release drugs could be particular useful .

• 4112

Imaging of DME in vitrectomized eyes

POURNARAS J A C
Jules Gonin Eye Hospital, LAusanne, Switzerland

Imaging modalities have greatly improved our recognition and understanding of the pathophysiology of diabetic macular edema. Fluorescein angiogram have shown vascular leakage in the presence of macular edema. It permits early detection of intraretinal morphological changes, hemodynamic and inflammatory modifications. Macular perfusion is nicely identified by this exam. Furthermore, OCT have greatly improved the detection of intraretinal fluid, anatomical changes in all retinal layers. It offers comprehensive analysis of the vitreoretinal interface. Quantitative, non invasive and non mydriatic procedure may be performed. Additional recent developments in imaging systems will be discussed.

• 4113

Pharmacokinetics of anti-VEGF and steroid agents in vitrectomized eyes with diabetic macular edema

PAPASTEFANOU V
Retina Department, London, United Kingdom

Anti-VEGF and steroid agents for diabetic macular edema (DME) in a vitrectomized eye is fraught with difficulties, bearing in mind the numerous confounding factors in DME. The pharmacokinetic parameters are affected as the vitreous cavity milieu is altered and the vitreous consistency is not reformed post vitrectomy (PPV). Pharmacokinetic data are largely based on experimental animal models.
VEGF clearance is increased in the vitrectomized eye compared to the non-vitrectomized eye, but there is little direct evidence that the protein expression profile in the vitreous cavity is altered after vitrectomy. Whilst some studies have demonstrated longer intravitreal retention for Bevacizumab compared to Ranibizumab and reduced half-life for both agents after PPV, other studies have found no changes. There is a characteristic lack of pharmacokinetic data for anti-VEGF agents in human vitrectomized eyes.
The vitreous half-life of triamcinolone acetonide (TA) after intravitreal injection was reduced in vitrectomized eyes in both animal models and human eyes. No pharmacokinetic differences between vitrectomized and non-vitrectomized eyes are noted in animal eyes following the injection of the Dexamethasone implant (Ozurdex, Allergan).

• 4114

The role of Anti-VEGFs in the management of DME in vitrectomized eyes

KOURENTIS C
Ophthalmology, Red Cross Hospital, Athens, Greece

The role of Anti-VEGFs in the management of diabetic macula edema (DME) is well established in large, randomized, controlled studies in eyes with naïve vitreous. The effect of Anti-VEGFs may be altered in vitrectomized eyes and the question arises whether there is a difference in the efficacy of Anti-VEGFs after vitrectomy. The replacement of the vitreous gel facilitates oxygen transport to the retina, as well as clearance of VEGF, thus VEGF and Anti-VEGF pharmacokinetics can be altered. Pharmacokinetic data are largely based on experimental animal models but there is also a clinical impression that vitrectomized eyes have augmented pharmacokinetics with a faster clearance of Anti-VEGFs and therefore their treatment could be less effective and requiring shorter treatment intervals, compared to non-vitrectomized eyes. According to a study presented January 2015, vitrectomized eyes fared as well as non.vitrectomized eyes after treatment with ranibizumab for diabetic macular edema.

• 4115

Steroids agents in the management of vitrectomized eyes with diabetic macular edema

ZAMBARAKJI H (1), Papastefanou V (2), Dooley I (2)

(1) Barts Health- Whipps Cross University Hospital NHS Trust, Eye Treatment Centre, London, United Kingdom

(2) Barts Health, Eye Treatment Centre, London, United Kingdom

Steroid treatments for diabetic macular edema (DME) include intravitreal Triamcinolone Acetonide (IVTA) or subtenon Triamcinolone Acetonide (STTA), the Dexamethasone 0.7 mg implant (Ozurdex, Allergan) and the Fluocinolone 190 µg implant (Iluvien, Alimera). Most IVTA studies in vitrectomized eyes have too many confounders including additional treatments such as macular laser or anti-VEG injections, variable outcome measures and follow up times. Furthermore, IVTA was usually given either at the time of pars plana vitrectomy (PPV) to better visualize the vitreous, or at the end of PPV and sometimes combined with an anti-VEGF. STTA data are based on small non-randomized studies with short-term follow up. Whilst some studies have shown limited benefit, studies that compared vitrectomized and non-vitrectomized eyes found no difference in VA. Current data based on the Ozurdex implant in vitrectomised eyes found short-term benefit for both visual acuity (VA) and macular thickness. No data is available at the present time for the use of the Iluvien implant for DME in previously vitrectomized eyes. Randomized controlled data are lacking to evaluate the role of steroids for the management of DME in the vitrectomized eye.

• 4121

Why do we need a subspecialty exam?

ACLIMANDOS W
United Kingdom

Abstract not provided

• 4122

What are the general requirements for candidates to sit the exam

MIDENA E
University of Padova, Department of Ophthalmology, Padova, Italy

The European Board of Ophthalmology (EBO) has recently decided to promote, at the European level, a subspecialty diploma in some selected areas of Ophthalmology. The first subspecialty diploma is related to Glaucoma. The guidelines for this kind of diploma have been developed with the European Glaucoma Society, because the aim of EBO is to have the already existing European subspecialty Societies (European Glaucoma Society, Euroepan Society of Cataract and Refractive Surgery, EURETINA, ...) as the driver of the EBO Subspeciality examination. The characteristics of the examination, and any information related to the curriculum and major requirements to sit the exam will be presented.

• 4123

How does EBO manage expertise of MCQ's ?

TASSIGNON M.-J.
Belgium

Abstract not provided

• 4124

EBO-EGS exam in glaucoma ; our first experience in 2015 ?

SUNARIC MEGEVAND G
Memorial Rothschild Foundation, Centre Ophtalmologique de Florissant, Geneva, Switzerland

The main goal of the EBO is to harmonize education and training in general ophthalmology within Europe and the main tool is the comprehensive EBO Diploma examination, organized annually since 1995, awarding successful candidates the title of the Fellow of the European Board of Ophthalmology (FEBO). More recently the EBO has established a Subspecialty European Board of Ophthalmology Diploma Examination with the goal to increase standards of knowledge and care in various subspecialties. The EBO is realising this goal by close collaboration with different European ophthalmological subspecialty societies who are actively taking part in the organization and realization of the EBO Subspecialty Examinations allowing an official and standardized evaluation and awarding of knowledge in various specialties.
The first of these subspecialty examinations to be introduced is in the field of glaucoma and is developed in close collaboration with the European Glaucoma Society (EGS). The goals, the organisation and requirements to sit the subspecialty exam as well as the first experience with the FEBO-Glaucoma exam and Diploma will be presented.

• 4125

Future plans: Exams in retina, paediatrics, cataract and cornea

CREUZOT C

Department of Ophthalmology, Dijon, France

Due to the heterogeity of ophthalmological practice all over Europe, there was currently no structured and standardised subspecialty training in the various fields of ophthalmology. Ophthalmologists who wish to pursue a more advanced training in the ophthalmological subspecialty of their choice mostly organize their own training and decide individually on their level of knowledge and capability. There was no formal process of assessment and recognition of their expertise. The goal of the EBO Subspecialty diploma is to award ophthalmologists who have completed an ophthalmological subspecialty training and achieved clearly defined prerequisites defined in collaboration with the different subspecialty societies. The first experiment has been organised this year with glaucoma with a close collaboration between EBO and EGS (European Glaucoma Society). In the future, EBO will act as an umbrella organization of the exam in close collaboration with the different European subspecialty societies. The assessment will be based on MCQs, clinical cases, oral examination, and discussion about published articles. If awarded, the candidates will be recognized as Fellow of the EBO in their field of expertise (ie retina, paediatrics, cataract ...)

• 4131

Infectious keratitis and the distribution in Asia

BEUERMAN R
Singapore Eye Research Institute, Singapore,

Abstract not provided

• 4132

Prevention of herpes simplex stromal keratitis by a glycoprotein B-specific monoclonal

BAUER D (1), Dirks M (2), Kasper M (1), Buch A (3), Dittmer U (2), Giebel B (4), Wildschütz L (1), Busch M (1), Goergens A (2), Schneweis K E (5), Eis-Hübinger A M (5), Sodeik B (6), Heiligenhaus A (1), Roggendorf M (7), Krawczyk A (7)
(1) Department of Ophthalmology at St. Franziskus Hospital, Ophtha-Lab, Muenster, Germany
(2)University Hospital Essen, Department of Virology, Essen, Germany
(3) Hannover Medical School, Department of Virology, Hannover, Germany
(4) University Hospital Essen, Institute for Transfusion Medicine, Essen, Germany
(5) University Medical Center Bonn, Institute of Virology, Bonn, Germany
(6) Hannover Medical School, Institute of Virology, Hannover, Germany
(7) University Hospital Essen, Institute of Virology, Essen, Germany

The increasing incidence of acyclovir (ACV) and multidrug-resistant strains in patients with Herpetic Stromal Keratitis (HSK) is a major health problem and often results in blindness. In the study we examined the effectivity of mAb 2c in preventing experimental HSK in BALB/c mice. Mice were infected with HSV-1 (KOS) and subsequently either systemically or topically treated with mAb 2c. Systemic treatment was performed by intravenous administration of mAb 2c 24 h prior to infection (pre-exposure prophylaxis) or 24, 40, and 56 hours after infection (post-exposure immunotherapy). For topical treatment antibody-containing eye drops or PBS as control was administered (5 times per day). Systemic antibody treatment markedly reduced viral loads and completely protected mice from developing HSK. The administration of antibody prior or post infection was equally effective. Topical treatment had no improving effect on the severity of HSK. In conclusion, our data demonstrate that mAb 2c proved to be effective for the treatment of corneal HSV-infections and for prevention of HSK and blindness. Moreover, the humanized counterpart (mAb hu2c) was equally potent in protecting mice from HSV-induced HSK when compared to the parental mouse antibody.

• 4133

Peptide versus gene therapy: Cathelicidin LL-37 and HSV-1 corneal infection

GRIFFITH M, Lee C J, Buznyk O
Linköping University, Dept. of Clinical and Experimental Medicine, Linköping, Sweden

We compared the performance of biosynthetic corneal implants based on collagen-phosphorylcholine (Coll-MPC) with anti–Herpes Simplex Virus (HSV)-1 activity achieved by sustained release of the cathelicidin LL- 37 from incorporated nanoparticles, to cell-based delivery of the peptide from human corneal epithelial cells (HCECs) transfected to produce endogenous LL-37. LL-37 released from the implants blocked HSV-1 infection of HCECs by interfering with viral binding. However, in pre-infected HCECs, LL-37 delayed but could not prevent viral spreading nor clear viruses from the infected cells. HCECs transfected with the LL-37 to confer viral resistance expressed and secreted the peptide. Secreted LL-37 inhibited viral binding in vitro but was insufficient to protect cells completely from HSV-1 infection. Nevertheless, secreted LL-37 reduced both the incidence of plaque formation and plaque size. LL-37 released from composite nanoparticle-hydrogel corneal implants and HCEC-produced peptide, both showed anti–HSV-1 activity by blocking binding. While both slowed down virus spread, neither was able on its own to completely inhibit the viruses.

• 4134

Antibiotic resistance and new types of antimicrobials

BEUERMAN R
Singapore Eye Research Institute, Singapore,

The World Health Organization has pointed out that all current antibiotics exhibit some level of resistance. Moreover, designing new antibiotics to avert resistance is difficult due to the ability of bacteria to mutate targets of current antibiotics. Conceptually, it was realized that to overcome resistance it was necessary to kill bacteria quickly and to avoid mutable targets. New molecules were designed using the fundamentals chemical interactions that would disrupt membrane organization. These small molecules were for both Gram positive and Gram negative bacteria, as well as mouse models of corneal infection. Specific chemical groups were attached to a series of small molecules that resulted in rapid kill time (<60mins), had no effect on healing of an epithelial wound in rabbits, and in a mouse model of MRSA infection of the cornea were effective at 3mg/ml compared to vancomycin at 50mg/ml. Simulation of resistance showed that these new classes of antibiotics did not develop resistance although in the same protocol, MICs for gatifloxicin, gentamycin and norfloxicin increased by 10-140 times. Conclusion: New drug designs based on more predictive behavior could bring a series of new drugs to the clinic to lessen the impact of resistance on healthcare.

• 4141

Uveal melanoma and other cancers

DESJARDINS L , Villaret J , Cassoux N , LumbrosoLeRouic L , Levy C , Plancher C , Savignoni A
Institut Curie, ophthalmic oncology, Paris, France

Purpose We evaluated in a retrospective study the frequency and nature of other cancers in uveal melanoma patients
Methods Patients and method
A prospective registry of uveal melanoma patients is pèrformed in our center including usual datas on patients and tumor characteristics and since 2000 cancer past history. Each patient is followed during ten years after initial treatment and occurence of second cancer after uveal melanoma is registered.
Results there are 6262 patients in the database with uveal melanoma and for 3934 history of previous cancer was registered.We had 548 cases of associated cancer: 423 had a past history of cancer before uveal melanoma was diagnosed and 102 patients dévelopged a second cancer after the diagnosis of uveal melanoma.Cutaneous melanoma and renal carcinoma were found to be more frequent than expected
Conclusions Recent genetic improvments led to new discovery of germinal mutations responsible for cancer. As known for BRCA mutations and breast cancer or Rb1 gene and retinoblastoma, BAP 1 mutations has been found to predispose to mesothelioma, clear cells renal cancer and cutaneous and uveal melanoma.For young patients or patients with multiple cancers or family high frequency of cancer genetic counseling has became essential.

• 4142

Uveal melanoma in Finnish patients with congenital ocular melanocytosis

MAMUNUR R , Kivelä T
University of Helsinki, Department of Ophthalmology Helsinki University Hospital, Helsinki, Finland

Purpose To described the characteristics of uveal melanoma in congenital ocular melanocytosis in Finland.
Methods For this retrospective observational case series, we identified all 15 of 867 (1.7%; 95% CI 1.0-2.8) uveal melanoma patients (5 male, 10 females) with congenital ocular melanocytosis during January 2000-May 2015 at the Ocular Oncology Service, Helsinki University Hospital. The patient was followed up at 3 and 6 months, every 6 months for 3 years, and thereafter annually. The diagnosis of uveal melanoma was based on clinical and ultrasonographic features, and metastases were screened with annual abdominal ultrasonography and liver function tests.
Results The mean age at diagnosis was 55 years as compared with 64 years for all 867 patients. The mean thickness and basal diameter of the tumours were 6.5 (SD 3.6) and 13.1 (SD 4.4) mm, respectively, as compared to 5.1 (SD 3.9) and 12.5 (SD 4.5) among all patients, respectively. The melanoma involved the ciliary body in 6 patients (40%). The tumours represented TNM stages I in 4 (27%) patients, II in 5 (33%), III in 5 (33%) and IV (metastases at the time of diagnosis) in 1 patient. Enucleation was done in 2 cases, I-125-brachytherapy in 7 cases, and 5 patients were treated with Ru-106. Recurrent tumour growth was observed in 2 patients. Overall 5- and 10-year survival was 68%(95% CI 35-87) and 13% (95% CI 1-43). Survival was associated with TNM stage: 100%, 80%, 33% and 0% at 5 eyars for stages I-IV, respectively. One patient survived for 10 years without metastasis.
Conclusions In our data set, uveal melanoma patients with congenital ocular melanocytosis are on average 9 years younger than uveal melanoma patients in general, and have a tendency to die of metastases.

• 4143

Spectral-domain EDI-OCT in small uveal melanoma and «pseudomelanomas»

SAAKYAN S (1), Neroev V (2), Myakoshina E (1), Zaitseva O (2)
(1) *Moscow Helmholtz Research Institute of Eye Diseases, Department of ophthalmooncology and radiology, Moscow, Russia*
(2) *Moscow Helmholtz Research Institute of Eye Diseases, Department of retinal pathologi, Moscow, Russia*

Purpose To reveal diagnostic symptoms of small uveal melanoma and «pseudomelanomas» by spectral-domain EDI-OCT.
Methods The results of complex research (ophthalmoscopy, ultrasonography, spectral-domain EDI-OCT) of 230 patients (230 eyes) aged from 13 to 75 (mean 49 ± 1.1) years with diagnosis «small uveal melanoma» were analyzed.
Results In 142 (61,7%) from 230 cases small uveal melanoma was diagnosed. The tomographycal symptoms were retinal thickness caused by neuroepithelium detachment, cystoid retinal edema; bow-shaped choroidal profile; retinal thickness in contiguous zone caused by neuroepithelium detachment. In 88 cases (38,3%) «pseudomelanomas» were diagnosed. In age-related macular degeneration (38) retinal pigment epithelium detachment, hyperreflective focus (subretinal membrane), equal choroidal profile; in subretinal hemorrhage (25) equal elevation of choroidal profile without retinal fluid; in peripheral retinal degeneration (12) retinal thinning, insignificant elevation of choroidal profile, hyperreflective foci on RPE level; in congenital hypertrophy of retinal pigment epithelium (13) equal choroidal profile, retinal thinning, thickness of retinal pigment epithelium were diagnosed.
Conclusions Thus, spectral-domain EDI-OCT allow to reveal small uveal melanoma and «pseudomelanomas» symptoms for adequate treatment.

• 4144

BAP1 correlates with metastasis in polyploid uveal melanoma

KILIC E (1), Yavuzyigitoglu S (1), Mensink H (2), Vaarwater J (1), Naus N (1), Paridaens D (2), De Klein A (3)
(1) *Erasmus MC, Ophthalmology, Rotterdam, The Netherlands*
(2) *Eye Hospital, Ocular Oncology, Rotterdam, The Netherlands*
(3) *Erasmus MC, Clinical Genetics, Rotterdam, The Netherlands*

Purpose Most of the Uvea melanoma (UM) display a near-diploid karyotype with only a few chromosomal changes. In contrast to these simple aberrations 10% of the UM samples show a polyploid character (> 58 chromosomes) and were associated with unfavorable prognosis. This study attempts to gain insight in polyploidy in UM and supplement the old data with the current knowledge on mutations in UM specific genes.
Methods Fluorescence-In-Situ-Hybridization (FISH) and/or Single-Nucleotide-Polymorphism (SNP) array was used to determine the ploidy status. Tumors showing signs of polyploidy (range tri- tetraploidy) were further investigated. Immune-histochemistry was used to determine the BAP1 expression and mutation analyses of *BAP1* (coding regions) or the hotspots for the *GNAQ*, *GNA11*, *SF3B1* and *EIF1AX* genes was carried out using Sanger Sequencing .
Results Polyploidy was seen in 23 tumor samples. Fourteen of the UM patients developed metastases with a median follow-up of 35 months. Thirteen tumors showed loss of BAP1 expression and all genetically tested polyploid tumors harbored a *GNAQ* or *GNA11* mutation. *SF3B1* mutations were found in three UM specimens and one of the tumors harbored an EIF1AX mutation. Univariate analyses showed a significant association with decreased survival for chromosome 1, 3 and 8 aberrations, *SF3B1* wild type and a loss of BAP1 expression. In the multivariate analyses, BAP1 expression was the only independent prognostic marker within the polyploid tumors (HR 10.1; p=0.008).
Conclusions Also for the tumors displaying polyploidy loss of BAP1 expression is associated with an increased risk of metastatic disease.

• 4145

Proteomic analysis of the uveal melanoma (UM) secretome reveals novel insights and potential biomarkers

ANGI M , Kalirai H , Coupland S
University of Liverpool, Liverpool Ocular Oncology Research Group, Liverpool, United Kingdom

Purpose UM is the most common primary intraocular tumour in adults. Despite successful ocular treatment, 50% of patients develop fatal metastatic spread, usually involving the liver. UM patients are stratified into high risk (HR) or low risk (LR) metastatic groups, according to clinical, histopathological and genetic features of their tumours. Blood biomarkers are urgently needed to detect the early development of metastatic disease. The aims of this work were to increase our understanding of UM metastasis processes, and to identify secreted biomarkers of UM metastatic disease.
Methods Comparative analysis of the secretome from short-term cultures of HR and LR UM patient samples was performed by nanoLC-MS/MS-based label-free quantitative proteomics. Normal (N) controls included the secretome of cultured normal choroidal melanocytes. Secreted proteins were predicted based on their sequences. Bioinformatic analyses were performed using Partek and Ingenuity Pathway Analysis software.
Results Eighteen UM (4LR; 14HR) and 5N cultures were established and their secretomes analysed. 1917 proteins were identified, and 1857 quantified in all subgroups. 627/1857 (34%) were classically and non-classically secreted, and 554/1857 (30%) represented exosomal proteins. 947 proteins were differentially expressed between UM and N; pathway analysis demonstrated upregulation of proteins involved in mTOR signalling amongst others. An 18-protein signature that discriminated between HR and LR UMs was identified.
Conclusions Our comparative study of the secretome of N versus UM has identified cancer-associated proteins linked to cell proliferation and cancer progression. Moreover, a UM secretome signature of metastatic risk was identified. Further studies on the exosomal fraction are also being performed.

• 4146

Selecting uveal melanoma for PRAME-TCR T cell immunotherapy

IAGER M J (1), Krijgsman D (1), Luyten G P M (1), Luk S J (2), Van der Velden P (1), Heemskerk M H M (2)
(1) LUMC, Ophthalmology, Leiden, The Netherlands
(2) LUMC, Haematology, Leiden, The Netherlands

Purpose To determine which uveal melanoma may be candidates for PRAME-directed immunotherapy using TCR-modified autologous T cells.
Methods Expression of PRAME was determined in uveal melanoma by an Illumina array. HLA polymorphisms were determined on peripheral blood leukocytes. Clinical and histological characteristics of UM were derived from clinical charts and pathology reports.
Results PRAME expression was highly variable; tumor size, thickness, and the presence of an inflammatory phenotype were associated with PRAME expression. 20/37 monosomy 3 cases expressed PRAME, and 8/20 disomy 3 tumors. 10-year survival data on 60 UM showed worse survival of UM with high PRAME compared to those with a low PRAME. However, six of the eight PRAME-positive disomy 3 cases died from metastases. With this information, all cases with PRAME-positive primary tumors who carry the HLA-A2 antigen should be followed closely for the development of metastases, as they can be candidates for PRAME-TCR autologous T cell therapy.
Conclusions Uveal melanoma may be good candidates for treatment with autologous T cells that have been modified so that they carry PRAME-specific T cell receptors. Large uveal melanoma with a high PRAME expression (independent of chromosome 3 status) in HLA-A2 positive patients are potential candidates for PRAME-TCR autologous T cell therapy. A high PRAME expression, also in disomy 3 tumors, was associated with an inflammatory phenotype and with death due to metastases.

• 4151

Comparison of retinal and choroidal involvement in tuberculous chorioretinitis in a non-endemic area.

MASSY R (1), Herbort C P (2)
(1) University of Lausanne, Centre for Ophthalmic Specialized Care, Lausanne, Switzerland
(2) University of Lausanne & Centre for Ophthalmic Specialized Care, Department of Ophthalmology, Lausanne, Switzerland

Purpose To assess the respective involvement of retina versus choroid in presumed ocular tuberculosis (POT) in a non-endemic area using dual fluorescein (FA) and indocyanine green angiography (ICGA).
Methods Retrospective study on patients with the diagnosis of POT seen in the Centre for Ophthalmic Specialized Care, Lausanne, Switzerland. Angiography signs were quantified according to an established FA and ICGA scoring system for uveitis (Int Ophthalmol. 2010;30:539-52 and Ocul Immunol Inflamm 2010;18:385-9).
Results Among the 1739 uveitis patients seen from 1995 to 2014, 53 patients were diagnosed as POT (3%) of which 28 had sufficient data to be included in the study. The choroid was predominantly involved in 22 patients and the retina in 6 patients. The mean angiographic score was 6.19/36 ±4.11 for the retina versus 13.48/36 ±7.06 for the choroid. For patients having sufficient angiographic follow-up, the scores decreased from 6.19 to 2.40 ±2.39 for FA and from 13.48 to 7.87 ±5.37 for ICGA after combined antituberculous and inflammation suppressive therapy.
Conclusions This study shows for the first time the respective involvement of retina and choroid in POT. Choroid is preferentially involved for which ICGA is the examination of choice. By looking only at FA, there is a risk of underestimating global ocular involvement and to miss the diagnosis. To evaluate correctly intraocular inflammation in POT and to have a better follow-up, the use of dual FA & ICG angiography is recommended. On the other hand, in case of a compatible uveitis having a positive IGRA test, in a non-endemic area, dual FA & ICGA should be performed to avert or help the diagnosis of ocular tuberculosis.

• 4152

Impact of disease modifying anti-rheumatic drugs (DMARDs) on the uveitis risk in juvenile idiopathic arthritis

TAPPEINER C (1), Klotsche J (2), Schenck S (2), Niewerth M (2), Minden K (2), Heiligenhaus A (3)
(1) Inselspital- University Hospital of Bern, Department of Ophthalmology, Bern, Switzerland
(2) Leibniz Institute, German Rheumatism Research Centre, Berlin, Germany
(3) St. Franziskus Hospital, Department of Ophthalmology, Muenster, Germany

Purpose To analyze the influence of methotrexate (MTX), Tumour necrosis factor (TNF) inhibitors, and their combination on uveitis occurrence in juvenile idiopathic arthritis.
Methods Data of a nation-wide prospective rheumatological and ophthalmological database in Germany were evaluated for the years 2002 to 2013. Patient with JIA disease duration of less than 12 months at initial documentation and with a follow-up of ≥ 2 years were included in this analysis. Discrete-time survival analysis was performed to evaluate the impact of disease modifying anti-rheumatic drugs (DMARDs) on the occurrence of uveitis.
Results A total of 3,512 JIA patients fulfilled the inclusion criteria (mean age 8.3±4.8 years, female 65.7%, ANA-positive 53.2%, mean age at arthritis onset 7.8±4.8 years, mean follow-up time 3.6 ± 2.4 years). Uveitis manifested in 180 patients (5.1%) within one year after JIA onset, and in further 251 patients (7.1%) after the first year. MTX (HR 0.63, p=0.022), TNF inhibitors (HR 0.56, p<0.001) and a combination of the two (HR 0.10, p<0.001) in the year before uveitis onset significantly reduced the risk for uveitis. MTX treatment within the first year after JIA diagnosis revealed the lowest uveitis risk (HR 0.29, p<0.001).
Conclusions DMARDs in JIA patients significantly reduce the risk for uveitis onset. A relevant protective effect was found especially for early MTX use within the first year of arthritis onset and for the combination of MTX with a TNF inhibitor.

Commercial interest

• 4153

Effect of dexamethasone intravitreal implant in the treatment of noninfectious uveitis

FRERE A (1,2), Janssens X (1), Makhoul D (1,2), Judice L (1,2), Postelmans L (2), Lefèbvre P (1), Caspers L (1), Willermain F (1,2)
(1) CHU Saint-Pierre, Ophthalmology, Brussels, Belgium
(2) Brugmann, Ophthalmology, Brussels, Belgium

Purpose To investigate the effect of dexamethasone intravitreal implant (Ozurdex; Allergan, Inc) in noninfectious uveitis
Methods Charts of patients with noninfectious uveitis treated by dexamethasone intravitreal implants were reviewed in a retrospective study. Uveitis etiologies, treatment indications, visual acuity, central retinal thickness measured by optical coherence tomography, intraocular pressure and number of injections were collected. Parameters were analyzed before injection (29±6 days), after 5-6 weeks (49±10 days) (short follow-up) and 4-5 months (134±2 days) (long follow-up) post Ozurdex injection.
Results We included 14 patients (20 eyes, 26 implants injections). Before injections, mean visual acuity was 0.5±0.5 logMAR and improved to 0.3±0.4 logMAR at short time follow-up and to 0.3±0.5 logMAR at long time follow-up. Macular thickness has decreased by 101±126 µm at short time follow-up and 83±162µm at long time follow-up. Mean intraocular pressure was 16±5 mmHg before injections, 17±6 mmHg at short time follow-up and 15±3 mmHg at long time follow-up.
Conclusions In noninfectious uveitis, dexamethasone implant can improve visual acuity and decrease macular thickness without significant increase of intraocular pressure. Although the effect seems limited in time.

• 4154

Sarilumab for the treatment of posterior segment non-infectious uveitis (NIU): The SATURN (SARIL-NIU) study

HEISSIGEROVA J (1), Sundaram P A (2), Erickson K (3), Varona R (4), Corp-dit-Genti V (4), Vitti R (3), Buggage R (5), Rihova E (1), Nguyen Q D (6)
(1) Charles University and General University Hospital, Ophthalmology, Prague 2, Czech Republic
(2) Sanofi R&D, Ophthalmology Division, Bridgewater, United States
(3) Regeneron Pharmaceuticals, Clinical Sciences Ophthalmology, Tarrytown, United States
(4) Sanofi R&D, Clinical Sciences and Operations, Chilly-Mazarin, France
(5) Sanofi R&D, Ophthalmology Division, Paris, France
(6) Truhlsen Eye Institute, College of Medicine- Department of Ophthalmology and Vision Sciences, Omaha, United States

Purpose Interleukin-6 (IL-6) and/or its soluble receptor are detected in the vitreous and aqueous humors of patients with uveitis. Inhibition of IL-6 signaling in a murine model of experimental autoimmune uveitis suppresses the development of uveitis. We designed an exploratory Phase 2 study to evaluate the efficacy and safety of sarilumab, a human monoclonal antibody directed against the alpha subunit of the IL-6 receptor complex in the management of posterior segment NIU.
Methods SATURN is a 52-week, multicenter, double-masked, placebo-controlled, parallel arm, randomized trial to evaluate the efficacy and safety of sarilumab (200 mg) administered subcutaneously every 2 weeks in patients with posterior NIU, who are treated with systemic steroids (as single therapy or with methotrexate). Efficacy and safety are assessed at each visit. The study primary endpoints are reduction from baseline in vitreous haze or systemic-steroid sparing effects, both measured at week 16. Other key endpoints assessed at week 16 include the change from baseline in: central retinal thickness, best-corrected visual acuity, and percentage of patients with retinal vessel leakage on fluorescein angiography.
Results The study has completed enrollment. As of April 6, 2015, 58 patients have been randomized and treated.
Conclusions The SATURN study may help clarify the role of IL-6 in the pathogenesis of NIU and the potential for IL-6 inhibition in the management of posterior segment NIU.

Commercial interest

• 4155

Long-Term Safety of Intravitreal Sirolimus for the Treatment of Non-infectious Uveitis (NIU) of the Posterior Segment: 12-Month SAKURA Study 1 Results

BODAGHI B (1), Pavesio C (2), Alfredo A C (3), Valentine M E (4)
(1) Hopital Pitie-Salpetrière, Ophtalmologie, Paris, France
(2) Moorfields Eye Hospital- London- United Kingdom, Uveitis, London, United Kingdom
(3) Hospital Clinic of Barcelona, Uveitis, Barcelon, Spain
(4) Santen- Inc-, Pharmacology, Emeryville, United States

Purpose Intravitreal sirolimus significantly reduced inflammation in subjects with NIU of the posterior segment and provided clinically relevant visual benefit, with an acceptable incidence of ocular adverse events (AEs), in the double-masked period of SAKURA Study 1, the first of 2 phase 3 randomized trials. Here, we report the long-term (12 month) safety findings from the combined double-masked and open-label treatment periods.
Methods Subjects with active NIU of the posterior segment (N=347) were randomized to 44 µg (active control), 440 µg, or 880 µg injections of intravitreal sirolimus, administered every 2 months. At M6, all subjects transitioned to 880 µg injections every 2 months.
Results 287 subjects entered the open-label treatment period and completed the M12 Vitreous Haze assessment. Of these, 211 received ≥1 intravitreal sirolimus injections. Through M12, the most common serious ocular AEs (study eye) occurring in ≥2% of subjects were ocular inflammation (2.9%-5.8%), cataract (3.8%), and medication residue (transient drug depot in the visual axis; 2.3%). The mean change in intraocular pressure was <2 mm Hg. The incidence of confirmed endophthalmitis was 0.06%/injection.
Conclusions There was a low incidence of serious ocular AEs over 12 months with intravitreal sirolimus in this heterogeneous group of subjects with NIU of the posterior segment.

Commercial interest

• 4156

Ophthalmologic manifestations of the granulomatosis with polyangiitis (Wegener)

TOUTEE A (1), Touitou V (2), Bodaghi B (2), Lehoang P (2), Saadoun D (3), Hie M (3), Schoindre Y (3)
(1) Hopital Kremlin Bicetre, Ophtalmologie, Le Kremliin Bicetre, France
(2) Hopital La Pitié salpétrière, Ophtalmologie, Paris, France
(3) Hopital La Pitié Salpétrière, Médecine Interne, Paris, France

Purpose Wegener's granulomatosis (WG) is a severe focal granulomatous inflammation with variable ophthalmic manifestations.
Methods Patients with a confirmed WG, seen in a single tertiary center between 2008 and 2014 were included retrospectively. WG was proven based on biological or histological analysis.
Results Five patients (3W/2M) aged 26 to 55 years, were included. Clinical features included one scleritis with dacryoadenitis, one bilateral episcleritis complicated with uveo-scleritis, one bilateral Mooren's ulcer and two orbital inflammatory pseudotumor. Time between the onset of symptoms and the diagnosis was 100 months (range: 1 to 276 months). All patients had anti-cytoplasm antibodies to polynuclear neutrophils and underwent biopsies. Histological features included vasculitis inflammatory necrotizing granulomas. Extraocular features were pulmonary lesions(100%), rhinosinusal involvment(80%), renal disease(40%), neurological injury(40%). All patients were initially treated with high-dose corticosteroids, wich were progressively decreased and received maintenance immunosupressive drugs. Immunosuppressive treatment was initiated on average 64 months after the onset of signs (range: 1 to 276 months).
Conclusions WG's ophthalmologic symptoms are variable. Scleritis remains the most common manifestation, followed by orbital inflammation. Atypical manifestations such as Mooren's ulcer or uveitis can delay the diagnosis. A multidisciplinary approach is mandatory to control this life threatening condition. WG should be considered in all cases of chronic orbital inflammation, scleritis or keratitis to ensure prompt diagnosis and improve the systemic prognosis.

• 4161
General structure of the retina

GRZYBOWSKI A
Poznan City Hospital, Department of Ophthalmology, Poznan, Poland

The invention of the ophthalmoscope in the 19th century led to the development of ophthalmology as a discipline. The retina is an accessible part of the central nervous system and has consequently been studied extensively. There is now a growing use of OCT to obtain information related to brain neurodegenerative disorders like multiple sclerosis, Alzheimer's and Parkinson diseases as well as migraine.
Two aspects of human retinal structure based on physiology and morphology can be distinguished. They are the various retinal layers that consist of either neuron perikarya or neuronal processes. The other, is the distinction between central (macula, fovea) and periphery parts of the retina. Major cell-types in the retina are pigment epithelial, photoreceptor, horizontal, bipolar, amacrine, ganglion and glial cells and an understanding of their roles in healthy and unhealthy retina remains a challenge. Ocular photoreception for example, was thought to be mediated exclusively by rods and cones until the beginning of the 21st century and only recently have photosensitive retinal ganglion cells (pRGCs) been discovered. The aim is to discuss certain aspects of retinal structure related to function.

• 4162
Retinal vasculature structure and function

SCHMETTERER L
Medical University of Vienna, Clinical Pharmacology, Vienna, Austria

The inner retina is supplied from the retinal vasculature, which gets it input from the central retinal artery (CRA). At the optic disc that CRA bifurcates into several branches that provide the blood supply of the entire inner retina. The venous part of the retinal circulation is arranged in a similar way. The central retinal vein leaves the eye through the optic disc and drains blood into the cavernous sinus. The diameter of the CRA before it enters the eye as well as the diameters of the branch arteries is typically below 200 mm. Hence, these vessels are functionally arterioles, and the venous vessels are functionally venules. The larger retinal arteries are surrounded by an avascular zone, because the surrounding tissue receives its oxygen from diffusion through the vessel wall. The capillary network of the retina is organized in two layers. The inner layer lies within the nerve fiber and RGC layer and is called inner plexus, whereas the outer layer lies within the inner nuclear and outer plexiform layers and is called outer plexus. Locally restricted to the region around the optic nerve head is a third capillary layer that is located in the nerve fiber layer consisting of radial peripapillary capillaries.

• 4163
The RPE/photoreceptor complex

OSBORNE N
Oxford University, Oxford, United Kingdom

The retinal pigment epithelium (RPE)/ photoreceptor complex constitutes the choroid, bruch's membrane and the photoreceptor outer segments. The RPE interacts with bruch's membrane and the photoreceptors, which it faces across the subretinal space. In these interactions the RPE acts as three types of cell - epithelium, macrophage, and glia. There are a number of selective interactions between the choroid, bruch's membrane, RPE and photoreceptors related to ion and water transport, vitamin A transport, phagocytosis of shed portions of outer segments, ensheathment of photoreceptors outer segments, and electrical responses. One purpose of the course is to discuss the RPE/photoreceptor complex in terms of structure and function.

• 4164
Retinal glial cells

REICHENBACH A
Paul Flechsig Institute of Brain Research, Leipzig Universität, Leipzig, Germany

Müller cells, the principal glial cells of the retina of all vertebrates, were discovered already in 1851 but it was only in the past decades that it became evident that these cells are essential players in vision. Müller cells constitute the 'core' of columnar units of clonally and functionally related groups of neurons. Their primary function is to support neuronal functioning (by increasing the signal-to-noise ratio of information processing) and survival (by maintaining a metabolic 'symbiosis' with the neurons). It has been shown that Müller cells increase the signal-to-noise ratio of retinal information processing by, for instance, (i) guiding the light towards the photoreceptor cells, (ii) removing excess neurotransmitter molecules from extracellular space, and (iii) performing an efficient clearance of excess extracellular potassium ions after neuronal excitation. The latter two functions are also crucial for neuronal survival – to prevent excitotoxic effects of glutamate – and are coupled to water clearance which is equally important for neuronal survival. As another case of glial homeostasis, the maintenance of appropriate microenvironmental biomechanics has recently been described. Normal glial cells are softer than the neurons, and thus provide a suitable substrate for neurite growth during development, and for functional plasticity. Finally it should be pointed out that Müller cells are capable of 'sensing' neuronal activity. They respond to physiological light stimulation of their adjacent photoreceptors with two distinct types of intracellular calcium rises. These calcium rises then may trigger the release of signal substances, incl. so-called 'gliotransmitters,' from Müller cells which thus even may modify neuronal signal processing in the retina (e.g., in cases of adaptation to bright light, as another mechanism to increase the signal-to-noise ratio of information processing in retina). In cases of reactive Müller cell gliosis, the dominant potassium conductance of the membrane is down-regulated and an increased expression of intermediate filaments is associated with increasing stiffness of the glial cell processes, such that all above-mentioned glial functions are impaired.

• 4165

The On/OFF system pathway of the retina

CASTELO-BRANCO M

IBILI - Institute for Biomedical Imaging and Life Sciences, Faculty of Medicine, Coimbra, Portugal

The ON/OFF pathways in the retina represent parallel systems with asymmetric properties. Here we discuss the basic anatomy and function of these pathways in health and disease, from the point of view of luminance, contrast and motion perception. We will also highlight how receptive field properties are shaped within each of these pathways and how they cross-talk within other parallel streams in the retina. Finally, we will address experimental and disease models that dissect the function of each of these pathways.

• 4171

MicroRNA-124 regulates transforming growth factor β1-induced epithelial-mesenchymal transition in the retinal pigment epithelium by Down-regulating expression of the RhoG

JUN J H (1), Joo C K (2)
(1) School of Medicine- Dongsan Medical Center- Keimyung University, Ophthalmology, Daegu, South-Korea
(2) Seoul St. Mary's Hospital- College of Medicine- The Catholic University of Korea, Ophthalmology and Visual Science, Seoul, South-Korea

Purpose MicroRNA-124 (miR-124) is thought to be involved in the epithelial-mesenchymal transition (EMT) of retinal pigment epithelium (RPE). In the present study, we investigated the regulation of miR-124 on EMT induced by transforming growth factor β1 (TGF-β1) in human RPE cells (APRE-19).
Methods The expression of miR-124 was evaluated after treatment of TGF-β1 by quantitative RT-PCR. Phenotypic alterations were analyzed by western blot analysis and immunocytochemical staining. Target validation was performed to identify the putative target of miR-124 by luciferase reporter assay.
Results The expression level of microRNA-124 (miR-124) was down-regulated during the progression of EMT. Overexpression of miR-124 upregulated the levels of zonular occludens 1 and RPE65, and down-regulated fibronectin, α-smooth muscle actin, and vimentin. Furthermore, inhibition of endogenous miR-124 increased and decreased the levels of mesenchymal and epithelial factors, respectively. TargetScan predicted two well-conserved and two vertebrate-only conserved miR-124 target sequences in the 3' untranslated region (UTR) of the RHOG mRNA. Direct targeting of this 3' UTR by miR-124 was demonstrated using a luciferase assay. Silencing of RHOG using a specific siRNA had identical effects on EMT regulation. Overexpression of miR-124 repressed TGF-β1-induced RPE cell-collagen gel lattice contraction by altering cell spreading/cell-to-cell adhesion.
Conclusions This study describes the regulation of EMT in RPE cells by TGF-β1/miR-124/RHOG signaling and suggests that the supplement of miR-124 expression would be a crucial therapeutic target for the prevention or treatment of proliferative vitreoretinopathy.

• 4172

Spontaneous and mechanically induced Ca2+ activity changes in hESC-RPE cells during maturation

ABLI KHAMIDAKH A (1), Juuti-Uusitalo K (2), Caetano dos Santos F (1), Skottman H (2), Hyttinen J (1)
(1) Tampere University of Technology- BioMediTech, Electronics and Communications Engineering, Tampere, Finland
(2) University of Tampere, BioMediTech, Tampere, Finland

Purpose The aim of this study was to investigate changes in spontaneous Ca2+ activity and mechanically induced intercellular Ca2+ communication in human embryonic stem cells-derived retinal pigment epithelium (hESC-RPE) during maturation.
Methods In this study, we assessed Ca2+ activity in hESC-RPE cells cultured for 9 or 28 days. Ca2+ imaging was done using a Ca2+-sensitive fluorescence dye fluo-4-AM. Spontaneous Ca2+ activity and mechanically induced intercellular Ca2+ communication were recorded in control conditions, in the absence of extracellular Ca2+, after depletion of intracellular Ca2+ stores with thapsigargin, in presence of a gap junction blocker α-glycyrrhetinic acid and a P2-receptor blocker suramin.
Results 9 days cells exhibited twice lower spontaneous Ca2+ activity and 4-fold higher mechanically induced intercellular Ca2+ communication compared to 28 days cells. Absence of extracellular Ca2+ reduced spontaneous Ca2+ activity in 9 days cells and almost completely inhibited it in 28 days cells, while having no effect on mechanically induced intercellular Ca2+ communication. Depletion of intracellular Ca2+ stores abolished spontaneous Ca2+ activity in 9 days and 28 days cells, as well as mechanically induced intercellular Ca2+ communication in 28 days cells, while not affecting the latter in 9 days cells. Blockade of gap junctions and P2-receptors had no effect on spontaneous Ca2+ activity or mechanically induced intercellular Ca2+ communication in cells from both time points.
Conclusions Our results show that hESC-RPE cells undergo significant Ca2+ signaling re-arrangements during maturation: the cells increase spontaneous Ca2+ activity, while decreasing their intercellular Ca2+ communication.

• 4173

Inflammasome activation by UVB irradiation in human corneal epithelial cells

KAUPPINEN A (1,2), Korhonen E (1), Püppo N (1), Hytti M (1), Kaarniranta K (1,2)
(1) University of Eastern Finland, Institute of Clinical Medicine / Ophthalmology, Kuopio, Finland
(2) Kuopio University Hospital, Department of Ophthalmology, Kuopio, Finland

Purpose Cornea is the outermost layer of the eye and mainly responsible for the absorption of ultraviolet B (UVB) radiation. An acute painful inflammatory damage caused by UVB radiation on the corneal epithelium is known as photokeratitis, snow blindness, or welder's burn. We have previously shown that UVB induces inflammation by increasing the production of cytokines IL-6 and IL-8 in human corneal epithelial (HCE) cells and now, we have continued this study by exploring the effects of UVB on the inflammasome signaling.
Methods *In vitro*-cultured HCE cells were exposed to UVB radiation after priming with TNF-α. Thereafter, inflammasome components and cytokines were determined using the ELISA, western blot, and activity assays.
Results Our results suggest that UVB is capable of activating inflammasome signaling in HCE cells.
Conclusions In addition to traditional pathways, UVB induces the activation of more recently found pro-inflammatory signaling system in the human corneal epithelium.

4174

Anatomical digital image analysis of the angle and optic nerve – a novel method for glaucoma imaging

RUSSELL G (1), Szabó A (2), Sziklai P (2), Facskó A (2), Kolko M (3), Petrovski G (2)
(1) Health Intelligence / University of Szeged, Clinical Development, Cheshire, United Kingdom
(2) University of Szeged, Department of Ophthalmology, Szeged, Hungary
(3) University of Copenhagen, Department of Neuroscience and Pharmacology, Copenhagen, Denmark

Purpose To devise a simple, fast and low-cost method for glaucoma imaging using anatomical digital image analysis of the angle and optic nerve in human subjects.
Methods A pilot study included 10 open-angle glaucoma patients attending the glaucoma services at the Department of Ophthalmology, University of Szeged, Hungary; colour photographs of the fundus, standard optic nerve images with OCT and additional digital slit lamp images of the angle where collected. Digital image conversion and analysis of the angle using Image J (NIH, USA) and adaptive histogram equalization Contrast Limited AHE (CLAHE) to prevent noise amplification. Angle and optic nerve images, were analyzed separately in the Red, Green and Blue (RGB) channels, then 3D volumetric analysis of the degrees of angle, cup volume of the optic nerve took place. Horizontal tomogram reconstitution and nerve fiber detection methods were developed and compared to a standard Topcon 3D OCT.
Results Angle measurements from digital angle images by gonioscopy all fitted within one standard deviation of Anterior OCT measurements. Comparative analysis of RGB channels produced volumetric cup and Horizontal tomogram results closely resembling those of OCT 3D appearance and B-scan of the cup, respectively. Similar RGB channel splitting and image subtraction produced a map closely resembling that of the thickness RNFL map on OCT.
Conclusions While spectral domain OCT is rapidly progressing in the area of optic disc and chamber angle assessment, rising health care costs and lack of availability of the technology, opens demand for alternative forms of image analysis of glaucoma. Volumetric, geometric and segmentational data obtained through digital image analysis correspond well to those obtained by high definition OCT imaging. A larger number of subjects is needed to further validate the method.

• 4175

Fisetin and Luteolin decrease inflammation and oxidative stress-induced cytotoxicity in ARPE-19 cells

HYTTI M (1), Piippo N (1), Korhonen E (1), Kaarniranta K (1,2), Kauppinen A (1,2)
(1) University of Eastern Finland, Department of Clinical Medicine / Ophthalmology, Kuopio, Finland
(2) Kuopio University Hospital, Department of Ophthalmology, Kuopio, Finland

Purpose Age-related macular degeneration (AMD) is the leading cause of blindness among the elderly in the western world. It represents not only a dramatic reduction in patients' quality of life but also a significant burden to the general healthcare system. Yet, despite the severity of the disease much questions regarding the pathways of disease formation and progression are still unanswered and viable treatment options still undiscovered. Here, we evaluate the cytoprotective and anti-inflammatory potential of fisetin and luteolin in human retinal pigment epithelial cells exposed to increased oxidative stress.
Methods ARPE-19 cells were treated with 4-Hydroxynonenal (HNE) to simulate high levels of oxidative stress. Thereafter, fisetin or luteolin were added to the culture medium. The MTT and the lactate dehydrogenase assays were used to assess cellular toxicity. Inflammatory cytokines, as well as activation of transcription factors were measured using the ELISA method and a DNA-binding transcription factor assay. To analyze the importance of SIRT1 and related pathways, the experiments were repeated after specific SIRT1 knock-out using siRNA. Levels of intracellular SIRT1 were measured using Western Blot.
Results Fisetin and luteolin protected retinal pigment epithelial cells from oxidative stress-induced cell death and exhibited potent anti-inflammatory properties even after the initial insult. These effects seemed to be independent of NF-κB or SIRT1.
Conclusions Bioactive polyphenols, fisetin and luteolin are powerful anti-inflammatory and anti-oxidant agents and show potential for the development of drugs aimed at specific intracellular pathways that affect inflammation in AMD.

• 4176

cis-Urocanic acid prevents inflammation and cell death in UVB-treated ARPE-19 cells

KORHONEN E (1), Piippo N (1), Hytti M (1), Kaarniranta K (1,2), Kauppinen A (1,2)
(1) University of Eastern Finland, Department of Ophthalmology, Kuopio, Finland
(2) Kuopio University Hospital, Department of Ophthalmology, Kuopio, Finland

Purpose cis-Urocanic acid (cis-UCA) is an endogenous ultraviolet (UV) absorbing chromophore that is mainly produced in the upper layers of epidermis. The aim of our study was to investigate the cytoprotective capacity of cis-UCA in UVB-irradiated ARPE-19 cells.
Methods ARPE-19 cells were pretreated with IL-1α and cis-UCA and then exposed to UVB radiation. Secretion of IL-1β and -18 was measured using the ELISA method. Moreover, the cells were observed under an inverted microscope and cell viability was measured by lactate dehydrogenase (LDH) release assay. The proper cis-UCA concentration was evaluated comprehensively beforehand using MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide), neutral red, and LDH tests.
Results Our results show that UVB after IL-1α priming activates IL-1β and -18 secretion in ARPE-19 cells and cis-UCA clearly alleviates that. cis-UCA also improves cellular viability.
Conclusions cis-UCA shows anti-inflammatory and cytoprotective properties in ARPE-19 cells.

• 4177

Anterior lens epithelium in cataract patients with retinitis pigmentosa - scanning and transmission electron microscopy study

ANDJELIC S (1), Draslar K (2), Hvala A (3), Hawlina M (1)
(1) University Medical Centre, Eye Hospital, Ljubljana, Slovenia
(2) Biotechnical Faculty- University of Ljubljana, Department of Biology, Ljubljana, Slovenia
(3) Medical Faculty- University of Ljubljana, Department of Pathology, Ljubljana, Slovenia

Purpose In retinitis pigmentosa (RP) patients, relatively minor lens opacity posteriorly centrally may cause disproportionate functional symptoms requiring cataract operation. To investigate possible structural reasons for this opacity development, we studied the structure of the lens epithelium of RP patients.
Methods The anterior lens capsule (aLC: basement membrane and associated LECs) were obtained from cataract surgery and prepared for scanning and transmission electron microscopy (SEM and TEM).
Results Both SEM and TEM show the holes in the anterior lens epithelium of cataract patients with RP. Mainly, the holes appear as thinning and degradation of the epithelium, with the dimensions from less than 1 μm to more than 10 ηm and covering the region of several aLECs. A step towards the formation of denuded regions with the dimensions even bigger than 50 ηm may be the detachment of the lens epithelium. Other type of holes in size up to 20 ηm, may be formed by gradual stretching of the lens epithelium. Another type of holes is formed between adjacent LECs where lateral connections are absent, with dimensions 0.1-2 ηm x up to 10 ηm.
Conclusions Showing of holes in the anterior lens epithelium supports the hypothesis that disturbed structure of the lens epithelium plays a role in water accumulation in the RP cataractous lens. We suggest that the lens epithelium has a role in the development of the cataract in RP patients.

• 4178

The study of needle tip aspirates and entry sites after intravitreal injections with different needle types

LYTVYNCHUK L (1), Savytska I (2), Sergiienko A (3), Binder S (4), Petrovski G (5)
(1) Lviv Regional Clinical Hospital, Ophthalmology Department #1, Lviv, Ukraine
(2) A.A.Shalimov National Institute of Surgery and Transplantology, Department of Experimental Surgery, Kyiv, Ukraine
(3) Professor Sergienko Eye Clinic, Ophthalmology, Vinnycia, Ukraine
(4) Rudolf Foundation Clinic- Karl Landsteiner Institute for Retinal Research and Imaging, Ophthalmological Department, Vienna, Austria
(5) Albert Szent-Gy¨orgyi Clinical Center- University of Szeged, Department of Ophthalmology, Szeged, Hungary

Purpose To compare the entry site and study the cellular content of different needle tip aspirates after transscleral intravitreal injection (IVI) on rat eyes.
Methods The intravitreal injections (IVI) were performed on 20 white outbred rat eyes (10 IVI with 30-gauge subcutaneous needles (SCN), 10 with 27-gauge Pencan needle (PCN) (B.Braun)). The 1.0 cc syringes were preloaded with 0.02 cc of balanced salt solution (BSS) and connected to the needles. The penetration was performed 1 mm posterior to the limbus, followed by aspiration of 0.01 cc vitreous body. Aspirated material was evacuated onto glass slides and stained by Azure-2-Eosin. Enucleation and histological analysis of the IVI entry site was performed at magnification 100 and 400 times.
Results Cellular content of the aspirated material was revealed in all cases. The aspirated cells represented conjunctival epithelial-, ciliary body non-pigmented epithelial-, sclerocyte-like cells and vitreous crystallised specimens. The amount of conjunctival epithelial cells prevailed in 27-gauge PCN IVI cases. The stained granular proteins were less significant in the case of 27-gauge PCN tips. The entry sites after 30-gauge SCN injection showed concrete cut of all tissues, while partial reassembling of the sclerocyte bindings was seen after 27-gauge PCN injections.
Conclusions The use of 30-gauge SCN and 27-gauge PCN needles for transscleral IVI has resulted in trauma of all layers of the rats' eye wall. Histological analysis of the needle tip aspirates showed less tissue damage by 27-gauge PCN; moreover, the SCN tips created complete cuts due to their sharp edges, in contrast to the PCN tips.

• 4211

Introduction and overview

DICK A
University of Bristol, Bristol, United Kingdom

Abstract not provided

• 4212

Parainflammation, ageing and loss of control

XU H
Queen's University Belfast, Center for Experimental Medicine, Belfast, United Kingdom

Abstract not provided

• 4213

Obesity, degeneration and senescence

SENNLAUB F
Departement thérapeutique, Institut de la Vision, Paris, France

Abstract not provided

• 4214

Feeding microglia to regulate vascular responses

LANGMANN T
Experimental Immunology of the Eye, Cologne, Germany

Abstract not provided

• 4221

Canaloplasty with the Stegmann Canal expander – two years results

GRIESHABER M (1), Schoetzau A (1), Stegmann R (2)
(1) University of Basel, Ophthalmology, Basel, Switzerland
(2) University of Southern Africa, Ophthalmology, Medunsa, South Africa

Purpose To assess the safety and efficacy of circumferential viscocanalostomy (canaloplasty) using a new canal expander in Caucasians with primary open-angle glaucoma (POAG).
Methods Thirty-five eyes of 35 consecutive patients with medically uncontrolled POAG underwent primary canaloplasty and implantation of the Stegmann Canal Expander into Schlemm's canal. Schlemm's canal was unroofed ab externo, and dilated with viscoelastic material and microcatheter. The Stegmann Canal Expander was implanted into the canal lumen, and the superficial scleral flap was closed watertight. Laser goniopuncture of the trabeculo-Descemet's membrane window was performed if postoperative intraocular pressure (IOP) exceeded 16 mmHg.
Results The mean IOP dropped from 26.6 ± 4.2 mm Hg preoperatively to 12.1 ± 2.6 mm Hg at 1 month, 13.1± 1.9 mmHg at 6 months, 13.0 ± 1.9 mm Hg at 12 months, and 13.4 ± 2.4 mm Hg at 24 months ($p < 0.001$). Laser goniopuncture was performed on 5 eyes (14.7%) 6.4 months after surgery; the mean IOP was 19.1 mm Hg before and 14.1 mm Hg after goniopuncture. The number of medications dropped from 2.9 ± 0.3 before surgery to 0.08 ± 0.3 after surgery ($p < 0.001$). The postoperative BCVA at last visit (0.12 ± 0.09; range, 0–0.39) was comparable to preoperative values (0.16 ± SD 0.10; range, 0–0.39) ($p = 0.35$). Complications were minor and included microhyphema (14 eyes) and transient elevated IOP (steroid responder; 4 eyes), partial peripheral Descemet's membrane detachment (2 eyes).
Conclusions Canaloplasty with implantation of the Stegmann Canal Expander reduced IOP significantly in POAG with a low risk for complications.

Commercial interest

• 4222

Risk of trabeculectomy with an initial diagnosis of glaucoma versus ocular hypertension in Gloucestershire, UK.

MCNAUGHT A (1), Turner S (2), Ivanova K (1), Crabb D (3)
(1) Cheltenham General Hospital, Gloucestershire Eye Unit, Cheltenham, United Kingdom
(2) Moorfields Eye Hospital, Glaucoma, London, United Kingdom
(3) City University, Division of Optometry and Visual Science, London, United Kingdom

Purpose Gloucestershire is a rural county in the UK, with a population of ~300,000 >40 years. Importantly, almost all glaucoma and OHT patients attend the Gloucestershire Eye Unit, under the care of one of two glaucoma specialists. Those treated privately will also be treated by the same clinicians: any audit of all the clinical activity of both might reasonably be extrapolated across the whole county. We use this approach to estimate risk of trabeculectomy in patients with an initial diagnosis of glaucoma versus OHT.
Methods An audit of the case notes of all trabeculectomies performed between 2010 and 2012 was undertaken. The initial clinical diagnosis at presentation was recorded e.g. whether POAG, NTG, ACG, secondary glaucoma or OHT, as was the initial untreated IOP/ severity of visual field loss (MD). Time elapsed between initial diagnosis and eventual surgery was calculated.
Results Considering only open-angle glaucomas and OHT, there were 127 trabeculectomies in 119 patients over the two years of the audit. Secondary glaucomas (n=14) were excluded. Annual risk of trabeculectomy in POAG was 2% per year based on an estimate of ~3000 glaucoma patients in the eye clinic. Median time from diagnosis to trabeculectomy: OHT (n=4) 131 months, POAG (n=93), 112 months, NTG (n=14) 89 months, and PEX (n=8) 55 months. Relative risk of trabeculectomy was 70 times higher in POAG compared with OHT, assuming prevalence of 2% POAG, 5% OHT in people >40 years (95% CI of RR 20-290).
Conclusions When compared with POAG, people with an initial diagnosis of OHT are 70 times less likely to need surgery. Patients with PXF had surgery much sooner than those with OHT. This audit provides prognostic predictions for glaucoma and OHT patients, and further, might suggest more resources be directed to patients with glaucoma, perhaps at the expense of patients with OHT.

• 4223

A minimally invasive approach to sub-conjunctival outflow: 1 year results of an ab-interno gelatin stent in combination with preoperative MMC injection for the treatment of primary open angle glaucoma.

STALMANS I (1), Fea A (2), Reitsamer H (3), Lavin C (4)
(1) UZ St. Rafael, Ophthalmology, Leuven, Belgium
(2) Universita degli Studi di Torino, Clinica Oculistica, Torino, Italy
(3) Paracelsus Medical University SALK, Ophthalmology, Salzburg, Austria
(4) Hospital Universitario La Paz, Ophthalmology, Madrid, Spain

Purpose To establish the safety and efficacy of an ab-interno gelatin stent, as a stand-alone procedure, in combination with a preoperative mitomycin C injection in reducing IOP and anti-glaucoma medications in patients presenting with primary open angle glaucoma. Mean IOP, IOP change, reduction in medications, and safety were recorded in 70 subjects through 12 months.
Methods In this prospective, non-randomized, multi-center evaluation, safety and efficacy parameters were evaluated. As a stand-alone glaucoma procedure, a trans-scleral gelatin stent is placed through a clear corneal incision using a preloaded injector with a 27 gauge needle. Once in place, the permanent gelatin implant is designed to connect the anterior chamber to the non-dissected Tenon's and subconjunctival space, thereby creating diffuse dispersion of aqueous while bypassing potential outflow obstructions. Effectiveness was assessed by comparing medicated baseline IOP and glaucomatous medications to postoperative values through 12 months. Safety was assessed by assessing complications at routinely scheduled exams through 12 months.
Results No major adverse events were reported, and 2 patients were converted to a tube shunt at 6 months. The mean preoperative (best medicated) IOP was 23.6 mmHg. The mean postoperative IOPs were: 13.3 mmHg (44% reduction) at 9 months, and 12.6 mmHg (47% reduction) at 12 months. From the preoperative mean of 3.5 (patients not washed out pre-surgery), 9 months medications were reduced by 69% and at 12 months medications were reduced by 66%. No infection, migration or erosion occurred in any patients.
Conclusions This "hybrid system", combining a minimally invasive ab-interno approach with a subconjunctival drainage, provided very satisfactory intra-ocular pressure control after one year with an excellent safety profile.

Commercial interest

• 4224

Glaucoma patients have a significant decrease in retrobulbar blood flow velocities during general anesthesia

ABEGAO PINTO L (1), Vandewalle E (2), Willekens K (2), Van keer K (2), Van Calster J (2), Stalmans P (2), Vertommen J (3), Deckers K (3), Marques-Neves C (1), Stalmans I (2)
(1) Centro Hospitalar Lisboa Norte / Faculty of Medicine of Lisbon University, Department of Ophthalmology, Lisbon, Portugal
(2) University Hospitals Leuven, Ophthalmology, Leuven, Belgium
(3) University Hospitals Leuven, Anesthesiology, Leuven, Belgium

Purpose Glaucoma patients are known to have an underlying vascular dysfunction and General anesthesia (GA) significantly decreases blood pressure, which might decrease ocular perfusion. This study was conducted to investigate the effects of GA on ophthalmic flow velocities and blood pressure.
Methods Prospective, case-control study. Glaucoma patients were scheduled for trabeculectomy or drainage device implantation; non-glaucomatous patients undergoing vitrectomy for macular hole or epiretinal membrane peeling were recruited as control subjects. Color Doppler imaging of the ophthalmic artery (OA) was performed immediately before and 1 minute after GA induction. The following parameters were analyzed: OA blood velocities and resistivity index, as well as cardiovascular parameters (diastolic and systolic blood pressure and heart rate). Statistical analysis was performed using Student's paired t test, Mann-Whitney, Fisher's exact test and Spearman's correlation.
Results 53 patients were included (glaucoma group: 25; control group: 28). The magnitude in blood pressure decrease after GA induction was similar between the two groups (p value 0.61-0,70). However, the decrease in OA blood velocities was significantly larger in the glaucoma groups than in the control group ($p<0.03$ in all comparisons). Unlike the control subjects, in the glaucoma group there was a significant association between the magnitude of blood pressure decrease and the lowering of the OA mean blood velocity ($r=0.69$, 95% IC: 0.36-0.87, $p<0.001$).
Conclusions These results suggest that glaucoma patients are unable to keep a stable blood velocity in the OA when subjected to acute significant decreases in blood pressure (such as the ones seen after GA induction).

• 4225

Receptor-targeted liposome-peptide-siRNA nanoparticles represent a novel and efficient siRNA delivery system to prevent conjunctival fibrosis.

YUI-WAI-MAN C (1), Tagalakis A (2), Manunta M (2), Hart S L (2), Khaw P T (1)
(1) NIHR BRC at Moorfields Eye Hospital and UCL Institute of Ophthalmology, Cell Biology & Ocular Biology and Therapeutics, London, United Kingdom
(2) Wolfson Centre for Gene Therapy of Childhood Disease, Gene Therapy, London, United Kingdom

Purpose Glaucoma is the leading cause of irreversible blindness worldwide and fibrosis is the main cause of failure of glaucoma surgery. We have previously described how the Myocardin-related transcription factor/ Serum response factor (MRTF/ SRF) pathway is intricately linked to all the key pathways in ocular fibrosis. Our aim was to develop a novel liposome-peptide-siRNA (LYR) nanoparticle as an efficient delivery system for MRTF siRNA in conjunctival fibrosis.
Methods The LYR nanoparticles were characterised with regard to particle size and zeta potential. Real-time qPCR and western blotting were used to compare the silencing efficiency in human Tenon's fibroblasts using different MRTF siRNA concentrations, targeting peptides, and liposomes. The cytotoxicity of the LYR nanoparticles was assessed using the MTT cell assay. Three-dimensional fibroblast-populated collagen matrices were also used as a functional assay to measure contraction in vitro.
Results All LYR nanoparticles were strongly cationic with sizes around 100 nm and PDIs < 0.4. The LYR nanoparticles efficiently silenced the MRTF gene by 76% and 84% using 50 nM and 100 nM siRNA respectively. The MRTF gene was also efficiently silenced by 76% and 75% using the targeting peptides Y and ME27 respectively. The MRTF protein expression was significantly decreased by the LYR nanoparticles. The non-PEGylated liposome formulations showed higher silencing efficiency than the cationic PEGylated formulations. The MRTF nanoparticles were also not cytotoxic at 50 nM siRNA concentration and prevented matrix contraction after a single transfection treatment.
Conclusions This is the first study to show that receptor-targeted liposome-peptide-siRNA nanoparticles represent an efficient and safe siRNA delivery system that could be used to prevent fibrosis after glaucoma surgery.

• 4226

Leuven Eye Study - Baseline and Methods

ABEGAO PINTO L (1), Willekens K (2), Van Keer K (2), Shibesh A (3), Vandewalle E (2), Molenberghs G (3), Stalmans I (2)
(1) Centro Hospitalar Lisboa Norte / Faculty of Medicine of Lisbon University, Department of Ophthalmology, Lisbon, Portugal
(2) University Hospitals Leuven, Ophthalmology, Leuven, Belgium
(3) University Hospitals Leuven, Bio-Statistics, Leuven, Belgium

Purpose Glaucoma is known to be associated with vascular dysfunction. However, integrating this knowledge in the clinical setting has been limited, considering the majority of vascular oriented studies have been either underpowered or only addressed a small segment of the vascular parameters in strictly selected patients. The Leuven Eye Study aims at bridging this gap by prospectively collecting the largest amount of vascular oriented data in a large real-life glaucoma clinic setting.
Methods Prospective, cross-sectional, case-control hospital-based study. Patients with primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), glaucoma suspect or ocular hypertension (OHT) and healthy volunteers were recruited. In addition to an ophthalmological examination, a vascular-oriented questionnaire was completed and ocular blood flow assessment (color Doppler imaging of retrobulbar vessels, retinal oximetry, dynamic contour tonometry, optical coherent tomography enhanced depth imaging of the choroid) was performed in each subject.
Results 620 subjects (297 male) were recruited between March and December 2013 (POAG: 214, NTG: 192; glaucoma suspect: 41; OHT: 27; healthy controls: 146). Mean age was 68,4±12,9 years. Other than IOP, there was no difference in demographic variables between glaucoma groups and healthy volunteers. Values for the ocular blood flow parameters are in line with the current literature.
Conclusions the Leuven Eye study stands as the largest clinical trial on ocular blood flow in glaucoma. The creation of this vast database may help integrate the vascular aspects of glaucoma into the clinical practice of glaucoma.

• 4227

Biomechanical properties of eyes with asymmetrical glaucoma defect

CELLINI M , GIZZI C , FINZI A , CAMPOS E C
Ophthalmology Service, 1.Department of Specialized- Diagnostic and Experimental Medicine, Bologna, Italy

Purpose To evaluate biomechanical properties in eyes of patients affected by primary open angle glaucoma (POAG) with marked asymmetrical defects by means of Ocular Response Analyzer (ORA) and Spectral Domain OCT with Enhanced Depth Imaging (EDI SD-OCT) function.
Methods We studied 20 patients (mean age: 56±12) with asymmetrical POAG. One eye was classified as mild glaucoma (MG) and the sound eye as severe glaucoma (SG) by visual field indexes: MD -4.21±1.51 vs -16.56±5.76 dB; p=0.011 and PSD 3.54±0.87 vs 10.95±3.51 dB; p=0.007. An EDI SD-OCT centered on the optic nerve head and an ORA examination were performed on each eye of every subject before and during a IOP increase of 12.5±2.1 mm/Hg induced by a compression of the globe with an ophthalmodinamometer. Corneal histeresis (CH), corneal resistence factor (CRF) and laminar displacement (LD) were statistically analyzed by Wilcoxon's rank sum test and Spearman's correlation test considering significant a p<0.05.
Results After IOP increase we found a decrease of CH: 9.3±3.66 vs 6.92±3.04 mm/Hg; p=0.012 in SG and 8.62±2.16 vs 7.23±2.29 mm/Hg; p=0.176 in MG. CRF instead increase: 8.61±2.31 vs 12.38±3.65 mm/Hg; p=0.016 in SG and 9.02±1.48 vs 12.22±5.68 mm/Hg; p=0.041 in MG. LD was positive in MD: 29.08±19.28 um and negative in AG-6.58±16.09 um. In AG eyes we found a correlation between LD and CRF (r=-0.658; p=0.019) and between LD and Scleral Rigidity (r=-0.693; p=0.012).
Conclusions This study demonstrates that in asymmetrical glaucoma the IOP increase changes the eye biomechanics with stiffening of the eye structures that involves not only the lamina cribrosa but also the corneal tissue.

• 4228

Multicenter Clinical Trial of High-Intensity Focused Ultrasound Treatment in Glaucoma Patients without Previous Filtering Surgery

APTEL F (1), Denis P (2), Rouland J F (3), Renard J P (4), Bron A M (5)
(1) University Hospital of Grenoble, Department of Ophthalmology, Grenoble, France
(2) Hospices Civils de Lyon, Department of Ophthalmology, Lyon, France
(3) Hôpital Claude Huriez- CHRU de Lille, Department of Ophthalmology, Lille, France
(4) HIA du Val de Grace, Department of Ophthalmology, Paris, France
(5) CHU Dijon, Department of Ophthalmology, Dijon, France

Purpose To evaluate the efficacy and safety of the ultrasonic circular cyclocoagulation procedure in patients with open-angle glaucoma naïve of previous filtering surgery.
Methods Prospective non-comparative interventional clinical study conducted in five French University Hospitals. Thirty eyes of 30 patients with open-angle glaucoma, intraocular pressure (IOP) > 21 mmHg and with no previous filtering glaucoma surgeries were sonicated with a probe comprising six piezoelectric transducers. The six transducers were activated with a 6-s exposure time. Complete ophthalmic examinations were performed before the procedure and at 1 day, 1 week, 1, 2, 3, 6 and 12 months after the procedure. Primary outcomes were surgical success (defined as IOP reduction from baseline ≥ 20% and IOP > 5 mmHg with possible retreatment and without hypotensive medication adjunction) at the last follow-up visit and vision-threatening complications. Secondary outcomes were mean IOP at each follow-up visit compared to baseline, medication use, complications and retreatments.
Results IOP was significantly reduced (p<0.05) from a mean preoperative value of 28.2 ± 7.2 mmHg (n = 3.6 hypotensive medications) to 19.6 ± 7.9 mmHg at 12 months (n = 3.1 hypotensive medications and n = 1.1 procedures) (mean IOP reduction of 30%). Success was achieved in 63% of eyes (19/30) at 12 months (mean IOP reduction of 37% in these eyes). No major intra- or postoperative complications occurred.
Conclusions The ultrasonic circular cyclocoagulation procedure seems to be an effective and well-tolerated method to reduce IOP in patients with open-angle glaucoma without previous filtering surgery.

Commercial interest

• 4231

Corneal neovascularization: a translational perspective

FERRARI G
Milan, Italy,

Development of corneal neovascularization (CNV) is a common finding in a number of disorders affecting the ocular surface. The role of infiltrating inflammatory cells, and specifically macrophages, is well described and associated with the development of CNV. Although CNV is commonly regarded as an ominous clinical sign due to its common association with vision reduction, the growth of neovessels can also beneficial in some instances. For example, CNV helps recruiting cellular immunity and provides protection against ocular perforation in corneal infections. Hence, avascularity of the cornea, constantly exposed to the outer environment, is the result of an evolutionary compromise between a prompt and effective reaction to aggression from the outside and the avoidance of corneal opacification. Specifically, the absence of vessels in the normal cornea is generally considered the result of the predominance of anti-angiogenic over pro-angiogenic factors. In this paper, we suggest a novel mechanism regulating corneal avascularity and its switch to corneal neovascularization. Potential translational implications are also discussed.

• 4232

New perspectives in dry eye treatment

BARABINO S
University of Genoa, Clinica Oculistica, Genoa, Italy

Dry eye syndrome is a chronic disease that affects tens of millions of people worldwide, representing one of the most common ocular pathologies. The traditional approach to treat dry eye focuses on tear replacement with artificial tears or on conserving the patients' tears through occlusion of the tear drainage system, but these therapies can be considered palliative in that they do not address the pathogenic process that underlines the disease. This presentation will discuss the recent major advances in managing dry eye patients, including a new algorithm of therapy and new technologies that can help in monitoring the effect of treatments, and the results of studies with new molecules-ocular surface modulators- aimed at restore the tear film-ocular surface epithelia equilibrium.

• 4233

New developments in DMEK and endothelial cell therapy

FUCHSLUGER T
University Hospital Erlangen, Dept. of Ophthalmology, Erlangen, Germany

This presentation provides an overview of current and future developments in endothelial transplantation. Aspects of clinical innovation, pharmacological options and developments in the pipeline are presented.

• 4234

Non-antagonistic influences of intrastromal corneal ring on primary human microvascular endothelial cells from adult donors in a tissue culture system

STORSBERG J (1), Träg S (2), Messner A (2), Rehfeldt S (1), Klöpzig S (1), Jentzen V (1), Bohrisch J (1), Schmidt C (1)
(1) Fraunhofer IAP, Functional Medical Polymers, Potsdam, Germany
(2) HumanOptics AG, Research, Erlangen, Germany

Purpose: Insertion of the Krumeich corneal intrastromal ring (KR) appears to restrict superficial vascularization of donor corneal tissue. The purpose of this report was to determine cytotoxic effects of the KR using tissue culture of primary HMVEC.
Methods: Soluble growth medium extracts of individual components of the KR alloy were prepared and HMVEC cells were exposed to these extracts in triplicates for one day and a subsequent MTT assay. Furthermore, HMVEC were grown for five days onto either KR or polypropylene discs coated with individual components of the KR alloy, followed by staining with FDA/PI.
Results: MTT assays revealed that higher doses of extracts appeared to reduce the viability of HMVEC, while highly diluted extracts of Mo powder appeared to increase the metabolic activity of HMVEC. FDA/PI staining showed few live HMVEC on either Co or Mo-coated propylene discs, compared to the respective Ti and Cr counterparts. Viable HMVEC appear attached to the KR after a five day incubation period.
Conclusion: The Krumeich ring does not appear to exert measurable cytotoxic effects in our chosen assay system. High dilutions of Mo powder extracts appear to increase the metabolic activity of HMVEC.

• 4235

Information technology in ophthalmology. www.retinarisk.com

STEFANSSON E

University of Iceland, Reykjavik, Iceland

A huge amount of epidemiological data has been accumulated in ophthalmology as in other fields of medicine. The use of these data in health care tends to be simplistic and makes too little use of information technology and mathematics. We have used published reports on risk factors for progression of diabetic retinopathy, DR, to create an algorithm that predicts an individual´s risk of sight threatening DR. The prediction is based on the type and duration of diabetes mellitus, blood glucose and pressure, DR stage and gender; see www.retinarisk.com. It predicts 80% of the risk as seen as the area-under-curve on ROC plots. The software provides individual predictions based on these risk factors. It educates the patient about DR risk and allows estimation of the effect of improving risk factors such as blood glucose. It has motivational and educational value. Current norm in DR screening is annual examination (every other year for eyes without DR). Individualized risk assessment allows individualized determination of the frequency of eye screening. High risk eyes are screened more frequently and low risk eyes less frequently. This improves safety for the high risk eyes and saves on resources for the low risk eyes. When compared with annual screening this provides cost savings of about 50%.

• 4241

Integrated multi-omic analysis of human retinoblastoma identifies novel regulatory networks

SURESHBABU V (1), Mallipatna A (1), Guha N (2), SA D (2), Lateef S (2), Gundimeda S (2), Padmanabhan A (2), Shetty R (1), Ghosh A (1)
(1) NARAYANA NETHRALAYA FOUNDATION, GROW RESEARCH LABORATORY, BANGALORE, India
(2) Agilent Technologies India, LSCI, Bangalore, India

Purpose
a) Elucidate the differential expression profiles in tumors & invitro models
b) Identify novel signal transductions and key regulators in retinoblastoma
Methods Institutional Ethics Committee approval was obtained prior to sample collection. We used enucleated eyes of 9 case samples & 2 pediatric deceased controls. Total RNA was extracted from tumor & control retina samples for mRNA, miRNA microarray and RT-PCR for gene expression validation in tumors. Patient's aqueous, vitreous and tears were analysed by LC/GC-MS to validate metabolic profiles of retinoblastoma. RB invitro models were developed using cell lines MCF-7, Y79 & Weri , for correlative analysis with patient data
Results We identified 8 key differentially regulated pathways and genes, from the mRNA expression profile. The miRNA expression profile helps to discover 18 novel miRNAs which regulates key target genes identified by mRNA microarrays. Multi- omics analysis of metabolomics data with gene expression profiles revealed key regulators belonging to common pathways. RB1 silenced MCF-7 showed significant overlap in key cell cycle genes & RB1 complemented retinoblastoma cell line Y79 mimics gain of function of molecular signature
Conclusions Overall, the study identifies molecular mechanisms driving retinoblastoma and provides an in-vitro modelling framework for further studies

• 4242

Anatomic features of choroidal naevi: Swept-source optical coherence tomography vs Enhanced depth imaging tomography. Preliminary results in 31 patients

PAPASTEFANOU V, Vázquez-Alfageme C, Xirou T, Degli-Esposti S, Patel P, Sagoo M S
Moorfields Eye Hospital, Medical retina, London, United Kingdom

Purpose To assess the anatomic retinal and choroidal features of choroidal naevi using swept-source optical coherence tomography (SS-OCT) and enhanced-depth optical coherence tomography (EDI-OCT).
Methods DESIGN: Observational case series. METHODS: Patients with choroidal lesions underwent clinical examination, B-scan ultrasound and imaging with SS-OCT and EDI-OCT. Location, dimensions, clinical and OCT retinal and choroidal features were recorded. Descriptive statistics were used.
Results Case series included 31 patients. 27/31 naevi imaged were melanotic and 4/31 amelanotic with a an overall median thickness of 0.7 mm. Naevus configuration was plateau in 17/31 cases, dome in 10/31 cases and mixed in 4/31 cases. RPE and photoreceptor layer disruption were noted in 14/31 cases and 13/31 had no retinal changes. Subretinal fluid was noted in 6/31 cases. Bruch`s membrane was found intact in 26/31 cases on both modalities. Intrinsic hyperreflectivity was noted in 29/31 cases on EDI-OCT and 30/31 cases on SS-OCT with less optical shadowing. The posterior margin of the naevus was visualized in 11/31 cases with SS-OCT and in 6/31 cases with EDI-OCT. Intratumour vessels were visualized in 28/31 cases with SS-OCT and 23/31 cases with EDI-OCT. For both modalities choriocapillaris appeared compressed and abnormal in 20/31 cases.
Conclusions These preliminary results indicate that imaging of choroidal naevi with SS-OCT enables better visualization of intratumour vessels and the posterior margin.

• 4243

Human choroidal nevi histopathology revisited

MADIGAN M C (1), Vader M (2), Ton H (1), Van der Velden P (2), Jager M J (2)
(1) University of NSW, Optometry and Vision Science and Save Sight Institute University of Sydney, Sydney NSW, Australia
(2) Leiden University Medical Centre, Ophthalmology, Leiden, The Netherlands

Purpose Choroidal nevi are relatively common lesions seen in normally asymptomatic eyes. They show low potential for progression to melanoma but may produce visual effects depending on location. We investigated vasculature and macrophages in pigmented choroidal nevi using histopathology and immunohistochemistry.
Methods 340 fixed post mortem adult human eyes with no history of choroidal melanoma were examined. Paraffin sections of eyes were subsequently cut, stained with hematoxylin & eosin or Periodic acid Schiff reagent and histopathology examined. We assessed localisation and distribution of macrophages immunolabelled with CD163 or CD68 antibodies.
Results Thirteen eyes (aged 54 to 90 years) with 16 pigmented lesions were found. Of these, 15/16 lesions occurred within the posterior pole region. H&E and PAS staining confirmed pigmented choroidal nevi, with a diameter of 1.5 to 6.8mm, and thickness <1.5mm. Lesions were located at varying depths within the choroid, comprised of densely pigmented nevi cells, and with a predominantly oval or dome shape (15/16). Overlying drusen were observed for 8/16 nevi. Large choroidal vessels bordered 11/16 nevi, and normal vessels were seen within nevi, however no microvascular patterns typically associated with melanoma were observed. Larger nevi located just beneath Bruch's membrane were more often associated with choriocapillaris (CC) thinning and RPE disruption. Nevus cells were seen within the CC pillars, abutting Bruch's membrane. Compared to surrounding choroid, numerous CD163+ and CD68+ macrophages (CD163+ > CD68+) were localised within and around nevi, often associated with vessels.
Conclusions These findings indicate that choroidal nevi can affect normal choroidal vessels including CC integrity. Nevi also share some histopathological characteristics with melanoma, including infiltrating macrophages.

• 4244

The Liverpool Uveal Melanoma Prognosticator Online (LUMPO) for prognosing metastasis free survival in the absence of cytogenetic data after ruthenium brachytherapy for uveal melanoma

ROSPOND-KUBIAK I, Wroblewska-Zierhoffer M, Twardosz-Pawlik H, Kociecki J
Poznan University of Medical Sciences, Department of Ophthalmology, Poznan, Poland

Purpose Liverpool Uveal Melanoma Prognosticator Online (LUMPO) is a tool developed by Eleuteri ***et al.*** to establish the prognosis for uveal melanoma patients according to the initial tumour characteristics and cytogenetic data. It has been validated with two separate cohorts of patients in United Kingdom and more recently in US. The aim of this study was to test the prognosticator in a homogenous group of patients treated with with ruthenium brachytherapy where genetic analysis was not performed.
Methods Material and methods: The records of the patients treated with ruthenium brachytherapy for uveal melanoma at the Department of Ophthalmology, Poznan University of Medical Sciences between 1994 and 2012 were retrospectively reviewed. The probability of 3-year, 5-year and 10-year metastasis free survival were obtained for each patient using the LUMPO accessed online and then compared with the existing follow-up data.
Results We identified 102 patients, 60 women, 42 men in a mean age of 59 years. Mean largest basal diameter of the treated tumours was 9.29 (range: 4.04 – 18.9)mm, mean tumour thickness: 4.8 (range: 2.6-7.01) mm. Follow-up ranged from 3 to 22 years, mean: 7,55 years. 33 patients died, 18 (17,65%) out of metastatic disease. The metastatic death was not related to patients' age (p=0,6866), LBD (p=0,3049) or tumour thickness (p=0,7063) alone. The probability of metastasis free survival according to LUMPO was significantly lower for the metastatic group comparing to the surviving group at 3 years (p=0,0017) and 5 years post treatment (p=0,0001).
Conclusions Conclusions: LUMPO is a useful tool for prognostication for uveal melanoma patients. However, the use of cytogenetic data makes this prognosis more precise.

• 4245

Immunohistochemical characterization of a retinal hamartoma

VAN GINDERDEUREN R , Stalmans P
UZ St. Rafael, Ophthalmology, Leuven, Belgium

Purpose To describe the immunohistochemical features of a retinal hamartoma.
Methods A 38 y old man was referred for preretinal fibrosis on his right eye. There was loss of vision for more than 8 years with metamorphopsia. The left eye was normal. Oct imaging showed an epiretinal fibrosis with extensive macular oedema. A 27Gauge vitrectomy was performed. The lamina limitans interna (ilm) was peeled after staining with Membrane Blue Dual and sent for histopathology.
Results After removal the epiretinal membrane was immediately fixed with PreservCyt® in a ThinPrep® container. The specimen was routinely processed by the Cellient® embedding system. Microscopy showed a folded Pas positive membrane, recognized as ilm with on one side some glial remnants and on the other side a cuboidal non-pigmented epithelium. The glial remnants stained with glial fibrillar protein (gfap), the epithelium with prekeratin AE1/AE3. CD 34 stain was positive in preretinal capillaries.
Conclusions A strange retinal fibrosis consisted of glial tissue and a row of superficial cuboidal non-pigmented epithelium cells. This kind of hamartoma with immunohistological description was never investigated or published.

• 4251

RNA sequencing in keratoconus: unraveling the molecular pathways

VALGAEREN H
Center of Medical Genetics, Edegem, Belgium

Abstract not provided

• 4252

Development of micro needle for retinal vein cannulation

WILLEKENS K
UZ Leuven, Ophthalmology, Leuven, Belgium

Abstract not provided

• 4253

Serine proteases as potential therapeutic targets for ocular inflammation and dry eye syndrome

JOOSSEN C
Laboratory for Microbiology, Parasitology and Hygiene, University of Antwerp

Abstract not provided

• 4254

Automatic detection of early keratoconus using topography and biomechanical measurements in the corneal horizontal and vertical axis

RUIZ HILDALGO I
University of Antwerp, Wilrijk, Belgium

Abstract not provided

• 4255

Tissue engineering in ophthalmology: regenerating the anterior cornea using self-aligning recombinant human collagen nanoscaffolds and corneal epithelial stem cells

HAAGDORENS M
University of Antwerp, Wilrijk, Belgium

Abstract not provided

• 4256

In vitro functional characterisation of tissue engineered corneal endothelial grafts

VAN DEN BOGERD B
University of Antwerp, Wilrijk, Belgium

Abstract not provided

• 4257

An in vitro and ex vivo study into the role of Müller cells in nanoparticle-based retinal gene therapy after intravitreal injection

PEYNSHAERT K
University of Ghent, Ghent, Belgium

Abstract not provided

• 4258

Detailed charactization of structural, functional and behavioral changes in a laser-induced mouse model for glaucoma

GEERAERTS E
University of Leuven, Leuven, Belgium

Abstract not provided

• 4261

Pathology of high myopia

OHNO-MATSUI K
Ophthalmology and Visual Science, Tokyo Medical and Dental University Yushima, Bunkyo-ku

Abstract not provided

• 4262

Epidemiology and the protective effects of time outdoors

MORGAN I (1), Rose K (2)
(1) Australian National University, Research School of Biology, Canberra, Australia
(2) University of Techology Sydney, Orthoptics, Sydney, Australia

There is a major epidemic of myopia in developed countries in East and Southeast Asia, where the prevalence of myopia is now 80-90% in those completing secondary school. More importantly, the prevalence of high myopia is now 15-20%, exposing the future adult population to a much increased risk of pathological myopia and vision loss. In Europe and North America, the prevalence of myopia is also increasing, and now appears to be of the order of 40-60%. Genetic change cannot provide an explanation of these increases, which must involve changes in environmental exposures. The two key factors appear to be increasingly intensive education, with study pressures extending to increased homework loads and extensive use of tutorial colleges after school hours. The other environmental factor at work is the amount of time that children spend outdoors, with increasing amounts of time outdoors protecting from the onset of myopia. The time spent outdoors by children is particularly low in East and Southeast Asia, and two clinical trials have now shown significant delays to the onset of myopia by increasing the amount of time that children spend outside at school. Similar interventions could help to control myopia in other parts of the world.

• 4263

Optical reduction of peripheral hyperopic defocus

TORII H, Negishi K , Tsubota K
Keio University School of Medicine, Ophthalmology, Tokyo, Japan

Purpose: To discuss the effectiveness of optical reduction of peripheral hyperopic defocus in preventing progression of myopia.
Methods: The relationship between reducing peripheral hyperopic defocus and slowing progression of myopia has been discussed with regard to glasses, contact lenses, and orthokeratology. Previous studies on optical reduction of peripheral hyperopic defocus mainly in Japan will be presented. We performed a prospective, randomized, double-blind clinical trial using a questionnaire to compare myopic progression between a single-vision lens and a lens that reduces peripheral hyperopic defocus. This study is part of a multicenter trial in Japan and the results of our institute will be presented.
Results: Many clinical trials have suggested that reducing peripheral hyperopic defocus possibly retards progression of myopia. Outdoor activity is an evidence-based environmental factor that protects against myopia; our data also show the importance of outdoor activities for preventing progression of myopia.
Conclusion: Not only reducing peripheral hyperopic defocus but also environmental factors such as outdoor activity is important to retard myopia. A greater number of eyes should be evaluated in future studies.

• 4264

Atropine treatment

GRZYBOWSKI A
Poznan City Hospital, Dept of Ophthalmology, Poznan, Poland

In the last years, there has been a marked increase in the prevalence of high myopia in younger generations in developed countries in East and Southeast Asia, and there are signs of similar, but less pronounced increases in North America and Europe. In some parts of the world, 70-90% of children completing high schools are now myopic, and as many as 20% may be highly myopic. Topical Atropine have been quite extensively used in clinical practice in Asian countries, and recent reports suggest that low concentrated atropine, which has less severe side-effects, is also effective. The beginning of an invasive treatment such as atropine drops, even at low doses, requires careful consideration of the risk of myopic progression. The current literature relevant to the prevention of myopic progression with atropine drops is reviewed.

• 4265

5. 7-methylxanthine treatment

TRIER K

Trier Research Laboratories, Clinic, Hellerup, Denmark

Several studies have shown that the caffeine metabolite 7-methylxanthine (7-mx) prevents myopia and eye elongation in animals subjected to form deprivation. A randomized, placebo-controlled clinical trial with up to 8 years of follow-up including a total of 750 myopic children aged 7-18 years has demonstrated that 7-mx is safe and without side effects. In the age-group 8-15 years the myopia progression and the corresponding eye elongation is reduced by around 60 % with one tablet of 400 mg 7-mx twice per day. The efficacy would probably improve if the serum concentration of 7-mx could be kept more constant by means of a sustained release formulation. 7-mx appears to work by blocking adenosine receptors in the posterior part of the eye and increasing the concentration of scleral collagen. The accelerated myopia progression found in periods with low ambient lighting may be related to increased accumulation of adenosine in the retina or retinal pigment epithelium. Thus, hypothetically, 7-mx offsets the myopia-enhancing effects of low ambient lighting.

• 4266

Defocus Incorporated Soft Contact (DISC) lens

LAM C S, Tang W C, To C H

The Hong Kong Polytechnic University, Centre for Myopia Research- School of Optometry, Kowloon, Hong Kong- China

Purpose: DISC lens is a concentric bifocal contact lens, combining myopia correction and constant myopic defocus. We investigate the effects of wearing time, eye dominance and pupil size on myopia control with DISC lens.

Methods: 128 children completed a 2-year double masked randomized clinical trial of myopic control (65 in DISC lens and 63 in single vision contact lenses). Refraction and axial length were measured with cylcoplegic autorefraction and IOL Master. Ocular dominance was determined with the Miles and Porta tests. Pupil images were captured by EAS-1000 (Nidek) for children wearing the DISC lens, the area ratio of the two optical zones was then calculated.

Results: Those who have worn the DISC lens for 8 hours daily reached a 60% reduction in myopia progression. There were no significant differences in eye dominance with refractive changes (t-test), association between myopic progression (chi-square test) and correlation between the zones ratio at pupil and myopic progression (multiple linear regression analysis).

Conclusions: We identified a dosage effect on the DISC lens in slowing myopia progression. Ocular dominance and pupil size do not have any effect on myopia control using the DISC lens.

• 4271

The Silk-protein Sericin Induces Rapid Melanization of Cultured Retinal Pigment Epithelial Cells by Activating the NF-κB Pathway

PASOVIC L, Utheim T P, Reppe S, Lyberg T, Olstad O K, Eidet J R
Oslo University Hospital, Department of Medical Biochemistry, Oslo, Norway

Purpose Restoration of the retinal pigment epithelial (RPE) cells to prevent further loss of vision in patients suffering from age-related macular degeneration represents one of the most promising novel treatment modalities in regenerative medicine. Development of RPE transplants in the laboratory, however, is a lengthy process requiring up to 3 months of cell differentiation. We explored whether the silk protein sericin can be used as a culture medium supplement to induce differentiation of human RPE.
Methods Microarray analysis determined the expression of RPE-associated transcripts in control cultures and cultures supplemented with sericin. Quantitative immunofluorescence (QIM), spectrophotometry and transmission electron microscopy (TEM) validated the findings.
Results Sericin supplementation increased the expression of RPE-associated transcripts (RPE65 and CRALBP). The NF-kB pathway was identified as one of the top sericin-induced regulators. Increased levels of RPE-associated proteins (including CRALB and the pigment melanin) in the sericin-supplemented cultures were confirmed by QIM, spectrophotometry and TEM. Sericin supplementation also increased cell survival following serum starvation. Inclusion of NF-kB agonists and antagonists in the culture medium showed that activation of the NF-kB pathway appears to be necessary, but not sufficient, for sericin-induced RPE pigmentation.
Conclusions Sericin promotes pigmentation of cultured human RPE by activating the NF-kB pathway.

• 4272

Cell penetrating peptide constructs: A novel drug delivery to the eye

SCOTT R (1), Hill L (2), De Cogan F (2), O'Neill J (2), Logan A (2)
(1) *Birmingham and Midland Eye Centre, Ophthalmology, Birmingham, United Kingdom*
(2) *University of Birmingham, School of Clinical and Experimental Medicine, Birmingham, United Kingdom*

Purpose In neovascular age-related macular degeneration (AMD) blood vessels grow from the choroid under the retina causing macular damage and scarring. Anti-VEGF drugs such as, ranibizumab or aflibercept are administered by intravitreal injection to treat AMD related neovascularisation, We present a novel cell-penetrating peptide construct (CPPC) topical delivery system to deliver Ranibizumab to the retina using drops.
Methods Peptides were produced using standard solid-phase peptide synthesis. They were analysed using mass spectrometry and purified using high-pressure liquid chromatography and used at a purity of >95 %. CPPC were built around the drugs by vortexing for 10 seconds and incubating at room temperature. Drug delivery experiments were carried out ex-vivo in freshly enucleated porcine eyes. In vivo experiments were carried out in C57 mice. Mice had a three 100 µm laser burns to the choroid to model neo-vascularisation in AMD. They then received a single intravitreal injection of an anti-VEGF agent or CPPC/Ranibizumab applied topically to the conjunctival sac twice daily for the duration of the experiment. Choroidal neovascularisation was measured by immunohistochemistry.
Results Ex vivo delivery to enucleated porcine eyes demonstrated that a single 60 µL drop could deliver 1.7 ± 0.4 µg/mL of ranibizumab to the vitreous cavity. Confocal images of immunohistochemistry on retinal wholemounts showed ranibizumab within the retina. In vivo experiments demonstrated both intravitreal injection and CPPC bound Ranibizumab reduced neovascularisation equally, compared to controls
Conclusions CPPC can be used topically to deliver therapeutic levels of Ranibizumab to the posterior segment.

• 4273

The improvement of Spoke-Wheel pattern foveoschisis in a patient with X-linked retinoschisis treated with topical dorzolamide observed by high-resolution adaptive optics camera

GOCHO K (1), Akeo K (1), Kameya S (1), Yamaki K (1), Mizota A (2), Takahashi H (3)
(1) *Nippon Medical School Chiba Hokusoh Hosp, Ophthalmology, Inzai, Japan*
(2) *Teikyo University School of Medicine, Ophthalmology, Tokyo, Japan*
(3) *Nippon Medical School, Ophthalmology, Tokyo, Japan*

Purpose The purpose of the study is to report the improvement of foveomacular cavities and spoke-wheel pattern retinoschisis observed by spectral-domain optical coherence topmography (SD-OCT) and high-resolution adaptive optics fundus camera in a patient with XLRS treated with topical dorzolamide.
Methods A 42 y.o. man with XLRS underwent detailed ophthalmic examinations. A mutation of RS1 gene was detected earlier. The ophthalmological examinations included SD-OCT, fundus autofluorescence imaging, and full-field and multifocal ERGs. Fundus images with microscopic resolution were obtained using the AO retinal camera (rtx1, Imagine Eyes, France). He was treated with topical dorzolamide three times a day. Transverse foveomacular cavities was observed by SD-OCT and the en-face images of spoke-wheel pattern foveoschisis was observed by AO fundus camera during a follow-up period.
Results His BCVA was 0.15 in the right eye and 0.3 in the left eye. The right eye showed atrophic macular degeneration and left eye showed spoke-wheel pattern foveoschisis. SD-OCT showed the thinning of retinal thickness in the right eye and cystoid foveoschisis in the left eye. AO images showed spoke-wheel pattern retinal fold in the left eye. The spoke-wheel pattern in AO was sharper compared to the images obtained by fundus photography and autofluorescence imaging. After 14 month of treatment with topical dorzolamid, improvement of foveomacular cavities in SD-OCT was observed. The spoke-wheel pattern retinal fold in AO become obscure after treatment, however still detectable even after foveomacular cavities in SD-OCT was almost disappeared.
Conclusions AO imaging showed detailed microstructure of spoke-wheel pattern foveoschisis and their improvement during a follow-up period. AO imaging may be helpful in clarifying the pathology of the foveoschisis in XLRS.

• 4274

Concordance between ophtalmologists and paramedical professionals in screening for retinal abnormalities with ultrawide field imaging

DURBANT E (1), Vardi K (1), Bordet J (1), Barbe C (2), Garcia T (1), Angioi K (3), Arndt C (1)
(1) *Hopital Robert Debré, Ophtalmologie, Reims, France*
(2) *Hopital Robert Debré, Unité d'aide méthodologique, Reims, France*
(3) *Hôpital de Brabois, Ophtalmologie, Nancy, France*

Purpose The decreasing number of ophthalmologists leads to evaluate preliminary screening procedures performed by paramedical professionnals. The ultrawide field retinography is a recent technique allowing to obtain, simply and reproducibly, central and peripheral retinal images with or without mydriasis.The main objective of this study was to evaluate the diagnostic agreement between the reading of the ultra wide field images by a paramedical professional compared to a doctor.
Methods A prospective diagnostic two-center study was performed in the ophthalmological departments of two University Hospitals (Reims and Nancy) including all patients eligible in an outpatient clinic. For each patient, an ultra wide field retinography was taken with an Optomap (Optos) and an image analysis was performed by both a paramedical professional and an ophthalmologist. The agreement (kappa coefficient) between both image readings was evaluated.
Results 901 patients were included from July 2011 to November 2014. A good agreement was found between paramedical professionals and ophthalmologists for the global analysis (normal or abnormal image) (k = 0.62 [0.59 to 0.66]).This good concordance was also found for retinal lesions, including the macula (k = 0.70 [0.66 to 0.73]) and particularly for the analysis of red lesions such as hemorrhages, dilated veins and retinal detachment. However, the agreement was poor for optic disc analysis (k = 0.38 [0.32 to 0.44]).
Conclusions In screening procedures, paramedical professionals were able to identify retinal abnormalities on ultra wide field image in a significant number of cases. However, the correct identification of optic disc abnormalities was poor.

• 4275

Research on ophthalmic examination apparatus to diagnose multiple diseases which result in loss of eyesight

SUZUKI N (1), Yamane K (2)

(1) National Institute of Technology- Numazu College, Department of Mechanical Engineering, Numazu, Japan

(2) Hiroshima University, Department of Ophthalmology and Visual Science, Hiroshima, Japan

Purpose In Japan, the four major diseases which cause the loss of eyesight are glaucoma, diabetic retinopathy, pigmentary retinal degeneration, and age-related macular degeneration. We developed an ophthalmic examination apparatus having the functions of fundus camera, microperimetry, electroretinography, and visual acuity testing, designed to diagnose multiple diseases which result in loss of eyesight.

Methods We constructed the experimental device with the same optical system as a fundus camera. The device has previously been used for research involving the diagnosis of early diabetic retionopathy. The microperimetry optical system was calculated using the optical engineering software OpTalix-LT and was added to the experimental device. In addition, we added an Edmund infrared camera EO-0413, a lens with a focal length of 25 mm, a 45-degree cold mirror, a 12V/50W halogen lamp, and an 8-inch monitor. The artificial eye consists of a plane-convex lens, a black spacer, and a hemispherical cup. A small section paper was stuck on the bottom of the hemispherical cup. The artificial eye was photographed for 10 times using the experimental device. The software was generated to show the examination target on the monitor and save examination data using C++Builder XE6.

Results The device was able to show the retinal fundus on the monitor, at a length and width of 1 mm with a resolution of 63.25 ± 3.51 and 64.13 ± 6.10 pixels, respectively.

Conclusions We succeeded in adding the function of microperimetry to the experimental ophthalmic device.

• 4411

Safety and effectiveness of intravitreal injections in the silicone oil-filled eye

ASCASO F (1,2,3)
(1) Hospital Clínico Universitario "Lozano Blesa", Medical & Surgical Retina Unit-Department of Ophthalmology, Zaragoza, Spain
(2) Instituto de Investigación Sanitaria de Aragón, IIS Aragón, Zaragoza, Spain
(3) School of Medicine- University of Zaragoza, Department of Surgery, Zaragoza, Spain

Silicone oil (SiO) use has gained acceptance in providing an effective long-term tamponade in retinal detachments complicated with proliferative vitreorretinopathy. As the use of injectable therapeutics grows and their indications broaden, it is important to know the safety and effectiveness of intravitreal injections in eyes containing SiO as a vitreous substitute. Thus, whereas intrasilicone injection of bevacizumab is safe and effective to treat patients with iris neovascularization after vitrectomy for advanced proliferative diabetic retinopathy, triamcinolone injection into the SiO-filled eye is inadequate given that it might significantly increase the IOP due to volume expansion. Furthermore, triamcinolone may not dissolve in SiO, preventing its diffusion to the macula surface, and its whitish crystals might opacify the visual axis. Unlike intravitreal triamcinolone, the DEX implant causes minimal volume expansion and no media opacity. It is biodegradable and injected without surgery and thus also advantageous over the fluocinolone implant. Additional studies are necessary to better understand the pharmacodynamics of sustained-release drugs from devices implanted or inserted into eyes filled with SiO as vitreous substitute.

• 4412

Silicone oil use in trauma

WEINBERGER D
Tel Aviv, Israel,

The use of Silicone oil and PFCL tamponades following vitrectomy in Penetrating ocular trauma and perforating injuries are highly advantageous due to their chemical-physical properties which enables them to displace aqueous humor from the retinal surface and maintain the adhesion between retina and retinal pigment epithelium. There are different types of silicone oils to which their dynamics depends on the interaction between buoyancy, interfacial surface tension, and viscosity. Therefore, depending on the type of oil, a short- to long-term tamponade would be provided to the retina. It has been shown that silicone oils and PFCL were successfully used to minimize the risk of postoperative bleeding, maintain the retina attached, and avoid phthisis in cases of hypotony following severely traumatized eyes. However, as in any vitreoretinal surgery, complications may occur such as re-detachment and PVR under the oil, increased IOP and damage to the cornea and AC. Herein, we will discuss the use of different type of silicone oils and PFCL,s their advantages and disadvantages in the use of ocular trauma surgeries.

• 4413

Silicone oil-induced anterior segment complications

AVITABILE T
University of Catania, Catania, Italy

Abstract not provided

• 4414

Controversies on heavy SiO endotamponade

LE MER Y
Fondation Ophtalmologique A. de Rothschild, Service Pr Sahel, Paris, France

Silicone oil (SIO) is a useful tool, mainly in retinal detachment cases complicated with PVR or in some specific cases .
A limitation of the tamponade effect of is due to its specific gravity lighter than water which means that recurrences of PVR are always in the inferior retina because of gravity leaving some liquid under the oil bubble where proliferative agents may concentrate.
An answer to this was given by modifying the chemical compounds of SIO, adding different substances increasing the specific weight over that of water, thus introducing the "heavier than water" SIO. Five different products are available, Densiron and Oxane HD being the most used.
There is still a lot of controversies on heavy SIOs regarding their potential toxicity due to the additional compounds and the stability of the mixture, regarding the potential interaction when directly exchanged with PFCL.
In an unfinished prospective study comparing "classical" SIO and heavy ones, the interim analysis after one year follow up in PVR cases didn't find any advantage in the use of heavy SIO. These results seem to finally close the last controversy on their usefulness in this indication.
Nevertheless, heavy SIO keep perhaps some indications in specific cases.

• 4415

Complications after SiO removal

KIILGAARD J F

Rigshospitalet, Eye Dept., Copenhagen, Denmark

Abstract not provided

• 4416

Neuronal complications of intravitreal SiO

GRZYBOWSKI A

Poznan City Hospital, Dept of Ophthalmology, Poznan, Poland

Intraocular silicone oil (SiO) complications include keratopathy, glaucoma, cataract and subretinal migration of the oil droplets, and can also lead to a severe optic neuropathy caused by retrolaminar migration. Intracranial migration of the SiO through the optic nerve posterior to the lamina cribrosa to the optic chiasm and brain is, however, uncommon. The mechanism is still under debate. Moreover, central scotoma may develop in eyes with SiO not only at the time of oil removal, but also during the period of tamponade. This review summarizes our current understanding of the specific pathogenic mechanisms of intraocular SiO neuronal side effects, concluding that pre-existing glaucoma and optic nerve abnormalities are the main risk factors associated with this damage. In their absence, the risk of extraocular SiO penetration is so low that the use of SiO endotamponade in complex retinal detachment patients does not need to be modified. MRI images to assess extraocular SiO migration are only necessary in very few and special cases, such as patients with optic nerve abnormalities and glaucoma.

• 4421

Turn off the tap: Inflow surgery comes of age with ECP

BLOOM P (1), Clement C (2), Sharkawi E (3), Grieshaber M (4)
(1) Western Eye Hospital, Imperial College Ophthalmic Research Group, London, United Kingdom
(2) Sydney Eye Hospital, Glaucoma Department, Sydney, Australia
(3) Hôpital Ophtalmique Jules-Gonin, Unité du Glaucome, Lausanne, Switzerland
(4) Universitäts-Augenklinik Basel, Augenchirurgie, Basel, Switzerland

For almost 50 years, trabeculectomy has been considered the 'gold standard' procedure in the surgical management of the Glaucoma patient. The operation undoubtedly works well in many surgeons' hands, and over the last 20 years small changes in surgical technique have improved the safety profile of guarded sclerostomy. 'Tube' surgery has also long been widely advocated and debate rages about which of these two mainstream treatments should be the de facto surgery for glaucoma.
In a continued attempt to improve the surgical risk/benefit ratio, there have more recently been advocated other surgical glaucoma procedures, which may in time take on the mantle of 'standard of care'.
Our SIS presents a selection of these new treatments as a basis for a robust discussion of why and how we offer surgery to control our patients' disease with the ultimate aim of preserving their vision as effectively and safely as possible.

Commercial interest

• 4422

Back to the future: The return of angle surgery

SHARKAWI E
Jules Gonin Eye Hospital, Lausanne, Switzerland

Micro invasive glaucoma surgery (MIGS) claims extremely high safety profiles and is a rapidly expanding field. In this session we will examine the efficacy and safety of ab interno angle surgery, and outline surgical tips and methods to maximize trabecular outflow in open angle glaucomas. We will also explore how angle surgery may improve results in angle closure eyes, over phacoemulsification alone. MIGS healthcare costs are not insignificant and efficacy can be limited. We will therefore examine cost effectiveness and quality of life issues that are paramount in moving this field forward. MIGS will be compared to more invasive glaucoma surgical approaches and real world indications discussed.

• 4423

Down under the sclera: Deep sclerectomy

CLEMENT C
Gordon, Australia

Deep Sclerectomy is an ab externo glaucoma filtration technique that aims to lower intra-ocular pressure without the need for a penetrating incision into the eye. The potential benefits are significant intra-ocular pressure reduction with a different complication profile to that of trabeculectomy. Deep Sclerectomy is not used by many glaucoma services world wide due to factors including restricted training, fear of intra-operative complications, a perceived steep learning curve and a perception that deep sclerectomy is ineffective or less effective than trabeculectomy. This presentation aims to address these issues by presenting data on the efficacy and complication profile of deep sclerectomy along with strategies to learn a safe and effective technique in a short period of time.

• 4424

Coming full circle: Canal surgery with / without implants

GRIESHABER M
University of Basel, Ophthalmology, Basel, Switzerland

Canaloplasty, one of the latest ab externo, non-penetrating procedures in glaucoma, reduces intraocular pressure by targeting the pathologically high resistance to aqueous outflow and restoring the natural outflow system. After (circumferential) viscodilation of Schlemm's canal, a polypropylene suture is looped through the canal and tightened to distend the trabecular meshwork; alternatively a new device, the Stegmann Canal Expander is implanted. The main advantage of canaloplasty over fistulating trabeculectomy is the independence of a filtering bleb. Furthermore, there is no need for antimetabolites and needling procedures. Canaloplasty as a stand-alone procedure or combined cataract extraction is proven to be safe and efficient. Technically, the surgeon must understand and respect the microanatomy of the outflow system and the mechanics of the procedure itself. This presentation guides the surgeon through standard canaloplasty and the implantation of the Stegmann Canal Expander, highlights tips and pitfalls, and presents new clinical data.

• 4431

Indications, patient selection, pre- and postoperative patient care

SZENTMARY N
Saarland University, Homburg/Saar, Germany

First we discuss different principle options of correction for corneal astigmatism, e.g. posterior chamber IOLs, phakic IOLs, and add-on IOLs. Major indication and inclusion /exclusion criteria for patients are shown and an overview on actual toric lenses with technical specifications and correction range are provided. Thereafter, we focus especially on toric intraocular lens implantation following penetrating keratoplasty. We summarize how to counsel patients about treatment options, preoperative and postoperative care and how to prepare the eye for the surgery. At the end, the postoperative care, evaluation and management of complications are discussed.

• 4432

Instrument assisted diagnostics – biometry, topography and wave-front analysis

EPPIG T (1), Spira C (2), Seitz B (2), Szentmáry N (2,3), Langenbucher A (1)
(1) *Saarland University, Experimental Ophthalmology, Homburg, Germany*
(2) *Saarland University Medical Center, Department of Ophthalmology, Homburg, Germany*
(3) *Semmelweis University, Department of Ophthalmology, Budapest, Hungary*

Patient selection and planning implantation of a toric intraocular lens requires sophisticated measurement of ocular biometry in order to facilitate a valid calculation of the implant. Biometric measurements such as videokeratometry or corneal tomography, may also assist in qualifying patients for toric lens implantation, e.g. detecting keratoconus, pellucide marginal degeneration or other contraindications. Keratometers mostly provide simulated keratometry values, which do not always reflect the amount of the regular astigmatism that could be corrected by a toric intraocular lens. Therefore, it is mandatory to differentiate between regular and irregular components of corneal astigmatism. Axial length measurements require additional attention, especially when using ultrasound biometry. Wave-front analysis may advance assessment of centration and rotation errors of toric implants.

• 4433

How to calculate toric intraocular lenses in clinical practice?

LANGENBUCHER A (1), Szentmáry N (2,3), Seitz B (2), Spira C (2), Eppig T (1)
(1) *Saarland University, Experimental Ophthalmology, Homburg, Germany*
(2) *Saarland University Medical Center, Department of Ophthalmology, Homburg, Germany*
(3) *Semmelweis University, Department of Ophthalmology, Budapest, Hungary*

There are several options for calculation of toric intraocular lenses, some are based on the classical intraocular lens calculation formulas and others utilize paraxial or numerical ray tracing techniques. Most online calculators use a two-step system based on precalculated data for the equivalent monofocal lens. Other methods calculate intraocular lens power separately for both cardinal meridians. Advanced methods directly calculate spherocylindrical power by matrix or ray tracing techniques. Especially when considering superposition of regular and irregular astigmatic components, postoperative implant rotation or anisometropia and aniseikonia, the classical formula approach might be inadequate for estimating toric intraocular lens power. Therefore surgeons dealing with toric intraocular lenses require deeper knowledge on advanced calculation techniques to improve patient satisfaction.

• 4434

Intraoperative optical coherence tomography (iOCT) in toric IOL implantation.

WYLEGALA E
Ophthalmology Clinic, Railway Hospital, Katowice, Poland

The effectiveness of the correction of astigmatism depends on the accuracy of the IOL position in the lens capsule. Removal of viscoelastic from the bag and the right IOL centration have a direct impact on the effectiveness of this IOL. Intraoperative use of OCT in real time (RESCAN 700 Zeiss) allows the evaluation of IOL in the bag position. iOCT plays role in the estimation of the distance from the posterior capsule of the lens. The use of iOCT allows to achieve an improved surgical results in patients with cataract and coexisting astigmatism.

• 4435

Surgical aspects of toric lens implantation, from perioperative marking to axis re-adjustment

BARRAQUER R I
Barraquer Institute, Barcelona, Spain

Which toric lens model is suitable for my patient? Which marking methods are available, what are the differences and which ones are suitable for toric lenses? How to assure that the lens will be properly implanted (centration, rotation and complication management)? A short overview on latest technology in surgical guidance systems.

• 4441

Correlation between radiation dose and damage to optic disc and macula in eyes treated with ruthenium brachytherapy

ESPENSEN C A (1,2), Fog L S (2), Klemp K (1), Aznar M C (2), Specht L (2), Kiilgaard J F (1)

(1) Copenhagen University Hospital, Department of Ophthalmology, Copenhagen, Denmark

(2) Copenhagen University Hospital, Department of Oncology- Section of Radiotherapy, Copenhagen, Denmark

Purpose Poor visual acuity and blindness due to retinal damage are challenging side effects to 106Ru-plaque treatments of malignant melanomas. In this study, we evaluated the dose to fovea and to the optic nerve and investigated the link between dose and the occurrence of macular and optic nerve damage.

Methods The study included 54 patients treated in 2005 and 2006 in Copenhagen University Hospital, Denmark. Six patients were excluded due to missing information on ocular outcome. Using dedicated commercial software, the tumour was retrospectively contoured on pre-treatment fundus images. The position of the plaque was determined from the radiation scar in post-treatment fundus images and enabled to recreate the dose distribution. The presence of ocular damage was determined from the same post-treatment fundus images. The dose to the fovea and optic nerve were reported and compared to the presence of ocular damage.

Results The estimated dose to the macula for patients with macular damage (median: 64 Gy, range: 7-668 Gy) was significantly larger than for patients with no macular damage (me- dian: 7, range: 0-31 Gy) (p=1.8·10^(−7)). Optic nerve doses for patients with optic nerve damage (median: 87 Gy, range: 38-257 Gy) similarly differed significantly from those for patients without damage (median: 17 Gy, range: 0-122 Gy) (p=1.7·10^(−4)).

Conclusions After 106Ru-plaque treatment, patients where ocular damage was identified had received a significantly higher dose to the macula and optic nerve compared to patients with no signs of ocular damage.

• 4442

Dexamethasone 0.7-mg intravitreal implant in patients with radiation macular edema after proton beam therapy for choroidal melanoma : 2-year results.

BAILLIF S, Maschi C, Caujolle J P

Saint Roch University Hospital, Ophthalmology, Nice, France

Purpose To evaluate over a 2-year period, the efficacy of dexamethasone 0.7-mg intravitreal implant in patients with radiation macular edema after proton beam therapy for choroidal melanoma.

Methods Nine patients' charts were retrospectively reviewed. The main outcome measures were visual acuity and mean central retinal thickness.

Results All patients received a radiation dose of 60 cobalt gray equivalent. Radiation macular edema occurred within a mean time of 41 months after irradiation. Mean preinjection visual acuity was 50 ETDRS letters. Mean central retinal thickness was 461.7 µm. Two months after injection, mean visual acuity was 57 ETDRS letters. It improved for 5 patients (+4, +9, +15, +15, and +19 letters) and remained unchanged for 4. Two months after injection, mean central retinal thickness was 321.6 µm. A complete resolution of radiation macular edema was observed for 7 patients. Four patients underwent several injections of dexamethasone performed 4 to 5 months after the last injection. Intraocular pressure increased for 2 patients over a mean follow-up period of 24 months. Two patients underwent cataract surgery after the third injection of dexamethasone implant.

Conclusions Intravitreal dexamethasone implant can improve visual acuity in radiation macular edema. The observed beneficial effect lasted up to 5 months.

• 4443

Radiation complications, Toxic Tumor Syndrome prevention

ROMANOWSKA DIXON B, Kubicka-Trzaska A, Morawski K, Bogdali A, Markiewicz A

Jagiellonian University Medical College, Ophthalmology, Krakow, Poland

Purpose After large melanomas radiotherapy (I-125, Ru-106 brachytherapy or proton-beam) tumor is damaged, which can cause the development of radiation-induced complications. Large tumor resection under the scleral flap (egzoresection) or during ***pars plana vitrectomy*** (endoresection) can prevent Toxic Tumor Syndrome. Aim: To present choroidal melanoma endoresections results. Tumors were resected in the Department of Ophthalmology and Ocular Oncology at the University Hospital in Krakow.

Methods The study included 10 patients with large melanoma located in the posterior pole after the proton beam irradiation. Patients were stratified for resection because of the risk of Toxic Tumor Syndrome. ***Pars plana vitrectomy*** and tumor endoresection was performed in all cases with endophotocoagulation and silicone oil endotamponade.

Results Removed melanomas were localized predominantly in the posterior pole of the eye, tumor base diameter ranged from 11,3 to 15,2mm, tumor thickness ranged 5.2 to 9,1mm. Endoresection was performed 1 to 3 months after proton beam irradiation. Intraoperative complications include minor bleeding occurred in all patients, postoperatively in 1 patient intraocular inflammation (treated with good effect intravitreal injections of steroids) and in 1 case of PVR. There was no recurrence of the neoplasm during the observation period.

Conclusions Choroidal melanoma endoresection should be used in some cases of large tumors localized back to the equator of the eye, mainly in the posterior pole of the eye. This prevents Toxic Tumor Syndrome and tumor recurrence.

• 4444

Proton beam irradiation of choroidal hemangiomas after unsuccessful photodynamic therapy

ZOGRAFOS L (1), Schalenbourg A (2)

(1) Cabinet Privé du Prof. L. ZOGRAFOS, Jules-Gonin Eye Hospital, Lausanne, Switzerland

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

Purpose To study the outcome of patients treated for a choroidal hemangioma with proton beam irradiation following unsuccessful PDT and compare the therapeutic results with that of a control group that received proton therapy as a primary treatment.

Methods Proton beam irradiation was applied to twelve cases of choroidal hemangioma that had been unsuccessfully treated with PDT (N of sessions: 1-5). Their functional results were compared to those of a control group of 48 cases treated only with proton therapy. The latter were matched (4 to 1) for the duration of symptoms before primary treatment, extent of retinal detachment as well as distance to the macula.

Results The mean follow-up following proton beam irradiation therapy was 28 months [range: 6 months-5 years] in the PDT group and 41 months [range: 6 months-10 years] in the control group. In all patients, the retinal detachment and macular edema disappeared following proton therapy. In the study group, final visual acuity was ≤ 0.1 in 25%, 0.2-0.5 in 25% and ≥ 0.6% in 50% of cases. Visual acuity improved in 50%, remained stable in 42% and decreased in 8% of cases. In the control group, final visual acuity was ≤ 0.1 in 4%, 0.2-0.5 in 38% and ≥ 0.6 in 58% of cases. Visual acuity improved in 65%, remained stable in 29% and decreased in 6% of cases.

Conclusions Proton beam irradiation is a valid therapeutic option after inconclusive results following PDT for choroidal hemangioma. Within the limits of this study, therapeutic results were slightly better for those patients that received proton therapy as a primary treatment.

• 4445

Stereotactic radiation therapy of diffuse choroidal hemangioma in Sturge-Weber syndrome

SCHALENBOURG A (1), Zografos L (2), Pica A (3)
(1) Jules-Gonin University Eye Hospital, Ophthalmology, Lausanne, Switzerland
(2) Cabinet Privé du Prof. L. ZOGRAFOS, Jules-Gonin Eye Hospital, Lausanne, Switzerland
(3) PSI, OPTIS, Villigen, Switzerland

Purpose To evaluate the outcomes following stereotactic radiation therapy of diffuse choroidal hemangioma related to Sturge-Weber syndrome (STW) and associated with secondary retinal detachment (RD).
Methods Retrospective case series of STW patients with diffuse choroidal hemangioma associated with RD, that were treated with stereotactic radiation therapy. The technique consisted of applying 19.8 to 25.2 Gray in 10 to 14 fractions, at the posterior pole.
Results Between June 2001 and August 2013, 13 patients (M/F ratio: 6/7) with a median age of 8.5 years (range: 3.0-32.0 years) were irradiated. Before, five of them had been unsuccessfully treated with PDT, silicone oil or propranolol in an attempt to reattach the RD. Median visual acuity at baseline was reduced to HM (range: NPL-0.7) with a median tumor thickness of 4.4 mm (range: 3.1-7.2). During radiation treatment, one patient complained of minor, transient conjunctival irritation. Mean follow-up (FU) was 39 months (range: 0-141 months). Complete retinal reattachment was observed in 9 cases, partial retinal reattachment in 1 case (FU 3 months) and no response in 1 case (RD duration of 3 years).Two patients were lost to follow-up. Four patients received panretinal photocoagulation for retinal ischemia. At the last control examination, median visual acuity was 0.04 (range: NPL-0.8), mainly related to pre-existing amblyopia, secondary retinal changes or glaucoma-associated optic atrophy. Median tumor thickness was 2.0 mm (range: 1.3-2.5).
Conclusions Stereotactic radiation therapy with 20 to 25 Gray is an efficient treatment for reapplying secondary RD in STW patients with diffuse choroidal hemangioma. No major complications were noted. However, visual outcomes remained poor, because of the complex ocular problems these young patients present, with often a delay in diagnosis and treatment.

• 4446

Choroidal osteoma in deep range imaging OCT (DRI-OCT)

MARKIEWICZ A (1), Romanowska Dixon B (1), Bogdali A (1), Jakubowska B (2)
(1) Jagiellonian University- Medical College-Cracow, Ophthalmology, Kraków, Poland
(2) University Hospital- Cracow- Poland, Ophthalmology, Krakow, Poland

Purpose A study presents features of choroidal osteoma in Deep Range Imaging Optical Coherent Tomography (DRI-OCT)
Methods We analysed 5 cases with choroidal osteoma. All patiens were diagnosed, treated and follow-up at the Ophthalmology and Ocular Oncology Department of University Hospital in Cracow during 2013 and 2015 years. Diagnosis of osteoma was established on basis of typical features found during fundus and ultrasonography examnations. Additionaly, DRI-OCT was performed in all choroidal osteoma cases. Images were evaluated by four experienced physicians in using DRI-OCT in differential diagnosis of intraocular tumors.
Results In all cases choroidal osteoma were observed smooth undulating tumor surface, multiple intralesional layers, sponge bone structure, transparency with visibility of sclero-choroidal junction and presence of vessels.
Conclusions Choroidal osteoma is a rare, benign tumor presents mainly at posterior pole of eye globe in young woman. Especially it should be distinguish from amelanotic choroidal melanoma or metastatic tumors. In these controversial cases DRI-OCT is very useful due to present very characteristic features of choroidal osteoma in this examination.

• 4451

An innovative mouse model for retinal alpha-synucleinopathy: taking a now look on Parkinson's disease

DE GROEF L
K.U.Leuven, Laboratory of Neural Circuit Development and Regeneration, Leuven, Belgium

Abstract not provided

• 4452

Unraveling the molecular and cellular mechanisms underlying deleterious ROCK signaling in neuronal survival and axonal growth

LEFEVERE E
University of Leuven, Leuven, Belgium

Abstract not provided

• 4453

Identification of the gene signature of retinal endothelial cells during classical experimental autoimmune uveitis, Th1- and Th17-dependent uveitis

LIPSKI D
Hôpital Erasme, Brussels, Belgium

Abstract not provided

• 4454

Development of a portable retinal oximeter using a hyperspectral image sensor

VAN KEER K
University Hospitals Leuven, Department of Ophthalmology, Leuven, Belgium

Abstract not provided

• 4455

3D printed human recombinant collagen scaffolds for corneal tissue engineering: determination of cell-scaffold interactions

MATTHYSSEN S
University Antwerp, Antwerp, Belgium

Abstract not provided

• 4456

Functional characterization of RCBTB1 as novel disease gene for syndromic retinal dystrophies

ASCARI G
University Ghent, Ghent, Belgium

Abstract not provided

• 4457

Integrated transcriptomics and genomics to identify hidden genetic variation of FRMD7 or novel candidate genes in idiopathic infantile nystagmus

ALMOALLEM B
Center for Medical Genetics Ghent, Ghent, Belgium

Abstract not provided

• 4458

Role of the transcription factor TonEBP/NFAT5 in the inflammatory response induced by hyperosmolar stress in RPE cells

LIBERT S
Université Libre de Médecine - Medicine Faculty, Laboratory of Physiopathological and Nutritional Biochemistry, Brussels, Belgium

Abstract not provided

• 4461

Acute exophthalmos in children

DE POTTER P
Cliniques Universitaires St.Luc, Brussels, Belgium

Abstract not provided

• 4462

Update in management of optic nerve glioma (part 2)

PARSA C
Quinze-Vingts National Eye Hospital / UPMC-Sorbonne Universities, Ophthalmology, Paris, France

Significant controversy exists in the treatment of optic nerve glioma because of the absence of evidenced-based trials demonstrating efficacy for various treatments administered over the years, from radiation therapy to various chemotherapeutic regimens and combinations thereof. Elements of tumor biology will be discussed along with fundamental properties of anti-mitotic regimens administered to date, as well as newer agents proposed targeting protein synthesis rather than DNA replication. Discussion of how tumor suppressor gene status (NF1) should be taken into consideration when deciding upon a treatment modality will also be discussed. Novel vision sparing surgical modalities applicable to NF1-associated orbital gliomas in particular will be reviewed.

• 4463

A novel method for measuring outcome of orbital decompression in Graves' orbitopathy

BALDESCHI L
Cliniques Universitaires St.Luc, Brussels, Belgium

To evaluate the outcome of a graded bone removal rehabilitative infero-medial orbital decompression in Graves' orbitopathy (GO) by means of a novel stratified appraisal (NSA) versus the traditional group analysis (TGA). This retrospective follow-up study included all the orbits decompressed (06/1999-12/2005), at the Department of Ophthalmology University of Amsterdam by one surgeon (L.B.), using the technique under evaluation. NSA assessed or quantified: 1) the invasiveness of surgery, allowing to calculate a mean index of invasiveness per orbit (MIIO) and per patient (MIIP) (25%≤values≤100%); 2) at ≥ 6 months postoperatively surgical targets (desired exophthalmos reduction, improvement of retroocular tension, reduction of peri-orbital puffiness, resolution of lagophthalmos) were scored as achieved or not allowing to calculate a mean index of targets achieved per orbit (MITAO) and per patient (MITAP) (0≤values≤1); 3) an index of diplopia (ID) (decompression-induced / decompressio-cured diplopia); (4) demographics and preoperative characteristics were compared after stratification of the included orbits for surgical target; surgical outcomes were assessed after stratification for amount of desired exophthalmos reduction and invasiveness of surgery. TGA examined the entire series as a single homogeneous cohort independently of the different targets and invasiveness of surgery. NSA and TGA were compared and complications noted. 151 orbits of 84 patients (78% female, mean age 45.5±9,7 years) were included. The NSA detected differences among groups within the studied cohort, the overall achievement of surgical targets was high, indices precisely quantified the extent of applied surgery and surgical results, at variance with results obtained with TGA. A negligible complication rate was recorded. The NSA may represent a step forward towards a more comprehensive and accurate evaluation of decompression surgery outcomes.

• 4464

Orbital implantation of biocompatible magnets for the treatment of intractable nystagmus

VERITY D H, Kennard C, Pankhurst Q, Geoffrey E R
Moorfields Eye Hospital, London, UK

Intractable acquired nystagmus causes debilitating symptoms and medical and surgical treatment is typically unsatisfactory. We describe a pilot study in which pairs of custom-designed titanium-encased magnets were sequentially implanted in an adult male patient with recalcitrant vertical nystagmus to achieve a reversible dampening of the nystagmus in the primary position. Under general anaesthesia, one magnet was sutured within the inferior retractor sheath, and, with the globe in the primary position, the fellow magnet was secured to the orbital floor with histoacryl glue, thereby dampening the nystagmus. The procedure was repeated on the fellow orbit several weeks later. This pilot study on a single patient was completed without complication, and has achieved a dramatic improvement in objective and subjective visual functions, including the spatial distribution of eye position during fixation in the primary position, together with a marked subjective improvement in quality of life. NIHR funding has been secured to extend this study to a larger cohort of patients to determine the extent and duration of this dampening effect in a larger cohort of patients.

• 4471

The prevalence and incidence of glaucoma in Denmark in a fifteen year period: A nationwide study

KOLKO M (1), Horwitz A (2), Thygesen J (3), Jeppesen J (4), Torp-Pedersen C (5)
(1) Roskilde University Hospital, Ophthalmology, Hellerup, Denmark
(2) University of Copenhagen, Department of Neuroscience and Pharmacology, Copenhagen, Denmark
(3) Copenhagen University Hospital Glostrup, Department of Ophthalmology, Glostrup, Denmark
(4) Copenhagen University Hospital Glostrup, Department of Cardiology, Glostrup, Denmark
(5) Aalborg University Hospital, Department of Health- Science and Technology, Aalborg, Denmark

Purpose The purpose of the present study was to describe the prevalence, incidence and demographic variation of glaucoma patients in Denmark in the period from 1996 to 2011. Moreover, the aim was to identify the treatment pattern of glaucoma medication within the studied period.
Methods The study population comprised all individuals living in Denmark in the period 1996-2011. The National Prescription Registry was used to identify all claimed prescriptions for glaucoma medication.
Results A total of 116,592 incident glaucoma patients were identified. Average age at onset was 66 years (range: 0-105 year), 55% were women. The over all prevalence of glaucoma increased from 0.79% to 1.72% during the investigated period. In 2011, glaucoma affected 3.76% of the population above 50 years and 10% in patients above 80 years.The highest prevalence of glaucoma was found in capital region of Denmark. Within the studied period the use of prostaglandin analogs and combination drugs increased, whereas the use of b-blockers, carbon anhydrase inhibitors and parasympathomimetic drugs decreased ($p<0.001$). Finally, the use of a2-adrenergic agonists remained unchanged within the studied period. A total of 75% of the patients were treated with two or more glaucoma medications.
Conclusions Over all, the present study is the first assessment of the frequency and the development of glaucoma in Denmark over a 15-year period. Glaucoma affects a little less than 2% of the total population and increases with age to reach a prevalence of more than 10% amongst people above 80 years.

• 4472

Optic nerve head hemorrhage and vitreous traction.

WILLEKENS K (1), Pinto L A (2), Vandewalle E (1), Stalmans P (1), Stalmans I (1)
(1) UZ Leuven, Ophthalmology, Leuven, Belgium
(2) Centro hospitalar Lisboa Norte, Ophthalmology, Lisbon, Portugal

Purpose During posterior vitreous detachment (PVD) the posterior hyaloid remains, for a certain period, attached to the optic disc. It can exert traction with development of optic nerve head hemorrhages (ONHH). ONHH are known to be associated with glaucomatous progression and retinal nerve fiber layer (RNFL) defects. Therefore this study aims at investigating the relationship between PVD formation and ONHH in open angle glaucoma patients.
Methods Patients presenting with an ONHH, from November 2014 on, were included. They underwent a comprehensive ophthalmological investigation, automated visual field test, confocal scanner (HRT III), OCT (HRT-Spectralis) scan and stereographic photos of the optic nerve head. This study is part of a larger, clinicaltrial.gov (NCT02290795) registered, study investigating vitreopapillary traction (VPT).
Results Eighteen eyes of 18 patients (11 normal tension, 6 primary open angle and 1 secondary open angle glaucoma) were included. Seven out of 18 (38,9%) eyes had concomitant VPT and 7 had a complete PVD. Seven ONHH were located infero-, 5 supero- and 6 temporal. In the non-VPT subgroup 5 out of 11 (45,5%) eyes showed matching retinal nerve fiber layer defects, with 2 out of 7 (28,6%) in the VPT subgroup.
Conclusions VPT could be a confounding factor in glaucoma assessment and ONHH development.

• 4473

Localized changes in retinal nerve fiber layer reflectance intensity are related to localized functional loss in glaucoma

GARDINER S , Demirel S , Reynaud J , Fortune B
Devers Eye Institute, Discoveries In Sight Laboratories, Portland, United States

Purpose Reflectance within the retinal nerve fiber layer (RNFL) may change prior to, or concurrent with, RNFL thinning in glaucoma. We hypothesize that reductions in RNFL reflectance intensity may be observed by optical coherence tomography (OCT), and may provide useful additional information beyond RNFL thickness.
Methods Participants enrolled in an ongoing longitudinal study of glaucomatous progression had peripapillary circle scans acquired using spectral-domain OCT, and performed automated perimetry, every 6 months. Data were analyzed from the most recent 8 visits with reliable results, from 211 eyes of 143 individuals. For each of the 52 visual field locations, intensity ratio and RNFL thickness were calculated within a 30° sector centered at the average location where corresponding nerve fibers enter the disc. Intensity ratio was defined as the mean intensity of pixels within the delineated RNFL boundaries divided by the mean intensity of pixels between the outer RNFL boundary and Bruch's Membrane. Rates of localized change were defined as the rate of change within each sector / location, minus the rate of global change. A mixed effects model was used to predict the rate of localized functional change from the rates of localized thickness and intensity ratio change within the corresponding sector.
Results In a combined model, the rate of localized functional loss was predicted by both rate of thinning and the interaction between the rates of thinning and intensity ratio change (both $p<0.0001$). For a given rate of RNFL thinning, a more negative rate of intensity ratio change predicted more rapid loss of sensitivity.
Conclusions Reduction of RNFL reflectance over time is associated with loss of sensitivity at corresponding locations. While these are early results, they suggest potential improvements to the interpretation and quantification of OCT scans.

• 4474

Visual field screening by opticians with Damato Multifixation Campimetry Online (DMCO)

OLSEN A S (1), Damato B (2), La Cour M (1), Kolko M (3,4)
(1) Rigshospitalet - Glostrup, Øjenklinikken, Copenhagen N, Denmark
(2) UCSF, Dept. of Ophthalmology, San Francisco, United States
(3) Roskilde University Hospital, Dept. of Ophthalmology, Roskilde, Denmark
(4) University of Copenhagen, Department of Neuroscience and Pharmacology, Copenhagen, Denmark

Purpose To study DMCO, a free of charge Internet-based visual field test, used as a screening device in optician shops in Denmark.
Methods Standard equipment was a computer, a wireless mouse and a 22" computer monitor. Optician shops in the region of Copenhagen were invited to participate. We used DMCO STANDARD 1+2, the best performing algorithm from our previous work, to screen. The algorithm demanded one or two successive DMCO tests with a cut-off at 4 or 5 missed points on a DMCO test. This algorithm has performed with sensitivity of 64.2% and specificity of 98.1, respectively (AUC = 0.9).
Results During 2014-2015 the DMCO STANDARD 1+2 algorithm has been evaluated in 12 optician shops. DMCO have been tested by 587 individuals of whom 31 demanded a full ophthalmology examination. The examinations revealed 7 glaucoma cases, 17 cases with different eye-brain-diseases, and 7 false positives. To date 46 individuals with a normal DMCO test have been examined: 44 healthy and 2 false negative cases. Preliminary results indicate DMCO to perform with sensitivity of 50% and specificity of 98.7%, respectively.
Conclusions This study demonstrated that DMCO was able to find various visual field defects when used by opticians. The chosen algorithm maintained high specificity but a decline in sensitivity was noticed. There is scope for future improvements of DMCO and more studies are needed to confirm the findings.

• 4475

Comparison of preservative-free latanoprost and bimatoprost in a multicenter, randomized, investigator-masked cross-over clinical trial.

STALMANS I (1), Cordeiro F (2), Hommer A (3), Oddone F (4), Ribeiro L (5), Sunaric Mégevand G (6), Rossetti L (7)
(1) UZ St. Rafael, Ophthalmology, Leuven, Belgium
(2) ICORG – Imperial College Ophthalmologic Research Group, Imperial College Healthcare NHS Trust, London, United Kingdom
(3) Hommer Ophthalmology Institute, Vienna, Austria
(4) G.B.Bietti Eye Foundation – IRCCS, Rome, Italy
(5) AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal
(6) Clinical Research Centre - Mèmorial A de Rothschild, Geneva, Switzerland
(7) Centre for Clinical Trials at San Paolo Hospital, University of Milan, Milano, Italy

Purpose To investigate the efficacy and safety of Bimatoprost Unit Dose Preservative Free (BUDPF) and Latanoprost Unit Dose Preservative Free (LUDPF) in a clinical setting.
Methods Prospective, randomized, investigator-masked, cross-over comparison. Patients with ocular hypertension or open angle glaucoma (OAG) with an IOP less than or equal to 21 mmHg with a preserved prostaglandin monotherapy at screening were washed out and randomized to receive BUDPF or LUDPF for 3 months and were then switched to the other respective treatment for another 3 months. IOP curves were performed at baseline and after each treatment period, and safety and tolerability were assessed at the two latter timepoints.
Results Both drugs were effective in lowering IOP, both at 3 and at 6 months (estimated differences compared to baseline pressures: -4,0±0.5 for both BUDPF and LUDPF, $p<0.01$ at 3 months; -5.2±0.5 for BUDPF, -3.4±0.5 for LUDPF, both $p<0.01$ at 6 months). Analysis at 6 months (primary endpoint) showed a difference of 1.6±0.5 mmHg between the two groups, favoring BUDPF ($p<0.01$). An intra-subject IOP difference of 0.9±0.2 mmHg in favor of BUDPF was observed ($p<0.01$).
Conclusions This study demonstrate a superior efficacy of BUDPF over LUDPF in lowering IOP.

Commercial interest

• 4476

Double-hump sign on gonioscopy: definitive plateau iris? A cross-sectional study using ultrasound biomicroscopy

CORDEIRO SOUSA D (1,2), Leal I (1,2), Caiado F (1), Goncalves I (1), Reina M (3), Marques-Neves C (1,2,4), Prior Filipe H (5), Abegao Pinto L (2)
(1) Hospital Santa Maria - Lisbon Academic Medical Center, Ophthalmology, Lisboa, Portugal
(2) Faculty of Medicine, Lisbon Academic Medical Center, Lisboa, Portugal
(3) Centro Hospitalar Lisboa Central, Ophthalmology, Lisbon, Portugal
(4) Centro de Estudos Ciencias Visao, Ophthalmology, Lisbon, Portugal
(5) ALM - Ofialmolaser Clinic, Ophthalmology, Lisbon, Portugal

Purpose Plateau iris configuration (PIC) is a rare condition involving an angle closure unrelated to pupillary block. It may be defined by a narrow angle and a double-hump configuration on gonioscopy. Plateau iris syndrome (PIS) may lead to acute angle-closure glaucoma due to an anterior displacement and rotation of the ciliary body. It has been proposed that ultrasound biomicroscopy (UBM) is helpful in PIC/PIS diagnosis. Our work aims to describe UBM quantitative and qualitative findings in patients whose gonioscopy suggested a PIC/PIS.
Methods Cross-sectional study involving patients with a double hump gonioscopic finding. UBM was then performed by a blinded observer and evaluated for the presence of following ultrasonographic (US) criteria: 1) a thick and flat iris, 2) a sharp, square root angulation on its insertion, 3) an anterior rotation of the ciliary body, 4) irido-ciliary sulcus narrowing, 5) iris-trabecular apposition and 6) a relatively normal anterior chamber (AC) depth. Only high-quality images were accepted.
Results From Sep/14-May/15, 35 patients (59 eyes) were recruited. Only 3 eyes presented the six US criteria, 23 eyes filled five of the criteria, 13 satisfied four criteria, 16 presented three criteria and 4 two criteria. The most commonly verified criteria (over 95% of them) were a thick and flat iris and a square root insertion. There was no association between any of these criteria and sex nor age ($p>0.10$). Furthermore, the presence/absence of these criteria did not correlate with either anterior chamber depth, lens vault and lens length ($p>0.10$).
Conclusions The majority of patients presenting with clinical iris plateau syndrome do not fulfill the entire US criteria for this condition. However, the US-based iris morphological parameters seem to be present in nearly all iris plateau patients.

• 4477

How accurate are optometrist referrals for glaucoma in the NICE era?

BOBAT H, Begum S , Lockwood A , Kirwan J F
Queen Alexandra Hospital, Eye Department, Portsmouth, United Kingdom

Purpose To determine if the reason(s) stated by the optometrist affect the positive predictive value (PPV) of referrals for suspected glaucoma.
Methods Optometrist referrals in Portsmouth are streamlined though the Glaucoma Referral Refinement Scheme (GRRS). We retrospectively analysed 100 'positive' and 100 'negative' referrals to the GRRS. Positives: those referred on to a secondary care glaucoma clinic; negatives: those discharged from the GRRS. Reason(s) for referral were determined and classified: intraocular pressure (IOP) optic disc changes (OD), visual field defect (VF), shallow anterior chamber depth (ACD). Since negative referrals to GRRS are four times more prevalent than positives, we calculated a 'corrected' PPV for each reason by multiplying the number of negatives by 4.
Results The overall PPV was 0.16. 70.4% cases were referred for a single reason (47.2% IOP, 12.2% OD, 8.8% VF, 2.4% ACD); the PPV was 0.11 for IOP and for OD, 0.05 for VF, 0.17 for ACD. 26.2% were referred for two reasons; the PPV was 0.47 for IOP + OD, 0.21 for OD + VF and 0.14 for IOP + VF. 4.2% were referred for IOP + OD + VF with a PPV of 0.62. Positive family history of glaucoma (21.4% referrals) did not increase PPV. The GRRS increased the PPV to 0.8.
Conclusions The majority of patients are referred for a single reason, yet the chance of a positive diagnosis is low. Accuracy is increased when IOP is reported in combination with OD, but VF adds little value as a second parameter. The highest PPV is found when all three reasons are stated (IOP+OD+VF). The proportion of referrals for IOP alone is similar to that found prior to the NICE guidelines. However, the PPV is considerably lower; 0.11 compared to 0.3 - 0.4 found in previous studies. In the NICE era, refinement schemes play an important role in reducing false positive referrals.

• 4478

A pilot study of survey on patient satisfaction and its meaning in an Glaucoma outpatient

POURJAVAN S (1), Vanhaecht K (2)
(1) Cliniques Universitaires St. Luc, Ophthalmology, Brussels, Belgium
(2) KULeuven, Public Health & Primary care, Leuven, Belgium

Purpose To assess the degree of patient satisfaction and its correlation with the subjective satisfactory score of the ophthalmologist.
Outcomes:
- The % of satisfied patients.
- The correlation between doctor-patient perception of care.
- The impact of the interpersonal chemistry and the mood of care provider.

Methods A prospective, blind study. A simple and short questionnaire is given to the patients. Patients were asked to fill in the questionnaire including 4 questions with a 1 (lowest) to 5 (highest satisfaction) scores.
1. The score the "care"?
2. the ophthalmologist?
3. Recommend of the outpatient?
4. Recommend of the specialist?

The ophthalmologist gives her subjective score in three fields:
1. The quality of consultation (QoC).
2. The interpersonal "click" with the patient.
3. Her "mood".

The consented patients will be called for more spontaneous explanation.
Results Patient's score: 98% gave high scores >3.
Ophthalmologists score: neg. click with 15%, natural: 48% and good click: 36%, her mood was 33% each in 3 scores (bad, natural and hyper), Her objective QoC was 95% high scores.
The click was significantly related with her mood and her mood was significantly related with QoC. The only correlation was between click & the high score on Q3.
On telephonic enquete were good outcome of the surgery, optimal care, location and their "like" for the specialist, important.
Conclusions All patients had a high satisfaction score & not influenced "Mood" or "QoC". Upon spontaneously explaining of the patients, the most important factors for their satisfaction were; good operation outcome, optimal care, correct diagnosis but the geographical location (nearby, parking space) and their affection for the specialist were also very important reason for their satisfaction.

Posters

• T001

Fisetin and Luteolin decrease inflammation and oxidative stress-induced cytotoxicity in ARPE-19 cells

HYTTI M (1), Piippo N (1), Korhonen E (1), Kaarniranta K (1,2), Kauppinen A (1,2)
(1) University of Eastern Finland, Department of Clinical Medicine / Ophthalmology, Kuopio, Finland
(2) Kuopio University Hospital, Department of Ophthalmology, Kuopio, Finland

Purpose Age-related macular degeneration (AMD) is the leading cause of blindness among the elderly in the western world. It represents not only a dramatic reduction in patients' quality of life but also a significant burden to the general healthcare system. Yet, despite the severity of the disease much questions regarding the pathways of disease formation and progression are still unanswered and viable treatment options still undiscovered. Here, we evaluate the cytoprotective and anti-inflammatory potential of fisetin and luteolin in human retinal pigment epithelial cells exposed to increased oxidative stress.
Methods ARPE-19 cells were treated with 4-Hydroxynonenal (HNE) to simulate high levels of oxidative stress. Thereafter, fisetin or luteolin were added to the culture medium. The MTT and the lactate dehydrogenase assays were used to assess cellular toxicity. Inflammatory cytokines, as well as activation of transcription factors were measured using the ELISA method and a DNA-binding transcription factor assay. To analyze the importance of SIRT1 and related pathways, the experiments were repeated after specific SIRT1 knock-out using siRNA. Levels of intracellular SIRT1 were measured using Western Blot.
Results Fisetin and luteolin protected retinal pigment epithelial cells from oxidative stress-induced cell death and exhibited potent anti-inflammatory properties even after the initial insult. These effects seemed to be independent of NF-κB or SIRT1.
Conclusions Bioactive polyphenols, fisetin and luteolin are powerful anti-inflammatory and anti-oxidant agents and show potential for the development of drugs aimed at specific intracellular pathways that affect inflammation in AMD.

• T002

cis-Urocanic acid prevents inflammation and cell death in UVB-treated ARPE-19 cells

KORHONEN E (1), Piippo N (1), Hytti M (1), Kaarniranta K (1,2), Kauppinen A (1,2)
(1) University of Eastern Finland, Department of Ophthalmology, Kuopio, Finland
(2) Kuopio University Hospital, Department of Ophthalmology, Kuopio, Finland

Purpose cis-Urocanic acid (cis-UCA) is an endogenous ultraviolet (UV) absorbing chromophore that is mainly produced in the upper layers of epidermis. The aim of our study was to investigate the cytoprotective capacity of cis-UCA in UVB-irradiated ARPE-19 cells.
Methods ARPE-19 cells were pretreated with IL-1α and cis-UCA and then exposed to UVB radiation. Secretion of IL-1β and -18 was measured using the ELISA method. Moreover, the cells were observed under an inverted microscope and cell viability was measured by lactate dehydrogenase (LDH) release assay. The proper cis-UCA concentration was evaluated comprehensively beforehand using MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide), neutral red, and LDH tests.
Results Our results show that UVB after IL-1α priming activates IL-1β and -18 secretion in ARPE-19 cells and cis-UCA clearly alleviates that. cis-UCA also improves cellular viability.
Conclusions cis-UCA shows anti-inflammatory and cytoprotective properties in ARPE-19 cells.

• T003

Nrf2- and PGC-1α-deficient mice: A novel animal model for impaired autophagy in AMD?

PATERNO J J (1,2), Smedowski A (1,2,3), Hytti M (2), Bjørkøy G (4), Amadio M (5), Levonen A L (6), Tavi P (6), Kauppinen A (1,2), Kaarniranta K (1,2)
(1) Kuopio University Hospital, Dept. of Ophthalmology, Kuopio, Finland
(2) University of Eastern Finland, Dept. of Ophthalmology, Kuopio, Finland
(3) Medical University of Silesia, Dept. of Physiology, Katowice, Poland
(4) NTNU- University College of Sør-Trøndelag HiST, CEMIR Centre for Excellence, Trondheim, Norway
(5) University of Pavia, Dept. of Drug Sciences, Pavia, Italy
(6) University of Eastern Finland, A.I. Virtanen Institute of Molecular Sciences, Kuopio, Finland

Purpose To clarify the complex role of impaired autophagy in RPE damage, we analysed mice deficient in both Nrf2 and PGC-1α. Increasing evidence of impaired autophagy as a contributor to AMD has raised the importance of animal models that fundamentally mimic autophagy decline in RPE.
Methods We analysed morphological and immunohistochemical changes in the retina of aged Nrf2 and PGC-1α double knock-out (dKO) mice and wild-type controls. The Keap1-Nrf2 pathway, an essential system involved in oxidative stress response, is regulated by proteasomes and autophagy. PGC-1α is a master regulator of ROS-scavenging enzymes, and it has a role in inducing autophagy/mitophagy. We performed immunostaining of proteins related to oxidative stress and autophagy (4-HNE, Beclin-1, HuR, LC3, p62, and ubiquitin).
Results RPE degeneration was prominent in dKO mice and it was associated with changes in autophagy and oxidative stress.
Conclusions Our findings suggest Nrf2 and PGC-1α deficiency increases oxidative stress and affects autophagy. This coincides with the retinal degeneration observed in the promising new AMD mouse model.

• T004

Hypoxia induces an inflammatory response in ARPE-19 cells

ARJAMAA O (1), Aaltonen V (2), Piippo N (3), Kaarniranta K (3), Kauppinen A (3)
(1) University of Turku, Department of Biology, Turku, Finland
(2) University of Turku, Department of Ophthalmology, Turku, Finland
(3) University of Eastern Finland, Department of Ophthalmology, Kuopio, Finland

Purpose To characterize further the link between hypoxia and inflammation in retinal diseases, we studied here the effects of hypoxic exposure on the secretion of inflammatory cytokines from ARPE-19 cell culture, pretreated with lipoplysaccharide (LPS, to induce inflammation).
Methods ARPE cell culture was exposed to 24h hypoxia, 24h hypoxia followed by 24h reoxygenation, and 24h or 48h normoxia with or without LPS. Experiments were performed using culture medium DMEM/F-12 supplemented with penicillin, streptomycin and L-glutamin without or serum and with or without LPS. Each treatment was repeated 6 times. Hypoxia (37 C, 1% O2, 5% CO2, 90% moisture) was induced in Ruskinn Invivo2 workstation, and normoxia and reoxygenation (37C, air, 5% CO2, 90% moisture) in a standard cell culture incubator. The culture media and cell lysates were collected under hypoxic or normoxic atmosphere, centrifuged and snap frozen for storage and further analyses. VEGF and cytokines were measured with ELISA and intracellular proteins (autophagy markers p62, LC3 and oxidative stress marker Nrf2) with immunoblotting.
Results As expected, hypoxic conditions increased significantly the secretion of VEGF from ARPE-19 cell culture as compared to the secretion in normoxic conditions. Also, the secretion of IL-6 and IL-8 showed a significant increase in hypoxia when measured at 24h. The intracellular protein levels were changed: p62 increased while LC3 and Nrf2 decreased in hypoxia (at 6h).
Conclusions An acute exposure to hypoxia induced an inflammatory response in ARPE-19 cell culture as characterized with an increased IL-6 and IL-8 secretion from cell culture. Intracellularly, the autophagic response decreased (seen with the increase of p62 and with the decrease of LC3) and the oxidative stress increased (seen with the decrease of Nrf2).

• T005

Autophagy stimulus affects different kinase pathways and promotes HuR protein activation and SQSTM1/p62 protein synthesis in ARPE-19 cells

AMADIO M (1), Marchesi N (1), Govoni S (1), Pascale A (1), Kaarniranta K (2,3)
(1) University of Pavia, Department of Drug Sciences - Section of Pharmacology, PAVIA, Italy
(2) Kuopio University Hospital, Dept. of Ophthalmology, Kuopio, Finland
(3) University of Eastern Finland UEF, Dept. of Ophthalmology, Kuopio, Finland

Purpose Age-related macular degeneration (AMD) pathogenesis is characterized by protein degradation impairment in retinal pigment epithelial (RPE) cells. We previously found that the expression of autophagy receptor SQSTM1/p62 is positively regulated by the RNA-binding HuR/ELAV protein. We investigated the effects of AICAR (autophagy inducer, 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside) and MG-132 (proteasome inhibitor) co-treatment on HuR activation, p62 expression, and the kinases potentially involved.
Methods ARPE-19 cells were treated with MG-132 (1μM) and/or AICAR (2mM) for increasing times (up to 2h) and subjected to cell fractionation. SQSTM1/p62 mRNA and protein levels were measured by qRT-PCR and Western blotting, respectively. HuR protein levels and its phosphorylated status were evaluated by Western blotting. The effects of puromycin (1mM, protein synthesis inhibitor) and various kinase inhibitors were also tested.
Results AICAR+MG-132 co-treatment for 2h induces HuR protein up-regulation, its cytoplasmic translocation and phosphorylation, as well as increased expression of p62 protein, being the latter one blunted by puromycin. AICAR+MG-132 co-treatment affects various kinases with differential outcomes.
Conclusions AICAR+MG-132 co-treatment leads to HuR activation and p62 protein translation. Different protein kinase pathways are likely involved in these events.

• T006

SQSTM1/p62 depletion leads to the Rab7 accumulation and inflammatory response in ARPE-19 cells

PIIPPO N (1), Hyttinen J (1), Hytti M (1), Korhonen E (1), Kaarniranta K (1,2), Kauppinen A (1,2)
(1) University of Eastern Finland, Institute of clinical medicine/ophtalmology, Kuopio, Finland
(2) Kuopio University Hospital, Department of Ophthalmology, Kuopio, Finland

Purpose SQSTM1/p62 is a central player in the selective autophagy directing ubiquitinated protein aggregates, mitochondria, and bacterial pathogens to autophagosomes. Autophagy culminates into the fusion of matured autophagosomes with lysosomes that contain degradative enzymes. One regulator of the fusion is Rab7, which also has a role in the movement of autophagosomes along microtubules. In this study, we have investigated the significance of SQSTM1/p62 in the functionality of human retinal pigment epithelial (RPE) cells and its possible role in the regulation of Rab7.
Methods SQSTM1/p62 was blocked in ARPE-19 cells using spesific siRNA. Proteasomes were inhibited with MG-132, which has been shown to induce autophagy flux by providing more substrate to the autophagic machinery. Additionally, AMPK-activator AICAR (5-aminoimidazole-4-carboxamide ribonucleotide) was used to induce autophagy. Rab7 protein levels were determined with western blot and the secretion of inflammatory cytokines using the ELISA method.
Results According to our results, interference of autophagy by SQSTM1/p62 depletion, especially in the presence of other stimuli, such as MG-132 or AICAR, leads to the accumulation of Rab7. Along with higher amounts of Rab7, increased inflammatory response was observed.
Conclusions Our results emphasize the importance of SQSTM1/p62 in the regulation of autophagy and inflammation in RPE cells that play the principal role in the pathogenesis of age-related macular degeneration (AMD).

• T007

Lack of collagen XVIII in mice evokes age-dependent deficiency in retinal pigment epithelium proteostasis

KIVINEN N (1), Felszeghy S (2), Aikio M (3), Pihjalaniemi T (3), Kaarniranta K (1)
(1) University of Eastern Finland, Clinical Medicine / Ophthalmology, Kuopio, Finland
(2) University of Debrecen, Department of Anatomy- Histology and Embryology, Debrecen, Hungary
(3) University of Oulu, Oulu Center for Cell-Matrix Research- Biocenter Oulu and Faculty of Biochemistry and Molecular Medicine, Oulu, Finland

Purpose Collagen XVIII is a unique component of basement membranes (BMs) with the structural properties of both a collagen and a proteoglycan. It has been found at the basement membrane/stromal interface and is thought to mediate their attachment. Proteolytic cleavage within its C-terminal domain releases a fragment, endostatin, which has been reported to have anti-angiogenesis effects. Age-dependent loss of vision in the collagen XVIII mutant mice is associated with pathological accumulation of deposits under the retinal pigment epithelium. We have recently shown that impaired proteasomal and autophagy clearance associate with the pathogenesis of age-related macular degeneration (AMD). In this study, staining levels of proteasomal and autophagy markers were studied in different ages of the *Col18a1*−/− mice.
Methods Enucleated eyes from 3, 12 and 18 months old mice were embedded in paraffin according to a routine protocol. Serial 5 μm-thick parasagittal samples were immunostained for proteasomal ubiquitin (Ub) and autophagy markers SQSTM1/p62 and Beclin. The extent of immunopositivity in the retinal pigment epithelial cells was evaluated during confocal microscopic analysis.
Results Lack of collagen XVIII in mice evoked age-dependent retinal pigment epithelium (RPE) degeneration and drusen-like deposit accumulation. Proteasomal Ub protein conjugate staining was prominent in both RPE cytoplasm and extracellular space. Autophagy markers SQSTM1/p62 and beclin stainings were prominent in the basal part of RPE cell cytoplasm in the *Col18a1*−/− mice.
Conclusions Disturbed proteostasis regulated by collagen XVIII may induce RPE degeneration, increase protein aggregation and finally predispose to the choroidal neovascularization.

• T008

Interventions against VEGF overexpression, available strategies and future developments

AMADIO M (1), Bucolo C (2), Govoni S (1), Drago F (2), D'Agata V (2), D'Amico A G (2), Cupri S (3), Pignatello R (3,4), Pascale A (1)
(1) University of Pavia, Department of Drug Sciences - Section of Pharmacology, PAVIA, Italy
(2) University of Catania, Department of Biomedical and Biotechnological Sciences, Catania, Italy
(3) University of Catania, Department of Drug Sciences, Catania, Italy
(4) University of Catania, NANO-i – Research Center on Ocular Nanotechnology, Catania, Italy

Purpose Neovascular diabetic retinopathy (DR) and age-related macular degeneration (AMD) are characterized by increased VEGF signaling. VEGF can be targeted using monoclonal antibody-based drugs (e.g. ranibizumab, aflibercept) or by modified oligonucleotides (e.g. pegaptanib). The main difference between the two classes is that antibodies recognize all VEGF isoforms while oligonucleotides may be more specific for certain isoform such as VEGF165. New ways of intervention stem out from the observation that VEGF expression can be post-transcriptionally regulated by the RNA-binding HuR/Elav-like1 protein. We evaluated if targeting HuR is a potential tool to hinder VEGF overexpression.
Methods 2.5μM HuR siRNA (naked or delivered by nanocarriers) was intravitreally administered in a DR model. Rats were sacrificed 48h after siRNA injection and retinal tissues collected for Western blot, ELISA, histological examination.
Results HuR siRNA treatment blunts both HuR and VEGF increase, restating normal VEGF content in DR retina. HuR siRNA exerts its protective effect when included in liposomal nanocarriers, since the naked molecule does not prevent diabetic retinal damage.
Conclusions An HuR-based strategy may be a target in the chain of events controlling VEGF expression synergizing with oligonucleotide-based interventions having the potential to modulate the expression of VEGF without fully blocking it.

Commercial interest

• T009

Reversal of ischemic retinopathy in ocular ischemic syndrome following carotid artery stenting

ESTEBAN O , Nuñez E , Ascaso J , Perez I , Idoate A , Sanchez J , Cristobal J
HCU Lozano Blesa, Ophthalmology, Zaragoza, Spain

Purpose Ocular ischemic syndrome (OIS), also known as hypoperfusion retinopathy is a rare ocular disease determined by chronic arterial hypoperfusion. The risk factors include age between 50-80 years, male gender (M:F = 2:1), arterial hypertension, diabetes mellitus, coronary disease (5% of the cases develop ocular ischemic syndrome), vascular stroke, hemodialysis. The reported incidence is 7.5 cases per million persons every year and the five-year mortality rate is 40%.
Methods Interventional case report showing the role of the early diagnosis and treatment with carotid artery stenting in a patient with OIS.
Results A 58-year-old patient with primary arterial hypertension, hypercholesterolemia obstruction of right renal artery presented with multiple episodes of amaurosis fugax with a 5-10 min of duration since three months ago in right eye. Physical examination revealed uncorrected distant visual acuity of 20/20 in each eye. Fundus examination showed dilated retinal veins and multiples microhemorrhages in the right eye. Peripheral retinal ischemia was identified with fluorescein angiography. Doppler ultrasound examination revealed a more than 90% stenosis of the right internal carotid artery. Retinal signs of ischemia improved and amaurosis fugax episodes disappeared two months following internal carotid artery stenting
Conclusions The early diagnosis and treatment of patients with OIS have a major effect on their visual prognosis.

• T010

Lactate transport and receptor actions: Potential roles in inner retinal function and disease

VOHRA R (1), Vosborg F (1), Henriksen U (1), Gurubaran I S (1), Hasan-Olive M (2), Holm E (1), Skytt D (1), Gjedde A (1), Storm-Mathisen J (2), Kolko M (1), Bergersen L H (2)
(1) Panum Institute, Department of Neuroscience and Pharmacology, Copenhagen, Denmark
(2) Institute of Basic Medical Sciences, Brain and Muscle Energy Group- Division of Anatomy, Oslo, Norway

Purpose In the brain and in adipose tissue activation of the lactate receptor GPR81 is known to promote downregulation of cAMP . Lactate is hereby involved in excitability, metabolism and inflammation. Neurodegenerative diseases in retina may in a similar manner be linked to disturbed lactate homeostasis.
Methods qPCR was performed on retina and brain extracts to investigate whether the lactate receptor GPR81 is expressed in the retina. Immunocytochemistry was performed on primary cell cultures of Müller cells (MC) and retinal ganglion cells (RGC) from mice to evaluate the presence of lactate receptors in neuronal and glial cells in the retina. Lactate assays were made to show the changes in lactate concentrations during different conditions of stress.
Results GPR81 mRNA was twice as high in retina as in hippocampus or cerebral cortex. Immunocytochemistry indicated lactate receptors in both RGC and MC. Lactate assays showed a decreased release of lactate from MC upon energy restriction. Interestingly, the combination of inhibited mitochondrial function and energy restriction significantly increased the amount of released lactate.
Conclusions The presence of lactate receptors in the retina as well as the changed levels of lactate in response to stress support the suggestion that lactate could be of great importance in retinal homeostasis and as such in the pathogenesis of inner retinal diseases.

• T011

The effect of macular edema on the measurement of retinal nerve fiber layer thickness and the thickness of peripapillary retina

KIM S (1), Lee S (2), Lee J (3)
(1) Maryknoll Medical Center, Ophthalmology, BUSAN, South-Korea
(2) Kosin University College of Medicine, Ophthalmology, BUSAN, South-Korea
(3) Pusan National University College of Medicine, Ophthalmology, BUSAN, South-Korea

Purpose With advanced in accuracy and reproducibility of spectral domain optical coherent tomography, It issuggested that the serial changes of retinal nerve fiber layer (RNFL) thickness could reflect the progression of glaucoma.But, patient may have accompany disease that affect retinal structure such as diabetes, venular occlusive diasese andmacular degenerative diasese. So, we investigated the factors that influence the measurement of RNFL and peripapillaryretina
Methods In this retrospective controlled case series, we reviewed the eyes with macular edema. Analyzed factorsassociated RNFL thickness and peripapillary retina ranging from 3mm and 5mm of optic disc included age, IOP, visualacuity, central macular thickness (CMT), central macular thickness changes and kinds comorbid diasese. All themeasured values were obtained at initial presentation and the presentation when macular edema was relieved. TheRNFL thickness and peripapillary retinal thickness were measured by SD-OCT (Spectralis OCT).
Results The measured value RNFL thickness and peripapillary retina were significantly fluctuate with the macularedema. The initial CMT, CMT changes were quantitively correlated with RNFL thickness alteration ($p < 0.01$). The initialCMT, CMT changes also significantly correlated with peripapillary retina ranging from 3mm and 5mm of optic disc, butthere was distinction associated with geographic difference. In the subgroup analysis, there were difference associationsaccording to kinds comorbid diasese.
Conclusions The macular edema effected the RNFL and the peripapillary retina. The measurements of RNFL andperipaillary retina were quantitively correlated in some kinds of comorbid diasese. The central macular thickness shouldbe considered in clinical application of detection about decreased RNFL thickness in patients who have macular edema.

• T012

Mitochondrial DNA haplogroups associated with neovascular age-related degeneration in a Spain population

ESTEBAN O (1), Ascaso F (2), Calvo T (3), Montoya J (4), Ruiz-Pesino E (4), Martinez M (2), Almenara C (2), Del Buey M (2), Cristobal J (5)
(1) HCE Lozano Blesa., Ophthalmology, Zaragoza, Spain
(2) HCU Lozano Blesa, Ophthalmology, Zaragoza, Spain
(3) Department of de Biochemisty and molecular biology., Universidad, Zaragoza, Spain
(4) Department of de Biochemisty and molecular biology, University, Zaragoza, Spain
(5) HCU Lozano Blesa, Ophtalmology, Zaragoza, Spain

Purpose To investigate whether mtDNA haplogroups are associated with neovacular AMD in a geographically defined area north east of Spain.
Methods AMD patients were ascertained at the Department of Ophthalmology of Lozano Blesa University Clinic Hospital, Zaragoza, Spain. We assessed the association between mtDNA haplogroups and neovascular AMD in 91 AMD patients and 656 unrelated controls residing in the same city. Late-stage neovascular AMD was defined as described in the international AMD calssification. Genetic analysis for mtDNA haplogroups was performed at the Department of Biochemistry and Molecular and Celular Biology at University of Zaragoza.
Results Haplogroup HV was the most frequent in AMD patients (54.9%) and controls (57.5%), followed by haplogroups U (20.9% and 22.6%, respectively), J (4.4% and 8.9%, respectively), and T (7.7% and 6.9%, respectively). There were no statistical significant differences between both groups ($P > 0.05$, chi-square test).
Conclusions Although findings of associations between different mtDNA haplogroup types and AMD lesions have been previously reported, suggesting that these haplogroups may be genetic markers indicative of an individual's susceptibility to AMD, present study did not show such association in our population.

• T013

Nuclear factor-erythroid 2-related factor-2 (Nrf2) and peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α) regulates proteolysis in cornea

SMEDOWSKI A (1,2,3), Paterno J J (1,4), Amadio M (5), Levonen A L (6), Tavi P (6), Kaarniranta K (1,4), Wylegala E (3)

(1) University of Eastern Finland, Ophthalmology, Kuopio, Finland
(2) Medical University of Silesia, Physiology, Katowice, Poland
(3) Medical University of Silesia, Ophthalmology, Katowice, Poland
(4) Kuopio University Hospital, Ophthalmology, Kuopio, Finland
(5) University of Pavia, Department of Drug Sciences, Pavia, Italy
(6) University of Eastern Finland, Department of Biotechnology and Molecular Medicine- A.I. Virtanen Institute for Molecular Sciences, Kuopio, Finland

Purpose The cornea is exposed to constant oxidative stress that may lead to protein homeostasis imbalance and tissue damage during aging process. The ubiquitin-proteasome pathway and the lysosomal pathway including autophagy are the major proteolytic systems to clean damaged proteins in cells. Our aim was to investigate the role of the Nrf2 and PGC-1α, the central transcription factors of the regulation of cellular detoxification and defense against oxidative stress, in corneas of double knockout mice (Nrf2-/PGC1α-).
Methods After fixation in 4% PFA, eyeballs were embedded in paraffin and 5 µm cross sections were cut using microtome. Tissue sections were deparaffinized, rehydrated and processed for immunostaining with primary antibodies against Beclin, HuR, p62 and LC3. Results were compared with age matching wild type controls.
Results Deficiency of Nrf2 and PGC-1α evoked accumulation of proteasomal ubiquitin and autophagy markers p62, Beclin and LC3 in one year old animals. Moreover, HuR that regulates p62 expression was highly up-regulated in the cornea epithelium.
Conclusions These results suggest that Nrf2 and PGC-1α deficiency associates with the impaired proteasomal and autophagy clearance in the corneal epithelium. This might be linked to corneal diseases, such as macular dystrophy (Kaarniranta et al, 2015).

• T014

Anterior lens epithelium in cataract patients with retinitis pigmentosa - scanning and transmission electron microscopy study

ANDJELIC S (1), Draslar K (2), Hvala A (3), Hawlina M (1)

(1) University Medical Centre, Eye Hospital, Ljubljana, Slovenia
(2) Biotechnical Faculty- University of Ljubljana, Department of Biology, Ljubljana, Slovenia
(3) Medical Faculty- University of Ljubljana, Department of Pathology, Ljubljana, Slovenia

Purpose In retinitis pigmentosa (RP) patients, relatively minor lens opacity posteriorly centrally may cause disproportionate functional symptoms requiring cataract operation. To investigate possible structural reasons for this opacity development, we studied the structure of the lens epithelium of RP patients.
Methods The anterior lens capsule (aLC: basement membrane and associated LECs) were obtained from cataract surgery and prepared for scanning and transmission electron microscopy (SEM and TEM).
Results Both SEM and TEM show the holes in the anterior lens epithelium of cataract patients with RP. Mainly, the holes appear as thinning and degradation of the epithelium, with the dimensions from less than 1 µm to more than 10 ηm and covering the region of several aLECs. A step towards the formation of denuded regions with the dimensions even bigger than 50 ηm may be the detachment of the lens epithelium. Other type of holes in size up to 20 ηm, may be formed by gradual stretching of the lens epithelium. Another type of holes is formed between adjacent LECs where lateral connections are absent, with dimensions 0.1-2 ηm x up to 10 ηm.
Conclusions Showing of holes in the anterior lens epithelium supports the hypothesis that disturbed structure of the lens epithelium plays a role in water accumulation in the RP cataractous lens. We suggest that the lens epithelium has a role in the development of the cataract in RP patients.

• T015

The study of needle tip aspirates and entry sites after intravitreal injections with different needle types

LYTVYNCHUK L (1), Savytska I (2), Sergiienko A (3), Binder S (4), Petrovski G (5)

(1) Lviv Regional Clinical Hospital, Ophthalmology Department #1, Lviv, Ukraine
(2) A.A.Shalimov National Institute of Surgery and Transplantology, Department of Experimental Surgery, Kyiv, Ukraine
(3) Professor Sergienko Eye Clinic, Ophthalmology, Vinnycia, Ukraine
(4) Rudolf Foundation Clinic- Karl Landsteiner Institute for Retinal Research and Imaging, Ophthalmological Department, Vienna, Austria
(5) Albert Szent-Gy¨orgyi Clinical Center- University of Szeged, Department of Ophthalmology, Szeged, Hungary

Purpose To compare the entry site and study the cellular content of different needle tip aspirates after transscleral intravitreal injection (IVI) on rat eyes.
Methods The intravitreal injections (IVI) were performed on 20 white outbred rat eyes (10 IVI with 30-gauge subcutaneous needles (SCN), 10 with 27-gauge Pencan needle (PCN) (B.Braun)). The 1.0 cc syringes were preloaded with 0.02 cc of balanced salt solution (BSS) and connected to the needles. The penetration was performed 1 mm posterior to the limbus, followed by aspiration of 0.01 cc vitreous body. Aspirated material was evacuated onto glass slides and stained by Azure-2-Eosin. Enucleation and histological analysis of the IVI entry site was performed at magnification 100 and 400 times.
Results Cellular content of the aspirated material was revealed in all cases. The aspirated cells represented conjunctival epithelial-, ciliary body non-pigmented epithelial-, sclerocyte-like cells and vitreous crystallised specimens. The amount of conjunctival epithelial cells prevailed in 27-gauge PCN IVI cases. The stained granular proteins were less significant in the case of 27-gauge PCN tips. The entry sites after 30-gauge SCN injection showed concrete cut of all tissues, while partial reassembling of the sclerocyte bindings was seen after 27-gauge PCN injections.
Conclusions The use of 30-gauge SCN and 27-gauge PCN needles for transscleral IVI has resulted in trauma of all layers of the rats' eye wall. Histological analysis of the needle tip aspirates showed less tissue damage by 27-gauge PCN; moreover, the SCN tips created complete cuts due to their sharp edges, in contrast to the PCN tips.

• T016

Clinical aspects of Autosomic Recessive Retinitis Pigmentosa Caused by USH2A Mutations in Consanguineous Tunisian Families

CHEBIL A (1), LARGUECHE L (1), KORT F (1), HASSAIRI A (1), HABIBI I (2), MUNIER F (3), EL MATRI L (1)

(1) Hedi Rais Institute of Ophthalmology, Research Laboratory of Oculogenetic LR14SP01- Department B of Ophthalmology, Tunis, Tunisia
(2) Faculty of Life Sciences- Ecole Polytechnique Fédérale de Lausanne- Lausanne-Switzerland, Institute for Research in Ophthalmology IRO- Sion- Switzerland, SION, Switzerland
(3) Jules-Gonin Eye Hospital- Faculty of biology and medicine- University of Lausanne-Switzerland., Institute for Research in Ophthalmology IRO- Sion- Switzerland, LAUSANNE, Switzerland

Purpose To assess the clinical phenotype in consanguineous Tunisian families with non syndromic autosomic recessive retinitis Pigmentosa (arRP) caused by an USH2A mutation.
Methods All accessible members of families were included and underwent full ophthalmic examination with best corrected Snellen visual acuity, kinetic visual field testing, fundus photography, optical coherence tomography and full field electroretinography. Haplotype analyses were used to test linkage in the families to 20 arRP loci, including ABCA4, LRAT, USH2A, RP29, CERKL, CNGA1, CNGB1, CRB1, EYS, RP28, MERTK, NR2E3, PDE6A , PDE6B, RGR, RHO, RLBP1, TULP1.
Results Thirty-four patients from five families were ascertained for the study. Twelve of the 34 members were clinically affected with arRP without hearing loss. Age range at baseline was 27 to 68 years (mean age was 42.5 years). For all affected members, night blindness appeared during the second decade. Visual acuity at baseline ranged from 20/40 to 20/32. Kinetic visual field was severely constricted. Fundus examination revealed typical RP changes with bone spicule-shaped pigment deposits in the mid periphery along with atrophy of the retina, narrowing of the vessels and waxy optic discs. Tomograms showed a thinning and even loss the outer nuclear layer of the fovea. ERG was unrecordable in scotopic conditions and the cone responses were markedly hypovolted.
Conclusions For these families, changes were typical of those that have been described in patients with moderate to severe forms of non syndromic recessive RP. Our findings support the need to consider possible involvement of USH2A not only in patients with Usher syndrome but also in patients with non syndromc arRP. Despite consanguinity, the presence of non-homozygous mutants illustrates the complexity of molecular analysis.

• T017

Exome sequencing confirms ZNF408 mutations as a cause of familial retinitis pigmentosa

HABIBI I (1), Chebil A (2), Kort F (2), Munier F (3), Schorderet D (1), El Matri L (2)

(1) Institute for Research in Ophthalmology IRO, Faculty of Life Sciences- Ecole Polytechnique Fédérale de Lausanne, Sion, Switzerland
(2) Research Laboratory of Oculogenetic (LR14SP01)- Hedi Rais Institute of Ophthalmology, Department B of Ophthalmology, Tunis, Tunisia
(3) Jules-Gonin Eye Hospital- Faculty of biology and medicine, University of Lausanne, Lausanne, Switzerland

Purpose The aim of this study was to identify the gene causing retinitis pigmentosa (RP) in a Tunisian family.
Methods Three members of a consanguineous Tunisian family were clinically examined and were given best-corrected visual acuity (BCVA), slit lamp biomicroscopy, fundus photography and optical coherence tomography scanning (OCT) testing. Blood samples were collected for DNA extraction. Regions of homozygosity were further analyzed in the index case and whole exome sequencing was performed. All detected mutations in candidate genes were validated by Sanger sequencing.
Results The phenotype was characterized by hemeralopia starting in the first decade of life. BCVA ranged from 20/100 to 20/40. Fundus examination revealed typical RP changes with bone spicule-shaped pigment deposits in the mid periphery along with atrophy of the retina, narrowing of the vessels and waxy optic discs. Tomograms showed macular edema. They also had high myopia and posterior subcapsular cataract. Mutation analysis in the region of homozygosity identified a c.653-1G>T mutation in the canonical splice site of exon 5 of the zinc finger protein 408 (*ZNF408*) gene. All three affected members were homozygous for this mutation.
Conclusions So far, only two different mutations have been identified (Avila-Fernandez et al, Hum Mol Genet. 2015). This family represents the third case of ZNF408 mutations and further expands the clinical spectrum of mutations.

• T018

Two Sisters with Congenital Blindness caused by Osteoporosis-pseudoglioma Syndrome due to new Mutations in the LPR5 Gene

WELINDER L (1), Robitaille J M (2), Boerkoel C F (3), Rupps R (3), Lyons C (4)

(1) Aalborg University Hospital, Ophthalmology, Aalborg, Denmark
(2) Dalhousie University and IWK Health Centre, Department of Ophthalmology and Visual Sciences, Halifax, Canada
(3) University of British Columbia- BC childrens Hospital, Genetics, Vancouver, Canada
(4) University of British Columbia- BC childrens Hospital, Pediatric Ophthalmology, Vancouver, Canada

Purpose To discover the reason behind two sisters being born blind with retinal detachment and microphthalmia with later findings of severe osteoporosis with low impact fractures
Methods Molecular testing identified biallelic lipoprotein receptor-related protein 5 (LRP5) mutations (NM_002335.3:c. [889dupA]; [2827 + 1G4A]) confirming a diagnosis of osteoporosis–pseudoglioma (OPPG) syndrome.
Results Two new mutations in the LPR5 gene were each found in the unrelated parents of the girls and were found heterozygote in the girls. Both parents were then discovered to have osteopenia, as did several relatives, who all started preventive treatment.
Conclusions OPPG is a autosomal recessive disease almost uniformly causing blindness from very early age with severe osteoporosis and low impact fractures, which was also the case of our two sisters. The diagnosis of OPPG was confirmed by sequencing the LPR5 gene, where two new mutations were found.

• T019

A novel mutation in CNNM4 (G492C) associated with Jalili Syndrome

LOPEZ TORRES L T (1), Schorderet D (2), Valmaggia C (3), Todorova M (1)

(1) University of Basel, Department of Ophthalmology, Basel, Switzerland
(2) Institute for research in ophthalmology IRO, Ophthalmology, Sion, Switzerland
(3) Cantonal Hospital St. Gallen, Department of Ophthalmology, St. Gallen, Switzerland

Purpose To describe a new G492C homozygous mutation in a consanguineous family from Saudi Arabia with autosomal recessive cone-rod dystrophy (arCRD) associated with amelogenesis imperfecta and mental deficiency (Jalili syndrome).
Methods Both parents and their five children were included in the study. They underwent a complete ophthalmic examination including fundus imaging and optical coherence tomography. Both affected children underwent electrophysiological evaluation including full-field ERG and EOG (ISCEV standard). Direct Sanger sequencing of all exons and intron-exon junctions of *CNNM4* was conducted.
Results ArCRD was diagnosed in two children with childhood-onset visual impairment and nystagmus. Ophthalmoscopy showed macular atrophy with pigment mottling, attenuated retinal vasculatur and optic disc pallor. Electrophysiology revealed non-recordable scotopic and photopic ERGs, completely attenuated off-response of the on-off ERG and reduced Arden-ratio of the EOG. Both affected children showed mental deficiency and had clinical signs of amelogenesis imperfecta presenting with dysplastic, hypomineralized teeth.Sanger sequencing identified a new c.[1474G>T] mutation in *CNNM4*, located in exon 2 leading to a substitution of the glycine amino acid to cystein at cDNA position 492. This mutation was homozygous in the two affected children and was heterozygous in the unaffected father, mother and both sisters. One unaffected son was homozygous normal.
Conclusions Genetic testing enabled to confirm the diagnosis of Jalili syndrome by identifying a yet unreported G492C mutation in *CNNM4*.

• T020

Genotypes & Phenotypes in Belgian Patients with Albinism

DE BLESER E (1), Tack M (1), De Baere E (2), Leroy B P (3)
(1) Ghent University Hosp. & Ghent University, Ophtalmology, Ghent, Belgium
(2) Ghent University Hosp. & Ghent University, Ctr for Medical Genetics, Ghent, Belgium
(3) Ghent University Hosp. & Ghent University, Ophthalmology & Ctr for Medical Genetics, Ghent, Belgium

Purpose To study the different genotypes and phenotypes in Belgian patients with albinism.
Methods Phenotypes and genotypes in a cohort of 89 patients were studied in detail. These patients were then grouped according to genotype.
Results A total of 40 patients with isolated oculocutaneous (OCA), and 11 with XL ocular albinism (XLOA) were molecularly confirmed. Nine syndromic OCA patients were identified. Genotypes of 29 patients were unknown at the time of study. Although not statistically significant due to small sample size, patients with a proper *TYR* mutation in combination with a temperature sensitive variant (TS) generally showed milder characteristics. A study of one specific family showed 3 affected siblings with this genotype. However, 2 normal children, each of a different patient, also had this genotype. There was perfect concordance between fundoscopic identification of lyonization in 15 female carriers of XLOA, and molecular confirmation of heterozygosity. Two adult patients with Chediak-Higashi syndrome showed OCA in combination with neurodegeneration. Systemic abnormalities in 7 Hermansky-Pudlak syndrome patients were very variable.
Conclusions Molecular analysis is essential to confirm clinical phenotyping in albinism. A causal relationship between a combination of a *TYR* mutation and the TS variant is as yet uncertain and requires more in depth analysis.

• T021

Retinitis pigmentosa : a new feature in hypohidrotic ectodermal dysplasia

MEUNIER A , Vilain C , Abramowicz M
Hôpital Erasme, Ophtalmology, Bruxelles, Belgium

Purpose Hypohidrotic ectodermal dysplasia is usually transmitted as an X-linked recessive trait. This is a really rare condition with a prevalence of 1 for 100000 births. Patients present a classical triad of hypotrichosis, anhydrosis or hypohydrosis and dental abnormalities. We report a 16 year old boy presenting a mild phenotype of HED and a hemeralopia due to a retinitis pigmentosa, without dysmorphia, intellectual deficiency or other associated feature. The parents were not consanguineous and the family history was unremarkable.
Methods A full field ERG according the ISCEV protocol, a goldmann visual field, color and autofluorescent fundu's photographies were recorded.
Results The scotopic responses were diminished bilaterally confirming the existence of a retinitis pigmentosa
Conclusions We report a patient with the association of HED and retinitis pigmentosa, a previously unreported association that might represent a novel genetic syndrome.

• T022

A variant rs613872 in TCF4 gene is responsible for the higher risk for Fuchs endothelial corneal dystrophy development- the results of study in Polish patients.

UDZIELA M (1), Oldak M (2,3), Ruszkowska E (2,4), Sciezynska A (2), Binczyk E (1), Ploski R (5), Szaflik J P (1)
(1) Medical University of Warsaw, Dep. Ophthalmology, Warsaw, Poland
(2) Medical University of Warsaw, Department of Histology and Embryology, Warsaw, Poland
(3) World Hearing Center- Institute of Physiology and Pathology of Hearing, Department of Genetics, Warsaw, Poland
(4) Medical University of Warsaw, Postgraduate School of Molecular Medicine, Warsaw, Poland
(5) Medical University of Warsaw, Department of Medical Genetics, Warsaw, Poland

Purpose The aim of the study was to investigate the connection between rs613872 polymorphism in *TCF4* gene and Fuchs Endothelial Corneal Dystrophy (FECD), and evaluation of *TCF4* gene expression within corneas of patients with FECD and individuals of Polish population control group.
Methods Genomic DNA was extracted from peripheral blood. Polymorphism rs613872 was genotyped in 227 subjects with FECD and 312 controls using real-time PCR and TaqMan sonds. Total RNA was isolated from Descemet's membranes, which were stripped during endothelial keratoplasty performed in patients with FECD (n=24) and from fragments of donors' corneas unused for transplantation (n=22). The difference in *TCF4* gene expression was estimated by quantitative method PCR.
Results The distribution of genotypes TT, GT, GG in control group was 74%, 23,4%, 2,6% and in FECD patients 21,6%, 64,8%, 13,7%, respectively. The rate of alleles T and G in patients' group was 245/454 (54%) and 209/454 (46%). In control subjects the results were 535/624 (85,7%) and 89/624 (14,3%). Allele G was much more common in patients with FECD compared to control group (OR=5.13, 95%CI: 3.84-6.86, $\chi 2$=132.63, p<0.0001). Within corneas from patients with FECD the tendency to increased *TCF4* gene expression was observed in comparison to the control group, but the disparity was not statistically significant.
Conclusions The results of our investigations revealed the rs613872 variant in TCF4 gene to be significant associated with FECD in Polish patients. The influence of changing expression of *TCF4* gene for FECD development requires the further studies.

• T023

Prospective study about activity of emergency unit in the Department of Ophthalmology (Nancy, University Hospital, France)

BAUDOT A (1), Ameloot F (2), Trechot F (2), Angioi K (2)
(1) Hôpitaux de Brabois, service ophtalmologie B, Gondreville, France
(2) Hôpitaux de Brabois, service ophtalmologie B, Vandoeuvre-les-Nancy, France

Purpose Ophthalmological emergencies are common. Actually, access to care is difficult because of the low medical demography. The Department of Ophthalmology (Nancy, University Hospital, France) created a unit devoted to emergency in 2012.
Methods We conducted a cross sectional study to describe this activity. All consecutive patients seen in the unit were included from February to April 2012 and from October to December 2014.We used a standardized evaluation (age, sex, access to care, geographic origin, symptoms, diagnosis, treatment, patient outcome). Every physician considered the real nature of the emergency.
Results 1496 patients were included during the first period (series 1) and 1116 during the second (series 2). The most common patient was a 45 years old man (55.3% and 56.3%). Many patients came by themselves without medical advice (40.1% and 58.4%). Principal symptoms were redness (31.5% and 24.8%), pain (28.5% and 25.0%), visual loss (22.6% and 17.7%), and irritation (20.6% and 17.8%). Traumatic context was frequent (about 25.0% of patients).The most prevalent diagnosis concerned the cornea. Serious infectious condition and vascular diseases were rare. 5.0% of patients were hospitalized and 6.0% received surgical treatment. 62.7% of them benefited only one consultation in emergency. They did not need another clinical control. 62.1% to 63.1% of consultations were qualified as real emergency.
Conclusions Actually, the management of ophthalmic emergencies is a real public health problem. It is important to train emergency physicians and general practitioners, to address wisely to the specialist. Structures such as our unit seem to be an effective way to access care.

• T024

Is there a seasonal relationship with idiopathic anterior uveitis presentation?

SAUNDERS D , Schulz C , Lockwood A
Queen Alexandra Hospital, Ophthalmology, Portsmouth, United Kingdom

Purpose Trigger mechanisms for relapse of idiopathic acute anterior uveitis (AAU) include psychological stresses and depression. Seasonality is known to affect other stress related diseases such as bipolar disorder, with depression episodes more common in autumn and winter. This study aims to investigate whether seasonality is related to AAU presentations.
Methods The electronic patient records for the eye casualty department were retrospectively searched between January 2010 and December 2014 for all new presentations of AAU. Time of presentation was grouped into seasons. The p value was calculated from two tailed z scores of the season sample means.
Results Two thousand, five hundred and sixty-three new presentations of AAU were recorded during the study period. Of these 634 (24.73%) presentations were in spring, 652 (25.44%) were in summer, 647 (25.24%) were in autumn and 630 (24.58%) were in winter. No temporal correlation was found for AAU presentations during either autumn (p=0.86) or winter (p=0.76).
Conclusions No seasonal relationship with AAU presentations has been found. Stress as a trigger for AAU relapses is still not fully understood but associations are more likely to be found at the individual level.

• T025

Frequency of refractive errors and binocular vision anomalies in children with learning disability

YEKTA A A (1), Khabazkhoob M (2), Hashemi H (2), Shadalouee Z (1), Ostadimoghaddam H (3), Rezvan F (2), Azimi A (1), Heravian J (1), Yekta R (4), Davari Ashteyani R (5)
(1) Mashhad University of Medical Sciences, Optometry, Mahhad, Iran
(2) Noor Eye Hospital, Noor Ophthalmology Research Center, Tehran, Iran
(3) Mashhad University of Medical Sciences, Refractive Errors Research Center, Mahhad, Iran
(4) Fadak Cclinic, Fadak clinik, Mashhad, Iran
(5) Shahid Beheshti University of Medical Sciences, Psychiatry, Tehran, Iran

Purpose To determine the frequency of refractive errors and binocular vision anomalies in children with learning disability
Methods In a cross-sectional study, 406 children with learning disability were selected by systematic sampling from the clinic of psychiatry, Emam Hosein hospital, Tehran, Iran. The mean age of the children was 8.56 ± 2.40 years (range: 5.00-14.00 years). After excluding the subjects with history of eye surgery and including criterias, examinations were carried out by experienced optometrist. Ophthalmic tests included: cycloplegic autorefraction, visual acuity, cover test, amplitude of accommodation, near point of convergence and stereopsis. Myopia and hyperopia were defined as spherical equivalent less than -0.50 Diopter (D) and more than +1.00 D. respectively. Astigmatism was defined as cylinder power worse than 0.75 D.
Results The frequency of myopia, hyperopia and astigmatism were 14.50% , 6.90% and 18.50% in children with learning diability respectively. Esophoria and exophoria were found in 1.00% and 6.40% of the children respectively. The optimal visual acuity was found in 98.50 % of the subjects.The frequency of exotropia, esotropia and cyclotropia were found in 1.50%, 1.00% and 0.20 % respectively. Suppression was found in 2.20% of the children. The means amplitude of accommodation and near point of accommodation were 15.53 diopter and 10.12 cm in these subjects, respectively.
Conclusions The results of this study indicated that the frequency of refractive errors and binocular vision anomalies in children with learning disabilities are similar to normal children and are not the main causes of learning disability.

• T026

Homocysteine and risk of wet age-related macular degeneration: a meta-analysis

PINNA A (1), Zaccheddu F (1), Boscia F (1), Solinas G (2)
(1) University of Sassari, Department of Surgical- Microsurgical and Medical Sciences- Unit of Ophthalmology, Sassari, Italy
(2) University of Sassari, Department of Biomedical Sciences- Laboratory of Epidemiology and Biostatistics, Sassari, Italy

Purpose Wet age-related macular degeneration (AMD) is an important cause of vision loss. We performed a meta-analysis review of the literature to assess the role of plasma total homocysteine (tHcy) concentration a as risk factor for wet AMD.
Methods Data sources included PubMed searches and searching reference lists of relevant articles and reviews. The literature review was performed according to the guidelines of Meta-analysis of Observational Studies in Epidemiology (MOOSE). Case-control studies were eligible for inclusion. Meta-analysis summary estimates were obtained using a random-effects model to account for between-study heterogeneity.
Results 9 case-control studies were identified, for a total of 422 cases and 467 controls. The mean tHcy was on average 1.18 micromol/L (95% confidence interval [CI] = 1.03-1.33) greater in the wet AMD cases compared with the controls (P<0.001), but patients' and controls' ages showed a high degree of between-study heterogeneity. After exclusion of the two studies with higher age heterogeneity, there were 243 cases and 277 controls and the mean tHcy was on average 0.7 micromol/L (95% CI =0.52-0.88) greater in the wet AMD patients compared to the controls (P=0.03).
Conclusions There is some weak evidence that elevated tHcy might be associated with wet AMD; however, this result should be interpreted cautiously because of a marked heterogeneity between the study estimates and the possible effect of publication bias on the tHcy findings.

• T027

The inhibitory effect of Itraconazole on Corneal neovascularization in Rabbits

YANG S (1), Won J Y (1), Lee H S (1), Joo C K (1), Chung S K (2)
(1) Department of Ophthalmology and Visual Science- Seoul St. Mary's Hospital- Catholic University of Korea- College of Medicine, Ophthalmology, Seoul, South-Korea
(2) Department of Ophthalmology and Visual Science- St. Paul's Hospital- Catholic University of Korea- College of Medicine, Ophthalmology, Seoul, South-Korea

Purpose To evaluate the inhibitory effect of itraconazole on corneal neovascularization in rabbits.
Methods Corneal neovascularization was induced in 36 eyes of 18 rabbits by suture placement in the corneal stroma. Seven days after suture placement, all rabbits were randomly divided into 4 groups and were treated four times daily with balanced salt solution (Group 1, 4 rabbits), topical 0.5% itraconazole (5 mg/mL , Group 2, 4 rabbits), topical 1% itraconazole (10 mg/mL , Group 3, 6 rabbits), and topical 2% itraconazole (20 mg/mL , Group 4, 4 rabbits). After one week, the surface area of corneal neovascularization was assessed on the digital photographs. In the corneal specimens, the concentration of VEGF A (vascular endothelial growth factor), VEGF R2, and PLGF (placental growth factor) mRNAs was measured by RT-PCR, and the concentration of ERK, p-ERK, Flk, and p-Flk was measured by Western Blotting.
Results The surface area of induced corneal neovascularization was significantly smaller in Groups 2, 3, and 4 compared to the control group on day 14 ($p<0.05$). RT-PCR analysis showed that the mean concentration of VEGF and PLGF in Groups 2, 3, and 4 was significantly lower than that in the control group after 7 days of treatment. Western Blotting analysis showed that the mean concentration of p-ERK, Flk, and p-Flk in Group 3 was significantly lower than that in the control group after 7 days of treatment.
Conclusions Topical itraconazole application was useful for effective inhibition of experimental corneal neovascularization.

• T028

Three dimensional meibography for diagnosis of dry eye syndrome

BYUN Y S (1), Yoo Y S (1), Eom T J (2), Na K S (3), Joo C K (1)
(1) Seoul St. Mary's Hospital, Ophthalmology, Seoul, South-Korea
(2) Gwangju Institute of Science and Technology- School of Information and Communication, Information and Communication, Gwangju, South-Korea
(3) Yeouido St. Mary's Hospital, Ophthalmology, Seoul, South-Korea

Purpose The dysfunction of meibomian glands which secrete components of lipid layer in tears is currently pointed out as one of the main causes occurring dry eye. The distribution of that is more than 70% in Asian, especially. This brought out the importance for the dysfunction of meibomian glands. Our study was aimed to confirm the efficacy of 3D meibography to evaluate the structures of meibomian glands.
Methods This study is a cross sectional study for patients who had diagnosed as dry eye disease associated with the dysfunction of meibomian glands at Seoul Saint Mary's Hospital from July to October, 2014. To confirm the structure of dry eye patients, 3D images using 3D OCT (optical coherence tomography) and 2D images using infrared camera were obtained. Patients who had the drop-out lesion in 3D and 2D images were divided as two groups, and differences between them were analyzed. At the same time, to find the clinical signification for structural changes of meibomian glands, all patients had an ocular surface and a tear function examination to define the degree of dry eye.
Results As compared between 3D and 2D images for dry eye patients who had the drop-out lesion on meibomian glands, 3D images was more useful for diagnosis of dry eye than 2D, especially in dry eye related with mild meibomian gland disease.
Conclusions Our study confirmed that the structural change of meibomian glands was reflected in optical coherence tomography 3D images. Especially, 3D meibography was more powerful than 2D infrared camera to find out the real state of drop-out lesion on meibomian glands. But, there was no statistical significance between the location of drop-out lesions; such as near lid margin, middle area, near superior conjunctival fornix, and clinical features in these study.

• T029

The use of matrix therapy in the Treatment of corneal perforation

LAZREG S
Cabinet Lazreg, Cabinet d'ophtalmologie, Dar el Beida, Algeria

Purpose Corneal perforation may be the most severe complication of ocular surface and corneal inflammation, the purpose of this study is to treat these small perforations
Methods Patients with corneal perforation in Sjögren's syndrome disease, we're treated by Cacicol at the dose regiment of one drop every other day for 3 weeks associated to an hydrophilic contact lens, the follow up visits were performed every day the first week , than every week the first month.
Results 5 cases of corneal perforation were treated , 4 females, mean age 73+/- 23 years, the size of the perforation was less than 1 mm in all cases, and the time between the perforation and the onset of the treatment was less than 24 hours, all the patients were treated for severe dry eye in Sjögren's disease since many years , the perforation were no painful in all cases, The beginning of corneal healing was observed between D 3 and D7, and the total cicatrization of the perforation was observed at d 15 for all patients.
Conclusions Matrix therapy can be helpful in small size corneal perforation associated to contact lens bandage in the absence of amniotic membrane,

• T030

An unusual germ responsible for fungal keratitis: Metarrhizium Anisopliae

ZAIDI M , Bazard M C , Dorin J , Machouart M , Angioi K
Universitary Hospital of Nancy, Meurthe et Moselle, Vandoeuvre les Nancy, France

Purpose Fungal keratitis remain rare, and often have a poor visual prognosis. About 30% require a keratoplasty. Many fungal agents may be involved. We report the first case of Metarrhizium Anisopliae keratitis in Europe.
Methods A 39-years old man complained about pain and redness in his right eye 15 days after having received earth on his face. His ophtalmologist diagnosed a corneal abscess and initiated a local treatment by Ciprofloxaxin. The patient was referred to our clinic 2 days later for worsening of local abscess. Visual acuity was limited to 2/10 RE and 10/10 LE. Slit-lamp examination revealed diffuse conjunctival redness, and a 3-mm diameter corneal abscess surrounded by diffuse corneal edema. After realization of a corneal scraping (which results happened to be negative), we introduced local antibiotherapy (Vancomycin-Ceftazidim), associated with Amphotericin B and Hexamidin. Despite these treatments and the realization of a therapeutic ptosis for persistent ulcer, the abscess enlarged and a deep stromal infiltration developed. As we suspected a fungal etiology, systemic Voriconazole was added. Despite all these treatments the abscess worsened dramatically and a transfixiant keratoplasty was performed.
Results Microbiological analysis of the cornea revealed neither bacteria nor amoeba or viruses, but presence of a filamentous fungus secondary identified as Metarrhizium Anisopliae by molecular biology.
Conclusions Metarrhizium anisopliae is usually known as an entomopathogenic fungus. It was first described in human pathology 18 years ago and only 9 cases have been reported worldwide, including 4 cases of keratitis. Our patient is the first case of Metarrhizium Anisopliae keratitis described in Europe. This report also shows that transfixiant keratoplasty is often the only treatment that allows visual rehabilitation in such dramatic cases.

• T031

Evaluation of a cyclosporine A ophthalmic ointment in an experimental mouse model of dry eye.

CIMBOLINI N , Antonelli S , Mauro V , Feraille L , Elena P P
IRIS PHARMA, Research Department, La Gaude, France

Purpose Dry eye syndrome is a common disease with multifactorial causes. Symptoms typically include irritation, dryness, burning and decreased or fluctuating vision. Anti-inflammatory drugs are widely used for the treatment of the inflammation produced by the disease with corticoid or cyclosporine A (CsA). Restasis® (Allergan), a CsA emulsion, was approved by the FDA but is not available in Europe. Here we propose to show the action of Optimmune® (MSD Animal Health) a marketed veterinary ophthalmic ointment that contains CsA in an experimental mouse model of dry eye induced by scopolamine, a tropane alkaloid drug with muscarinic antagonist effects
Methods Animals were divided in three groups of ten pigmented mice: Two groups were exposed to desiccating conditions (relative humidity <25%, air-flow 15L/min, temperature 20-22°C) with transdermal scopolamine administration (0.5 mg/72h) for 14 days. Animals were treated topically three times a day with 0.2% CsA ointment or vehicle. Controls were saline-treated animals placed in a normal environment. Tear production was measured with the phenol red thread test, corneal defects were examined by slit-lamp observation using blue light after 0.5% fluorescein eye drop. These examinations were performed in both eyes before exposure and on days 3, 7 and 14. A histological study was performed at the end of the study.
Results Cyclosporine A eye ointment appeared to show efficacy in this model.
Conclusions Cyclosporine A eye ointment significantly reduced clinical signs of dry eye by decreasing corneal defect more than cyclosporine A ophthalmic emulsion (internal studies).

Commercial interest

• T032

Correlation of Osmolarity Measurements with Signs and Symptoms in the Norwegian Dry Eye Clinic

BADIAN R A (1), Eidet J R (1,2), Ræder S (1,2), Utheim Ø (1,3), Chen X (4), Stojanovic A (4,5), Utheim T P (1,6)
(1) The Norwegian Dry Eye Clinic, The Norwegian Dry Eye Clinic, Oslo, Norway
(2) SynsLaser Kirurgi, SynsLaser Kirurgi, Oslo, Norway
(3) Oslo University Hospital, Department of Ophthalmology, Oslo, Norway
(4) SynsLaser Kirurgi, SynsLaser Kirurgi, Tromsø and Oslo, Norway
(5) University Hospital of North Norway, Department of Ophthalmology- University Hospital of North Norway, Tromsø, Norway
(6) Unit of Regenerative Medicine-Oslo University Hospital, Department of Medical Biochemistry, Oslo, Norway

Purpose To evaluate the relationship between osmolarity and signs and symptoms of dry eye disease (DED) in a Norwegian cohort of patients with DED.
Methods Clinical signs and symptoms were evaluated for 365 subjects at the Norwegian Dry Eye Clinic. All patients received an extensive ophthalmological work-up, including tear meniscus height, blink rate, corneal sensibility, tear film break-up time, Ocular Protection Index, vital staining, Schirmer I, meibum quality and meibum expressibility. Pearson correlations between signs and symptoms were performed. P values below 0.05 were considered significant.
Results High osmolarity correlated with lower ocular protection index (0,32) and higher blink interval (0,12), but no other parameters.
Conclusions Osmolarity did not correlate strongly with any parameters of dry eye disease.

• T033

A case of significant refractive change in nodular posterior scleritis

YOON S , Jeong H , Kim H , You T
Pureun eye center, Department of Ophthalmology, Jeonju, South-Korea

Purpose The aim of this study is to report refractive change in a patient with nodular posterior scleritis.
Methods A 43-year-old woman visitied clinic with a complaint of near vision discomfort associated with ocular pain and conjunctival injection. Her past ocular history was myopia of both eye, refractive error was -1.00D and uncorrected visual acuity was 20/40.
Results On ocular examination, uncorrected visual acuity was 20/20 in her right eye. But, refrective error of right eye changed -1.00D to +0.25D. Fundus examination revealed an large submacular mass associated with subretinal fluid surrounding it. B-scan ultrasonography, optical coherence tomography, fluorescein angiography, and indocyanine green angiography findings confirmed a nodular posterior scleritis. But, brain and orbit MRI was normal finding except posterior scleritis. As treatment, nepafenac eye drops 3 times a day, and flurbiprofen tablet 100 mg twice a day were prescribed. After 4 weeks of treatment, the ocular pain was relieved, refractive error was changed +0.25D to -1.00D and subretinal mass totally regressed.
Conclusions In case of severe nodular posterior scleritis, refractive error changes can appear at chief complain. So, In the case of refractive error change associated with ocular pain, nodular posterior scleritis should be evaluated.

• T034

Comparison of CKC- and BAK-cationic emulsions in a rat model of corneal wound healing

DAULL P (1), Feraille L (2), Elena P P (2), Garrigue J S (1)
(1) Santen SAS, Novagali Innovation Center, Evry, France
(2) Iris Pharma, R&D, La Gaude, France

Purpose Dry eye disease (DED) is a chronic disorder that afflicts 20% of the population. One prominent feature of DED is the ubiquitous presence of inflammatory cells and corneal epithelium damages in DED patients. The aim of the present study is to compare the efficacy of unpreserved cationic emulsions (CEs) with cetalkonium (CKC) or benzalkonium (BAK) chloride as cationic agents on debrided rat corneas healing and inflammatory response.
Methods The CEs were assessed in a rat model of corneal scraping. The upper part of the corneal epithelium was scraped prior to a 5-day treatment with the CEs. Paces of corneal recovery and clinical evaluations (in vivo confocal microscopy (IVCM) and Draize tests) were used to evaluate the healing process. Inflammatory cells count in the corneal stroma was assessed by IVCM.
Results Corneal healing was only marginally affected by the different treatments, and was almost complete at day 5. However, cornea wounds closed more rapidly when treated with CKC-CEs than with BAK-CEs. Interestingly, both Draize and IVCM scores indicate that treatments with the CKC-CEs resulted in a better healing process when compared to BAK-CEs. The number of inflammatory cells was also at its lowest following treatments with CKC-CEs.
Conclusions By restoring a hydrated ocular surface the different treatments promote corneal healing. Inflammatory cells count in the stroma was at its lowest with the preservative-free CKC-CEs, suggesting that CKC and BAK have indeed different properties and effects on the ocular surface. Hence, Ikervis®, a CKC-CE of cyclosporine, represents a promising treatment option for the management of corneal lesions and inflammation in DED patients.

Commercial interest

• T035

From devastation to restoration: trichosporon asahii can be beaten

AYDIN YAZ Y (1), Yildirim N (2), Oz Y (3), Sahin A (2), Yaz Y (4)
(1) Eskisehir State Hospital, Opthalmology, Eskisehir, Turkey
(2) Eskişehir Osmangazi Üniversitesi, Ophthalmology, Eskişehir, Turkey
(3) Eskişehir Osmangazi Üniversitesi, Microbiology, Eskişehir, Turkey
(4) Ekişehir Yunusemre State Hospital, Ophthalmology, Eskişehir, Turkey

Purpose To report the first case of fungal keratitis caused by ***T.asahii*** which is treated succesfully with penetran keratoplasty.
Methods A 79-year-old woman was attended to our clinic with pain and hyperemia in her left eye. The patient had undergone phacoemulsification and intraocular lens implantation surgery from her left eye 9 months ago, and after the surgery visual acuity had been reported 0,8. 4 months after the surgery bullous keratopathy was occurred and treated with bandage contact lens and topical steroids. When she was evaluated visual acuity was light perception and slit lamp examination showed in anterior segment a large keratitis area, central of keratitis area was melted, anterior chamber was shallow and hypopyon was occurred. In direct examination hyphae formation was seen.
Results Fluconazole 200mg 2x1, Cefazolin 50mg/ml gtt per hour, Voriconazole %1 gtt per hour, Cyclopentolate %1 3x1, Phenilephrin %2.5 3x1, Tropicamide %1 3x1, Acetozolamide 250 mg 2x1 treatment were started empirical until the culture and antibiograme were resulted. Culture was resulted and ***Trichosporon asahii*** was isolated. The microorganism was sensitive for voriconazole and fluconazole, resistant for amphotericin B. According to the antibiograme results, systemic fluconazole and topical voriconazole treatment were continued. The keratitis area was healed with medical treatment but cornea was spontaneously perforated in 15th day of treatment and penetrating keratoplasty was performed immediately. After penetrating keratoplasty visual acuity was reached 0,1 and corneal graft was clear.
Conclusions Fungal keratitis is vision threatening corneal disease causing by corneal ulceration. ***Trichosporon*** is one of the uncommon agent for fungal keratitis. This is the first case reported as a fungal keratitis caused by ***T.asahii*** treated successfully with penetrating keratoplasty.

• T036

Blepharitis and thin corneal thickness : An unexpected association

TRECHOT F (1), Conaert J B (1), Perone J M (2), Angioi K (1)
(1) CHU Nancy, Ophthalmology, Nancy, France
(2) CHR Metz-Thionville, Hopital de Mercy, Metz, France

Purpose The aim of this study is to measure central corneal thickness in patients with blepharitis associated with meibomian gland dysfunction. Local inflammation and alteration of the tears film might result to corneal thinning.
Methods All consecutive patients seen in consultation with blepharitis in our Department of Ophthalmology in November 2014 were included. Blepharitis clinic criteria were those reported by MGD workshop. Meanwhile a control group was set up. Patients with ophthalmic associated pathology, or recent history of ophthalmic surgery were excluded. The central corneal thickness was measured with a non contact pachymeter (NT 530P,Nidek, Jp).
Results The study group was made of 40 eyes of 20 patients (11 men) with blepharitis, mean age was 58.5±14.4. Forty eyes of 20 healthy patients (9 men) were used as a control group, mean age was 56.75±13.39. The study group and the control group were comparable in gender and in age. In the study group, the mean central thickness was 527.5µm±29.8 and in the control group mean central corneal thickness was 554.9µm±24.7. There was statistically significant difference between the two groups using a Z normal distribution test.
Conclusions Blepharitis may be associated with a thinner corneal thickness. Increased of osmolarity in the tear fluid and ocular surface inflammation are likely to be the cause of this decrease.

• T037

Safety and Efficacy of a Polyethylene Glycol/Propylene Glycol Based Lubricant Eye Drop in Patients with Dry Eye.

LABETOUILLE M (1), Messmer E (2), Ogundele A (3), Mouriaux F (4), Baudouin C (5)
(1) CHU Bicetre- South Paris University, Ophthalmology, Le Kremlin Bicêtre, France
(2) Ludwig-Maximilian-University, Ophthalmology, Munchen, Germany
(3) Alcon Research- Ltd., Ophthalmology, Fort Worth, United States
(4) CHU Rennes, Ophthalmology, Rennes, France
(5) Quinze-Vingts Institute, Ophthalmology III, Paris, France

Purpose The objective of this study was to compare the efficacy and safety of a polyethylene glycol/propylene glycol based eye drop (PEG/PG; Systane® Ultra) to an osmoprotective-carboxymethylcellulose based eye drop (CMC/O; Optive®) in patients with dry eye.
Methods This was a multicenter, observer masked, parallel-design study, subjects were randomized to PEG/PG or CMC/O QID for 35 days (Phase 1) and then as needed for 55 days (Phase 2). Eligible subjects were diagnosed with dry eye and exhibited signs and symptoms at screening. Supportive efficacy assessments included the total ocular staining score (TOSS) score change from baseline to Day 90 (15-point Oxford scale).
Results Demographic characteristics were similar between the PEG/PG (n=46) and CMC/O groups (n=48). The efficacy of PEG/PG was similar to CMC/O at Day 90 (LS mean treatment difference in TOSS score change from baseline to Day 90 of -0.10 units in favor of PEG/PG). In addition, ocular surface staining associated with dry eye decreased following treatment with PEG/PG with a mean TOSS score change from baseline at Day 90 of -2.7 units. No treatment-related serious adverse events were reported. Five subjects discontinued due to treatment-related AEs (2 PEG/PG and 3 CMC/O subjects).
Conclusions PEG/PG based drop demonstrated comparable efficacy to the CMC/O based drop after 90 days treatment with a favorable safety profile in patients with dry eye.

Commercial interest

• T038

Clinical Efficacy of an Oil-based Lubricant Eye Drop in Dry Eye Patients with Lipid Deficiency.

LABETOUILLE M (1), Maurino V (2), Ogundele A (3), Rossi G C M (4), Van der Meulen I (5), Mrukwa-Kominek E (6), Galarreta D (7), Boehringer D (8), Baudouin C (9)
(1) CHU Bicetre- South Paris University, Ophthalmology, Le Kremlin Bicêtre, France
(2) Moorfields Eye Hospital, London, United Kingdom
(3) Alcon Research- Ltd., Fort Worth, United States
(4) IRCCS- Policlinico San Matteo Clinica Oculistica, Pavia, Italy
(5) Academic Medical Center, Ophthalmology, Amsterdam, The Netherlands
(6) University Center of Ophthalmology and Oncology Silesian University of Medicine, Katowice, Poland
(7) Hospital Clinico Universitario de Valladolid, Valladolid, Spain
(8) Eye Center- University Hospital Freiburg, Freiburg, Germany
(9) Quinze-Vingts Institute, Ophthalmology III, Paris, France

Purpose To demonstrate the superior efficacy of a propylene glycol-based, micro-emulsion eye drop (SYSB; Systane® Balance) over Preservative-Free 0.9% Saline (PFS) Solution in patients with lipid-deficient dry eye.
Methods This was a multicenter, observer masked, parallel-design study (powered to show superiority). Subjects were randomized to receive SYSB or PFS QID for 35 days (Phase 1) and then as needed for 55 days (Phase 2). Eligible subjects had lipid-deficient dry eye with meibomian gland dysfunction.
Results A total of 279 patients were enrolled, 214 were randomized and 210 received the assigned study treatment. Baseline and demographic characteristics were similar between SYSB (n=110) and PFS (n=100) groups. At the end of the study, the mean change from baseline (±SEM) in TFBUT at Day 35 was 1.5 (0.2) and 0.5 (0.2) for SYSB and PFS respectively, representing a difference of 1.0 (0.3), significantly in favor of SYSB (p=0.0011). Twenty one (19.1%) patients receiving SYSB and 8 (8.0%) patients receiving PFS experienced ocular treatment-emergent AEs.
Conclusions SYSB demonstrated superior efficacy to PFS in patients with lipid-deficient dry eye and was well tolerated over the 90 day of treatment.

Commercial interest

• T039

Semi-automated reconstruction of inflammatory infiltration in infectious keratitis

SMEDOWSKI A (1,2,3), Tarnawska D (1,4), Wylegala E (1)
(1) Medical University of Silesia, Ophthalmology, Katowice, Poland
(2) Medical University of Silesia, Physiology, Katowice, Poland
(3) University of Eastern Finland, Ophthalmology, Kuopio, Finland
(4) University of Silesia, Department of Biophysics and Molecular Physics- Institute of Physics, Katowice, Poland

Purpose To perform reconstruction of inflammatory cells infiltration in infectious keratitis.
Methods First we performed in vivo confocal microscopy (HRT III, Rostock Cornea Module) in 118 patients diagnosed for the infectious keratitis (45 viral, 40 bacterial, 23 fungal, 10 amoebal). Inflammatory cytology has been analyzed according to morphology and size of cells forming infiltration. Microscopic scans were then processed with stereological software (MicroBrightField Inc, VT, USA) to track inflammatory cells within scans. Representative reconstructions of inflammatory cells infiltration has been created for each etiology of keratitis based on previous characterization of cells.
Results Overall inflammatory cells densities showed no specificity for keratitis etiology, however there was clearly different participation of morphological types of cells depended on keratitis etiology. Leukocyte-like, round cells represented approximately 4.4% of inflammatory cells in viral, 91.2% in bacterial, 50.4% in fungal and 54.4% in amoebal keratitis. Rest of cells were represented by different forms of dendritic cells, which were possible to track in stereology.
Conclusions In vivo analysis of corneal epithelial cytology provides useful information about keratitis etiology. Reconstruction of inflammatory cells infiltration can help to create diagnostic algorithm for infectious keratitis diagnosis.

• T040

Experience with the monoclonal anti IgE antibody Omalizumab in severe refractory vernal keratoconjunctivitis in children

DOAN S (1), Amat F (2), Gabison E (1), Just J (2), Cochereau I (1)
(1) Hopital Bichat and Fondation A de Rothschild, Ophthalmology, Paris, France
(2) Hopital Trousseau, Allergology, Paris, France

Purpose Vernal keratoconjunctivis (VKC) is a severe form of pediatric ocular allergy, characterized by acute and chronic corneoconjunctival inflammation that may lead to visual sequelae. Although topical cyclosporine is usually effective, severe forms may be refractory and require prolonged steroid therapy. Omalizumab is a monoclonal anti IgE antibody, administered systematically and authorized for severe asthma. We report our clinical experience with omalizumab in severe VKC children.
Methods We retrospectively reviewed the files of 4 boys treated with omalizumab because of severe VKC, defined as persistent corneal inflammation despite continuous topical 2% cyclosporine and steroid eye drops.
Results Four boys, aged 7 to 13 years old, were treated. All children had asthma and 1 had severe lid eczema. Two patients had required supratarsal steroid injections. Omalizumab was administered every 2 weeks by subcutaneous injections, at doses varying from 450 to 600 mg per injection. Three patients out of 4 responded to the treatment, with a decrease in frequency and in duration of the inflammatory flares, and also a decreased need for topical steroid. However, the response was incomplete and they still had inflammatory corneoconjunctival flares despite continuous topical cyclosporine. On the other hand, asthma and lid eczema were completely controlled in these 3 patients. The fourth child did not respond to o and needed oral steroids for his VKC and his asthma. Noticeably, this patient did not have detectable sensitization to any allergen, contrary to the other cases. The treatment was stopped in this refractory case, but is still ongoing in all other cases, with a median duration of 16 months (6 to 26 months).
Conclusions Omalizumab is an interesting treatment in severe refractory forms of VKC, but its efficacy is incomplete in these very severe cases.

• T041

Assessment of the size spectrum of epithelial lesions of punctuate superficial keratitis during dry eye

COURRIER E (1), Lepinet T (2), Hor G (1), He Z (1), Chikh M (3), Thuret G (4), Gain P (1)
(1) Jean Monnet University, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint-Etienne, France
(2) University of Lyon- Jean Monnet University, Hubert Curien Laboratory UMR 5516 CNRS, Saint-Etienne, France
(3) University Hospital, Ophthalmology, Saint-Etienne, France
(4) Jean Monnet University, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine AND Institut Universitaire de France- Bd St Michel- Paris, Saint-Etienne

Purpose Quantification of staining of the ocular surface by fluorescein and lissamine green is important for diagnosis and follow up of dry eye syndromes, especially in clinical trials. Analysis of digital pictures may help improving the reliability of this quantification but require objective data on the basic lesions constitutive of punctuate superficial keratitis (PSK) to develop adequate algorithms. Aim: to evaluate the size spectrum of epithelial lesions of PSK during dry eye to improve the existing diagnosis tools.
Methods Fluorescein was instilled to six patients suffering from dry eye graded according to the Oxford scheme. Pictures (3008x1960px) were taken using a Topcon slit-lamp using the Cobalt blue light without barrier filter. Two magnifications (x10 and x16) were used and calibrated using a certified standard reference grating. It allowed determining the size of observed objects with the software ImageJ. The most visible and isolated PSK lesions (green dots) were selected. The size of 180 different PSK lesions (30/patient, 15/magnification) were measured by tracing the light intensity profile and manually measuring the width at half maximum.
Results All patients combined, the mean was 21.6±4.8µm (15.2-30µm, 10°-90° percentile). Lesion diameters ranged between 11.4 and 30.4µm.
Conclusions Lesions seem to be smaller than epithelial cells (approximatively 25µmx50µm for superficial cells) and might correspond to the beginning of cell detachment with fluorescein retained between cells. These new quantitative data will help developing automatic recognition algorithm to obtain reliable objective classification of the corneal staining.

• T042

The inhibitory effect of Itraconazole on Corneal neovascularization in Rabbits

WON J Y (1), Chung S K (2)
(1) Seoul St. Mary's Hospital, ophthalmology center, seoul, South-Korea
(2) St. Paul's Hospital, Department of Ophthalmology, Seoul, South-Korea

Purpose To evaluate the inhibitory effect of itraconazole on corneal neovascularization in rabbits.
Methods Corneal neovascularization was induced in 36 eyes of 18 rabbits by suture placement in the corneal stroma. Seven days after suture placement, all rabbits were randomly divided into 4 groups and were treated four times daily with balanced salt solution (Group 1, 4 rabbits), topical 0.5% itraconazole (5 mg/mL , Group 2, 4 rabbits), topical 1% itraconazole (10 mg/mL , Group 3, 6 rabbits), and topical 2% itraconazole (20 mg/mL , Group 4, 4 rabbits). After one week, the surface area of corneal neovascularization was assessed on the digital photographs. In the corneal specimens, the concentration of VEGF A (vascular endothelial growth factor), VEGF R2, and PLGF (placental growth factor) mRNAs was measured by RT-PCR, and the concentration of ERK, p-ERK, Flk, and p-Flk was measured by Western Blotting.
Results The surface area of induced corneal neovascularization was significantly smaller in Groups 2, 3, and 4 compared to the control group on day 14 ($p<0.05$). RT-PCR analysis showed that the mean concentration of VEGF and PLGF in Groups 2, 3, and 4 was significantly lower than that in the control group after 7 days of treatment. Western Blotting analysis showed that the mean concentration of p-ERK, Flk, and p-Flk in Group 3 was significantly lower than that in the control group after 7 days of treatment.
Conclusions Topical itraconazole application was useful for effective inhibition of experimental corneal neovascularization.

• T043

Long-term results of the phase I/II clinical trial: standardized, non-xenogenic, cultivated limbal stem cell transplantation.

BEHAEGEL J , Ni Dhubhgaill S , Koppen C , Tassignon M J , Zakaria N
UZ Brussel, Ophthalmology, Brussels, Belgium

Purpose To evaluate the long-term success rate of transplanted non-xenogenic, bio-engineered, composite grafts of cultured limbal epithelial stem cells on standardized amniotic membranes in patients with limbal stem cell deficiency.
Methods We report the extended outcome of standardized cultivated limbal stem cell transplantations of our previous phase I/II trial. Between July 2008 and May 2012, 18 patients with partial or total limbal stem cell deficiency received either autologous (n=15) or allogenic (n=3) stem cell explants, using a protocol free from xenogenic products and a reduced manipulation surgical technique.
Results Six of the 18 patients were lost to follow-up. The remaining 12 patients had a mean follow-up of 46,6 months. Two of 10 patients experienced an evisceration, not related to the stem cell transplantation. 7 of the remaining 8 (87,5%) patients retained a persistent intact epithelium. Although we did see a significant reduction in corneal neovascularization of the corneas post transplantation, we did not see a significant improvement in visual acuity of the total cohort, although one patient gained a visual acuity from finger counting to 0,5 post limbal stem cell transplantation and post penetrating keratoplasty.
Conclusions This standardized culture system and surgical approach is safe and effective in restoring a functional epithelial cell layer, with satisfying long-term results. Due to the limited number of patients and the comorbidities, we did not see a significant improvement in visual acuity of the total cohort. We maintain that in selected cases this technique, followed by a penetrating keratoplasty can significantly improve visual acuity.

• T044

Analysis of the efficacy of the tissue regenerating agent (RGTA) 0.01% poly-carboxymethylglucose sulfate in the treatment of neurotrophic corneal ulcers and persistent epithelial defects

DEL BUEY M A (1), Casas P (1), Caramello C M (1), Esteban O (1), Martinez M (1), Sánchez N (1), Pinilla I (1), Lanchares E (2)
(1) " LOZANO BLESA" CLINICAL UNIVERSITY HOSPITAL, OPHTHALMOLOGY, ZARAGOZA, Spain
(2) Universidad de Zaragoza, Engeniering, Zaragoza, Spain

Purpose To report the results obtained in a series of 58 eyes with chronic corneal ulcers and persistent epithelial defects resistant to conventional therapy and treated with 0.01% poly-carboxymethylglucose sulfate based on tissue regenerating agent technology (RGTA, Cacicol®).
Methods A prospective study was made of 58 eyes. The ulcers were essentially chronic and slow-evolving, with mean vertical and horizontal diameters of 2.4 and 2.7 mm, respectively (range 1-5.5 mm). The patients received an initial dose of one drop every 48 hours during 10 days. After evaluation of the effects of treatment, new dosing schemes were prescribed for those patients who had improved their clinical condition though without complete resolution of the disease.
Results Important variation was observed in the time to recovery of corneal integrity, ranging from a few days to some weeks, depending on the severity and etiology of the case. Full healing was recorded in 50 patients. The patients with large neurotrophic ulcers showed improvement of the lesions, with a decrease in lesion size after 15 days of treatment. All patients reported subjective improvement. The drug showed immediate efficacy in 11 eyes with epithelialisation disorders following PRK or trauma, with recovery of tissue integrity after the first treatment period.
Conclusions The tissue regenerating agent (RGTA Cacicol®) is an interesting and effective topical adjuvant product for the treatment of severe and chronic corneal ulcers resistant to conventional treatment. Its efficacy remains to be confirmed in the context of double-blind, randomised clinical trials.

• T045

Ocular Sarcoidosis Surgery as the most effective option to avoid blindness

MARTINEZ M , Del Buey M , Perez I , Idoate A , Sánchez J I , Ascaso J , Cristobal J
Lozano Blesa" University Clinic Hospital, Ophthalmology, Zaragoza, Spain

Purpose To present the clinical evolution and diagnosis of a patient with binocular and no simultaneous affection of posterior synechiae, associated to bombe iris and neovascular glaucoma, without medical treatment response.
Methods Clinical case
A 63 year-old male is assisted in the ER because of progressive and painless visual loss in his left eye; visual acuity was only light perception. Anterior segment(AS) showed a synechia, ambarin atypical membranous tissue and neovascularization in the pupillary area, causing an iris bombe with no acute inflammatory signs and an IOP of 60 mmhg. Ocular sonogram and ultrasound bio microscopy didn't show tumor growth. The treatment with anti-inflammatory, hypotensive and mydriatic eye drops could not break the synechiae nor reach normal IOP. One year later, the patient came to the ER because of right eye visual loss. AS showed a similar synechial tissue, no tyndall effect and IOP of 20 mmhg. Due to the left eye experience, we decided to practice surgery in the right eye.
Results We took aqueous humor sample + synechiotomy + iridian biopsy + phacoemulsification with IOL. 20/20 visual acuity after surgery. After many medical tests and the anatomopathological study, the patient was released from the hospital with probable pulmonary and ocular sarcoidosis.
Conclusions If we have a patient with atypical progressive posterior synechiae without inflammatory signs and with no treatment response, we should think about sarcoidosis ocular as the diagnosis. Our experience shows that an early surgery is the most effective option to avoid blindness in these cases.

• T046

Study of Xailin night physical Properties versus marketed ocular lubricant products

PILOTAZ F (1), Pecout A (2), Do M (2)
(1) Nicox, Valbonne, France
(2) Octalia Technologies, Vallauris, France

Purpose Xailin Night is a multi-dose preservative free lubricating eye ointment for night-time relief of dry eye sensations. It contains white soft paraffin 57.3% w/w, white mineral oil 42.5% w/w and lanolin alcohols 0.2% w/w. Comparative studies were performed with Xailin Night against other marketed products in the EU in order to assess its key physical properties.
Methods Tested products cover the whole range of ocular lubricants from oily formula to aqueous compositions. The parameters studied were the following: Viscosity and rheological behaviour (25°C and 35°C), capacity to slow down evaporation at 40°C and 70°C, spreading capacity at room temperature and 35°C, long-lasting assessment. The products marketed in the EU assessed in this study were: Viscotears liquid gel, Lipolac, Celluvisc 4mg/0.4mL, Siccafluid 2.5mg/g, Bepanthen, Vismed multi, Hyabak 0.15%, Artelac Nighttime Gel.
Results At room temperature, Xailin Night viscosity shows an intermediate profile included between low viscosity gels (Siccafluid) and very highly viscous products (Bepanthen, Viscotears and Lipolac). As expected, temperature has an effect on the rheological behaviour of ointments but not on the other products. No evaporation is observed for Xailin Night whatever the temperature, while all the other tested products show a slight evaporation. Lipolac and Viscotears have a superior spreading capacity compared to pure aqueous-based products but remain significantly lower than ointments. As an ointment, Xailin Night has a superior long-lasting effect than aqueous products.
Conclusions Xailin Night is an ocular ointment with a strong long lasting effect and shows no evaporation compared to aqueous based ocular lubricants.

Commercial interest

• T047

Study of XAILIN HA Physical Properties versus Marketed Hyaluronate Based Ocular Lubricants

PILOTAZ F (1), Saldo J (2), Boix M (2)
(1) Nicox, R&D, Valbonne, France
(2) Octalia Technologies, R&D, Vallauris, France

Purpose Xailin HA is a multi-dose lubricating eye drop for alleviating symptoms of moderate to severe dry eye sensations. It contains sodium hyaluronate (HA) 0.2% w/w and sodium perborate in aqueous buffered vehicle. Perborate is a disappearing preservative that turns into water and oxygen upon contact with the ocular surface.
Comparative studies were performed with Xailin HA against other EU marketed HA products in order to assess its key physical properties.
Methods The parameters studied were the following: Macroscopic appearance, pH, osmolality, viscosity at 25°C, drop size and surface tension. The marketed products assessed in this study were: Xailin HA, Vismed multi, Hyabak, Hyalistil, Optive Fusion, Hylo-Comod, Hylo-vision HD, Artelac Splash MDO, Hylo-Gel.
Results All products are clear and colourless and their pH range is between 6.8 and 7.4. The tested products remain in the common range of osmolality for topical ophthalmic forms except Vismed multi (hypotonic, 150 mOsm/kg). Xailin HA presents the next lower osmolality (260 mOsm/kg). Four categories from less to more viscous products are observed: • Hyabak and Hylo-Vision • Artelac Splash MDO, Hyalistil, Optive Fusion, Hylo-Comod and Vismed Multi • Xailin HA • Hylo-Gel Xailin HA is significantly different from all others products with the lowest surface tension recorded.
Conclusions Xailin HA is a new hyaluronan-based ocular lubricant. Its low surface tension property should reflect a better distribution and spreading capacity on corneal surface than the other marketed products tested.

Commercial interest

• T048

Eyelid disorders evaluation in the Ophthalmic current practice in Belgium, Denmark, France, Netherland, Portugal and Turkey: The Meibum Study

DIAZ VALLE D (1), Doan S (2), Yagmur M (3), Benitez del Castillo J M (1)
(1) Hospital Clinico San Carlos, Servicio de Oftalmologia, Madrid, Spain
(2) Hôpital Bichat- Fondation A de Rothschild- Paris- France, Département ophthalmologie, Paris, France
(3) Cukurova University, The Medicine Faculty Balcalı Hospita, Adana, Turkey

Purpose To determine the incidence and characteristics of eyelid inflammatory disorders during general ophthalmological consultations and to demonstrate the association between palpebral pathologies and ocular surface pathologies in 6 of the 9 European countries involved in the MEIBUM survey
Methods Multi-center, international, transversal and epidemiological survey. The primary objective was to assess the percentage of eyelid disorders in patients attending a current ophthalmologic consultation. The secondary objectives were to assess the association between palpebral pathologies and ocular surface pathologies, the impact of eyelid disorders on patient's daily life (on vision, on daily life activities/work, on leisure, on contact lens wearing, on emotions and on sleep) .
Results A total of 1398 were included by ophthalmologists from Belgium, Denmark, France, Netherland, in Portugal and Turkey.The mean age was 56.2 (±17.5). At least an ocular history was found in 78.4 % of the patients. The main antecedents were "Dry eye" (25%), "Glaucoma" (15,7%) and "Cataract" (19,8%). The percentage of eyelid disorders was 73.4%. The diagnostic of Meibomian Gland Dysfunction (MGD) was established in 45.4% of the total patients and dry eye in 63.4%. The impact of MGD on daily life was mainly on vision for 60.2% of the patients, on daily activities/work (49.7%), on leisure (40.8%), but also on emotions (22.1%) and sleep (15.8%). MGD were treated by eyelid hygiene recommendations: warming (68.5%), massaging (67.7%) cleansing (78.9%), and eye drops for dry eye (79.5%).
Conclusions MGD was diagnosed in nearly half of the patients with a strong link to dry eye. The impact on daily life is notable. Only dry eye symptoms seem to be taken in charge more often than MGD

• T049

Neurotrophic keratitis (NK) in carotid cavernous fistulae (CCF)

STEPHAN S , Rouger H , Doan S , Lamirel C , Cochereau I , Gabison E
fondation A. de Rothschild, ophtalmology, paris, France

Purpose Carotid cavernous fistulae (CCF) are rare, with a poor visual outcome. In addition, lesions of trigeminal nerve induced by an elevated venous pressure in the cavernous sinus may induce a neurotrophic keratitis (NK). Embolization is the standard care.
The objective of this study was to assess NK in a group of patients treated by embolization of their CCF using in vivo confocal microscopy.
Methods Patients treated for an indirect CCF from January 2004 to May 2013 were prospectively included. The diagnostic of NK was assessed by Oxford's test, Cochet-Bonnet's esthesiometry and a study of corneal nerves by in vivo confocal microscopy. Results were compared using Student t-test.
Results 13 patients, 5 men and 8 women, with a median age of 67 years old were included with a median follow-up of 51 months: 38% (5/13) had a NK, of which 40% (2/5) bilateral. 60% (3/5) were clinically cured, with a minimal to moderate NK; and 40% (2/5) had persisting CCF symptoms with a moderate to severe NK.
Conclusions To our knowledge, NK resulting of a compression of the trigeminal nerve by CCF has never been studied. On the other hand, NK is a challenging diagnosis because of a poor clinical presentation. Recently, in vivo confocal microscopy has been developed for corneal nerves analysis and should therefore be considered as an interesting tool to assess NK in patients treated for a CCF. NK are frequent (38%) in patients treated for CCF. NK are minime to moderate and sometimes bilateral. Early diagnosis using in vivo confocal microscopy should avoid corneal complication.

• T050

Meibomian Gland Dysfunction (MGD) and Tear Cytokines after Cataract Surgery according to Preoperative Meibomian Gland Status

JUNG J W (1), Cho D (2), Kyoung Yul S (3)
(1) Inha University School of Medicine, department of ophthalmology, Incheon, South-Korea
(2) Ministry of unification, Hanawon, Hwacheon, South-Korea
(3) Severance Hospital- Yonsei University College of Medicine, Department of Ophthalmology, Seoul, South-Korea

Purpose To investigate the possible mechanisms by which cataract surgery aggravates meibomian gland dysfunction (MGD), we evaluated the changes in tear cytokines and ocular surface parameters after cataract surgery according to the preoperative MGD grade.
Methods Fifty patients who underwent cataract surgery were enrolled and classified into two groups: Group I had no or minimal MGD, and group II had grade 2-4 MGD. Ocular surface parameters were measured, including tear film break-up time (TBUT), Schirmer I test, ocular surface staining, and Ocular Surface Disease Index (OSDI), and tear cytokine levels were measured.
Results In group II, preoperative MGD grade, ocular surface staining, TBUT, and OSDI were worse and mean interleukin (IL)-2, IL-6, and TNF-α levels were higher than those of group I. MGD and ocular surface parameters were worsened to a greater degree after surgery in group II than in group I ($P < 0.050$). In group II, IL-6 and TNF-α levels significantly increased at postoperative 1 month, and there were significant correlations between changes in ocular surface parameters and tear cytokines (IL-2, IL-6, and TNF-α; $P < 0.050$).
Conclusions The extent to which the MGD grade was aggravated following cataract surgery differed based on preoperative MGD grade. In patients with definite MGD, which was associated with high cytokine levels, an increase of tear cytokines indicated an aggravation of severe MGD after cataract surgery. Preoperative MGD and ocular surface status should be carefully evaluated.

• T051

Dry Eye Disease Therapy: who are the non-responders?

EIDET J R , Ræder S , Chen X , Badian R , Utheim Ø , Utheim T P
Oslo University Hospital, Center for Clinical Research, OSLO, Norway

Purpose To investigate the parameters that characterize the patients that responds or do not respond to dry eye disease (DED) therapy as recommended by the International Dry Eye WorkShop 2007.
Methods 217 DED patients were consecutively included at the Norwegian Dry Eye Disease Clinic in Oslo, Norway. All patients underwent a comprehensive ophthalmological examination. The patients' symptoms were reported by means of three self-questionnaires (Ocular Surface Disease Index [OSDI], McMonnies Dry Eye Inventory [MDEIS] and the Sjögren's syndrome [SS] questionnaire [SSQ]). Patients were defined as treatment-responders if their dry eye severity level (DESL) score had improved following 6 months of treatment, and non-responders if their DESL score was unchanged or worse.
Results Non-responders were older (P=0.019), had lower baseline DESL score (P<0.001), had less pathological tear meniscus height (P=0.007) and used fewer systemic prescription drugs (P=0.046). Linear regression analysis showed that age, DESL and number of systemic prescription drugs used were independently associated with treatment response (P<0.05). Furthermore, patients were more likely to respond to therapy if it was initiated during winter, which suggests a seasonal effect. Females and males, as well as meibomian gland dysfunction (MGD) patients and non-MGD patients, were equally likely to respond to treatment.
Conclusions As the recommended therapy for DED is based on the DESL score of the patient our results may either indicate that the therapy recommended for the higher levels of DESL are more effective than that recommended for the lower levels of DESL or that effect is easier to detect in patients with more pronounced DED. Future studies should investigate whether patients with mild DED should be treated more aggressively.

• T052

Utility of peripheral lamelar corneal graft in PUK with corneal perforation treatment

SANCHEZ MARIN J1 , Del Buey M A , Perez I , Almenara C , Esteban O , Martinez M , Idoate A , Ascaso F J
Hospital Clínico Universitario Lozano Blesa, Ophthalmology, Zaragoza, Spain

Purpose Peripheral ulcerative keratitis (PUK) is a destructive inflammation of the limbal corneal stroma with oval morphology. It is characterized by a sectorial affection with corneal thinning, usually associated with an epithelial defect, cell infiltration and progressive lysis of the stroma, which can progress to corneal perforation. We present a case of a 88 years old woman who came to our hospital with epifora and foreign body sensation in the left eye. It was observed perforated marginal corneal ulceration in inferonasal quadrant with iris incarceration. She was treated with therapeutic contact lens and topical antibiotics and was programmed for surgery. In order to maintain the corneal integrity and due to the dimensions of the perforation, we decided to employ a lamellar corneal grafting because the use of tissue adhesives or amniotic membrane coating would be insufficient. This prevents the elimination of healthy cornea and keep better the anatomy. In the same surgery the graft was covered with amniotic membrane patch securing it with biological glue and coated with therapeutic contact lens.
Methods The lamellar corneal grafting was obtained by manually cutting one of the corneoscleral edges of a donor cornea, in which the central corneal button was drilled and used for another patient in a penetrating keratoplasty the same day of surgery.
Results The postoperative time coursed with no complications and showed good integration of corneal graft, through images of the anterior segment and AS-OCT.
Conclusions Lamellar corneal graft seems to be a good treatment option for maintaining the tectonic integrity in perforated patients due to peripheral ulcerative keratitis

• T053

Advancing age does not strongly correlate with symptoms and signs of Dry Eye Disease in a large Norwegian cohort

BADIAN R A (1), Eidet J R (2), Ræder S (2), Utheim Ø (3), Chen X (4), Stojanovic A (5), Utheim T P (6)
(1) *Innlandet Hospital Trust, Department of Ophthalmology, Oslo, Norway*
(2) *The Norwegian Dry Eye Clinic, The Norwegian Dry Eye Clinic, Oslo, Norway*
(3) *Oslo University Hospital- Oslo- Norway, Department of Ophthalmology- Oslo University Hospital, Oslo, Norway*
(4) *SynsLaser Kirurgi, Norway,*
(5) *SynsLaser Kirurgi, SynsLaser Kirurgi, , Norway*
(6) *Unit of Regenerative Medicine- Oslo University Hospital, Department of Medical Biochemistry, , Norway*

Purpose To evaluate the relationship between age and signs and symptoms of dry eye disease (DED) in a Norwegian cohort of patients with DED.
Methods Clinical signs and symptoms were evaluated for 957 subjects at the Norwegian Dry Eye Clinic. All patients received an extensive ophthalmological work-up, including tear meniscus height, blink rate, corneal sensibility, tear film break-up time, Ocular Protection Index, vital staining, Schirmer I, meibum quality and meibum expressibility[CJ1] , and in many cases osmolarity measurements. Pearson correlations between signs and symptoms were performed. P values below 0.05 were considered significant. [CJ1]This is not a real word, but may be in ophthalmology it is common.
Results No correlations above r2 = 0.28 were found between age and signs or symptoms. Increasing age was only correlated with lower protection index (0.13), lower Schirmer I values (0.22), lower corneal sensibility (0.15) and higher Meibum expressibility (0.28).
Conclusions Advancing age did not correlate strongly with any parameters of dry eye disease. This is particularly interesting as advancing age is regarded as a considerable risk factor for the development of dry eye disease.

• T054

Healing of a resistant neurotrophic corneal ulcer using a new matrix therapy agent (RGTA): A case report

Zghal I , ZAHAF A , Fekih O , Zayani M , Bouguila H , Nacef L
Institut d'ophtalmologie, Tunis, Tunis, Tunisia

Purpose We report a case of a resistant neurotrophic corneal ulcer successfully treated by the matrix regenerating agent (RGTA) Cacicol(®).
Methods We report a case of an 18-year-old female patient, who developed a persistent epithelial ulcer after cataract surgery complicated by endophthalmitis, with no improvement despite 4 weeks of artificial tears. A new ophthalmologic solution based on a regenerating agent (RGTA, Cacicol20®) was then used, with a dosage of two eye drops per week for 8 weeks.
Results Improvement was observed in 2 weeks, and complete healing was obtained in less than 5 weeks, with no side effects.
Conclusions This heparin mimetic, which may stimulate extracellular matrix healing, may be a possible alternative therapy to autologous serum or amniotic membrane transplantation in severe neurotrophic ulcer. However, randomized studies are necessary to confirm this encouraging result.

• T055

Corneal nerve activity during ocular inflammatory processes

LUNA C , Quirce S , Belmonte C , Gallar J , Acosta M C
Instituto de Neurociencias UMH CSIC, Neurobiologia Ocular, San Juan de Alicante, Spain

Purpose To study the changes in sensory nerve activity of the eye associated with ocular inflammation in two different experimental models developed in the guinea-pig.
Methods Allergic keratoconjunctivitis (AK): Ovalbumin sensitization was induced and blinking and tearing rate was measured before and after the allergic challenge. UV photokeratitis: One eye of the anesthetized guinea-pig was exposed to 254 nm radiation during different times. Blinking rate and tear secretion were measured before and 48 h after UV. In both models, nerve activity was recorded in vitro in the whole eye or the excised cornea superfused with physiological saline at a controlled temperature. Spontaneous (SA) and stimulus-evoked electrical activity were recorded. Mechanical, thermal and chemical sensitivity were tested in control and inflamed eyes.
Results In AK model tearing and blinking rate increased significantly. In nociceptors, mechanical threshold decreased, the percentage of units with SA increased and the impulse response to chemical stimulation increased significantly in inflamed eyes compared with controls. On the contrary, SA and response to cold of cold thermoreceptors decreased during inflammation.
Conclusions In ocular pathological processes primarily characterized by local inflammation, nociceptors became sensitized while cold thermoreceptors became desensitized, due to changes in the expression and/or activity of ion channels present in sensory nerve terminals. Disbalance in the sensory input from the different functional types of sensory nerve fibers innervating the ocular surface in inflammatory conditions may be in the bases of the unpleasant sensations evoked by inflammatory pathological processes affecting the ocular surface in humans.

• T056

Corneal surface temperature and tear secretion in young and adult aqueous tear deficient guinea pigs

GALLAR J , Luna C , Alonso E , Revert R , Quirce S , Aracil A , Belmonte C , Acosta M C
Instituto de Neurociencias- UMH-CSIC, Ocular Neurobiology, San Juan de Alicante, Spain

Purpose To evaluate changes in ocular surface temperature and tear secretion in young and adult control and tear-deficient (DE) guinea-pigs.
Methods Tearing rate (TR) was measured using phenol red threads (30s). Tear break-up time (TBUT) was measured after fluorescein instillation. Corneal surface temperature (CST) was recorded continuously in the full open eye during 30s after the eye opening using an infrared thermal camera (InfRec R300SR, Nippon Avionics). Images were analyzed using dedicated software.
Results Tearing rate was significantly higher and TBUT was significantly lower ($p<0.05$) in adult (12-18 months) compared with young (2-4 months) animals ($p<0.001$). CST immediately after the eye opening had a value around 36.5ºC in control eyes in young and adult animals. Most tear deficient eyes had initial CST over 37ºC. The slope of temperature decrease during the interblink period was similar for all ages. As expected, DE animals had significantly lower TR ($p<0.001$) and TBUT ($p<0.01$) than intact animals, although their initial CST and the slope of interblink temperature decrease were similar to age-matched control eyes.
Conclusions Tear-deficient eyes show higher CST values immediately after blink suggesting the presence of inflammation. Temperature reduction during the interblink period was not modified in DE, despite the reduced stability of tear film.

• T057

The Effect of Ikervis® (1mg/mL Ciclosporin cationic emulsion) on severe keratitis in patients with dry eye disease participating in a phase III study

LEONARDI A (1), Labetoulle M (2), Ismail D (3), Garrigue J S (4), Rancho L (5), Brignole-Baudouin F (5), Amrane M (3), Baudouin C (6)
(1) PADUA HOSPITAL, OPHTHALMOLOGY, PADUA, Italy
(2) KREMLIN-BICETRE HOSPITAL, OPHTHALMOLOGY, KREMLIN-BICETRE, France
(3) SANTEN SAS, MEDICAL AFFAIRS, EVRY, France
(4) SANTEN SAS, RESEARCH AND DEVELOPMENT, EVRY, France
(5) VISION INSTITUTE, OPHTHALMOLOGY, PARIS, France
(6) QUINZE-VINGT HOSPITAL, OPHTHALMOLOGY, PARIS, France

Purpose The treatment of severe keratitis in Dry eye disease (DED) represents a real therapeutic challenge. The effect of Ikervis®, an unpreserved 1mg/mL ciclosporin A cationic emulsion, in this condition was evaluated.
Methods Sansika study was a 12 month phase III, multicenter, double-masked, vehicle controlled, in which 246 DED patients with severe keratitis (corneal fluorescein staining, CFS, grade 4 on modified Oxford scale), were randomised to one drop of Ikervis® or vehicle daily at bedtime for 6 months. Vehicle patients switched to Ikervis® after 6 months.
Results The proportion of patients achieving by M6 at least a two-grade improvement in CFS and a 30% improvement in symptoms [Ocular Surface Disease Index (OSDI)] was 28.6% with Ikervis® vs 23.1% with vehicle, p=0.326. There was a greater improvement in Ikervis® treated patients over vehicle in mean CFS change from baseline (CFB) at M6 (-1.81 vs -1.48, p=0.037). The mean OSDI CFB was -13.6 with Ikervis® and -14.1 with vehicle at M6, p=0.858. There was a reduction in the ocular surface inflammation assessed with Human Leukocyte Antigen-DR (HLA-DR) expression in favour of Ikervis® at M6 (p=0.021). Post hoc analysis showed a greatest proportion of patients achieving a 3-grade improvement in CFS with Ikervis® over vehicle (28.8% vs 9.6%) at M6.
Conclusions This study confirmed the positive benefit/risk ratio of Ikervis® for the treatment of severe keratitis in DED. The availability in Europe of Ikervis® represents a significant progress in the management of this disease.

Commercial interest

• T058

Posterior corneal anatomy in a newborn baby

FARAJ L , Yeung A , Said D , Branch M , El Alfy M , Dua H
University of Nottingham, Ophthalmology, Nottingham, United Kingdom

Purpose In view of the recent developments in our understanding of posterior corneal anatomy and the description of a unique layer and zone in adults, we investigated two corneas from a three-week-old baby.
Methods both corneas were subjected to intra stromal air injection using a 30G needle. The type of big bubble formed was identified. The wall of the big bubble and the posterior stromal interface with Descemet membrane was studied using light microscopy, electron microscopy and immune-histological studies.
Results Intra stromal injection of air resulted in the formation of characteristic type 1 big bubble in one cornea and another characteristic type II big bubble in another. The wall of the type I big bubble bubble was made of endothelial cells, Descemet's membrane and a thin collagen layer anteriorly (previously described as Dua's layer [DL]). DL was made of 7-8 collagen lamellae of compactly opposed collagen. This was made of predominantly type I collagen with abundance of collagen VI. Thrombospondin was characteristically seen along the posterior surface of DL extending to the trabecular meshwork. The interface between DL and DM was not distinct but presented a transition zone. The wall type II big bubble was made of Descemet membrane only, which was extremely thin.
Conclusions We demonstrated here that the human infant cornea behaves similarly to adult cornea when subjected to air injection (dissection). We also demonstrated the presence of DL in a 3 week old baby and presented its histological characteristics.

• T059

Microfluidic in vitro Drug Release from Contact Lens Materials

FILIPE H P (1), Paradiso P (2), Valente A R B (2), Mata J L G (2), Saramago B (2), Henriques J M (3), Serro A P (2,4)
(1) IOGP, Ocular Surface- Ocular Imaging- Cataract Surgery, Lisboa, Portugal
(2) Instituto Superior Têcnico, Centro de Química Estrutural, Lisboa, Portugal
(3) Instituto Dr. Gama Pinto, Retina Cirúrgica, Lisboa, Portugal
(4) IST/ISCSEM, Centro de Química Estrutural Centro de Investigação Interdisciplinar Egas Moniz, Lisboa, Portugal

Purpose Over 90% of ophthalmic drugs are commonly applied as eye drops. However, drug tear film residence time is less than 5 min, and only 5% of the administered drug is absorbed, leading to a final poor drug bioavailability and eventual side effects Efforts have been made to develop more effective drug delivery systems. Therapeutic contact lenses (CLs) have demonstrated to be a good vehicle for a controlled release of a variety of drugs owing to their biocompatibility, high degree of comfort, and prolonged contact with the eye.
Methods CLs materials were prepared as a) a conventional hydroxyethylmethacrylate (HEMA) based hydrogel and as b) a silicone based hydrogel. The different materials were loaded with an antibiotic- levofloxacin (LVF), and one of two non-steroidal anti-inflammatory drugs (NSAID) -diclofenac (DCF) and ketorolac (KET). To simulate physiological human eye conditions such as temperature, tear volume and flow rate, drug release tests were carried out in a novel microfluidic cell.
Results Results showed that a) HEMA based hydrogel allows a drug release up to 10 hours with predicted concentrations in the eye as >129 µg/mL for LVF, >918µg/mL for DCF and > 251 µg/mL for KET whereas b) Silicone based hydrogel releases both NSAID for at least 4 days, with concentrations >163µg/mL for DCF and >31µg/mL for KET.
Conclusions Drug eluted CLs biomaterials can be used as a platform for ocular drug delivery applications.

• T060

Comparison between i-gel and endotracheal tube in corneal grafts: a randomized clinical trial

GUERRIER G (1), Rondet S (1), Hallal D (1), Levy J (1), Boutboul D (1), Sjögren L (2), Legeais J M (2), Nicolau R (2), Mehanna C (2), Bourges J L (2), Samama C M S (1)
(1) Hôpitaux Cochin Hotel-Dieu, Anesthésie-réanimation, Paris, France
(2) Hôpitaux Cochin Hotel-Dieu, Ophtalmologie, Paris, France

Purpose To assess the safety of the laryngeal mask I-Gel® in keratoplasty (KP) performed under general anaesthesia.
Methods Patients with indications for KP (n=110) were enrolled in a prospective study and randomly assigned to I-Gel® (n=55; 30 lamellar KP and 25 penetrating KP) or tracheal tube (n=55; 29 lamellar KP and 26 penetrating KP). Peri-operative complications and recovery time were compared between two groups using t-test or $\chi 2$ test. Contraindications to elective use of the laryngeal mask airway were exclusion criteria (oesophageal reflux, extreme obesity, oropharyngeal pathology, expected difficult intubation).
Results No surgical peri-operative complications were reported in either group. There was a significantly greater incidence of coughing at extubation and after extubation in the tracheal group (25/55; 45%) than in the laryngeal mask group (3/55; 5%) ($p<0.001$). Recovery time was shorter in the I-Gel® group (80min; 95%CI [75-86]) compared with the tracheal tube group (88min; 95%CI [82-95]) ($p=0.03$). There were no significant differences in the incidence of sore throat and hoarseness between the two devices.
Conclusions The use of I-Gel® for keratoplasty under general anaesthesia is safe, reduces the risk of potential ocular hypertension during recovery and saves recovery time.

• T061

Investigating the blue sclera in osteogenesis imperfecta by in vivo confocal microscopy.

JUILLIENNE R (1), Brehon A (1), Perrot J L (2), Forest F (3), Cinotti E (2), Labeille B (2), Peoc'h M (3), Thuret G (1), Gain P (1)
(1) University Jean Monnet- Faculty of Medicine, Laboratory Biology- engineering and imaging of Corneal Graft- EA2521, Saint-Etienne, France
(2) University Jean Monnet- Faculty of Medicine, Department of Dermatology, Saint-Etienne, France
(3) University Jean Monnet- Faculty of Medicine, Department of Pathology, Saint-Etienne, France

Purpose The blue sclera appearance is a distinctive clinical sign for osteogenesis imperfecta (OI), a connective tissue disorder caused by an abnormality of type I collagen. It is a challenging diagnosis because multiple bone fractures, occurring in early childhood, can be the only sign of the non-lethal forms of OI. In these situations, child abuse is a major concern for Paediatricians. Aim: To investigate the in vivo confocal microscopy (IVCM) of the sclera and its characteristics as a diagnostic test for OI.
Methods A father and his daughter suffering from OI gave informed consent for non-invasive ocular examination. The cornea and sclera were examined with a handheld dermatological IVCM (VivaScope 3000, MAVIG GmbH/Lucid), which we pioneered for ophthalmological examination. The examination of two age matched healthy volunteers and corneoscleral donor tissues served as a control.
Results The IVCM in OI shows a very specific and reproducible pattern where the collagen fibres have a well organised parallel alignment as would be expected within the clear corneal stroma. Collagen fibres were cross striated in the control.
Conclusions These findings were consistent with the electron-microscopic features previously described. The blue appearance results from the visualisation of the underlying choroid through the translucent sclera, which displays a specific parallel orientation of the collagen fibres. To the best of our knowledge, this is the first report of IVCM of the blue sclera. This rapid and non-invasive imaging technique is an interesting diagnostic tool for challenging cases, especially in children, with multiple bone fractures.
GRANT: GIRCI RAA

• T062

Upgrading wide field contact specular microscope

HOR G (1), Gavet Y (2), Gain P (1), Thuret G (1), Bernard A (1), Pinoli J C (2)
(1) Laboratory BiiGC- EA2521, Faculty of Medicine- Jean Monnet University, Saint Etienne, France
(2) CRNS UMR5307- Laboratoire Georges Friedel, Institut Mines de Saint Etienne, Saint Etienne, France

Purpose Non-contact specular microscopes (SM) developed 25 years ago highly facilitated image acquisition while eliminating contaminations risk. Nevertheless their very small field of observation (SM Topcon SP2000: 0,1 mm2) constitute major limitations for the assessment corneas. Aim: to upgrade a wide field contact SM with a digital camera and dedicated software.
Methods The original camera film was replaced by a digital camera (Canon EOS 6D with full-frame 35mm sensor) connected to a computer. The new camera was fixed on the SM (Konan SP5500, x40 zoom) with 3D print custom adaptor and uses its optics. After acquisition of wide field images (0.6 mm2), they were processed using a segmentation algorithm (watershed with markers method). Software, using several libraries (ITK, OpenCV, Qt, MySQL), has been developed allowing the acquisition of images (camera control), image processing, and storage of results in a database.
Results A segmented image showing only cell borders in black over white background and document which presents ECD number (1000 cells counted) and cell's characteristics showing quality of cells (regarding their size). Stored in a database, these results are available for operators.
Conclusions The upgraded wide field contact SM counts a great number of cells. Consequently, it estimates the ECD with less bias than other methods. Also, it can be used for the assessment of heterogeneous endothelium like in Fuchs corneal endothelial diseases for which noncontact SM are obviously unsuited.
GRANT: ANR 2012 CORIMMO project

• T063

Genotype and phenotype correlation of monogenic corneal dystrophies in population of central Poland

UDZIELA M (1), Oldak M (2,3), Sciezynska A (2), Ploski R (4), Szaflik J P (1)
(1) Medical University of Warsaw, Department Ophthalmology, Warsaw, Poland
(2) Medical University of Warsaw, Department of Histology and Embryology, Warsaw, Poland
(3) World Hearing Center- Institute of Physiology and Pathology of Hearing-, Department of Genetics, Warsaw, Poland
(4) Medical University of Warsaw, Department of Medical Genetics, Warsaw, Poland

Purpose To assess the genotype-phenotype correspondence in monogenic corneal dystrophies caused by *KRT*,*TGFBI* and *UBIAD1* genes mutation.
Methods 61 patients from 30 Polish families with clinically diagnosed epithelial and stromal corneal dystrophies participated in the study. Corneal phenotypes were assessed by slit lamp, AS-OCT,and confocal microscopy ***in vivo***. Genomic DNA was obtained from blood samples and respective exons (hot spots) were PCR amplified and sequenced on both strands.
Results Molecular genetic testing revealed heterozygous missense p.E498V mutation (exon 7) of KRT3 in one family with Meesmann corneal dystrophy phenotype, p.R555W (exon 12) mutation in nineteen patients diagnosed with granular type I dystrophy (GCD1). In two patients p.R124H mutation (GCD2, Avellino) was found. In three patients (2 families) heterozygous p.R124L (exon 4) mutation was identified and diagnosed as Reis-Buecklers dystrophy. In two unrelated patient p.R555Q (exon 12) mutation typical for Thiel-Behnke dystrophy was found. Heterozygous p.R124C (exon 4), p.T538R (exon 12) and p.H626R (exon 14) mutations were identified, respectively, in ten patients diagnosed with lattice corneal dystrophy (LCD1). A novel p.L565P mutation was found in one family with late-onset LCD. Among 18 idividuals (4 families) suffering from stromal Schnyder corneal dystrophy (SCD) molecular genetic testing revealed 3 different *UBIAD1* gene mutations: p.N102S, p.D112N, p.T120R.
Conclusions The genotype typical for monogenic corneal dystrophies caused by *KRT* and *UBIAD1* genes mutation corresponds with its clinical phenotype. *TGFBI* is associated with phenotype heterogenity and in some cases only genetic tests may confirm the proper diagnosis. This indicates that a relatively straightforward molecular analysis can be a practical use in diagnosis of these conditions and associated genetic counseling.

• T064

Visual acuity increases up to 7 years after Descemet Stripping Automated Endothelial Keratoplasty

HANSEN M S , Correll M H , Julian H
Copenhagen University Hospital Rigshospitalet Glostrup, Dept. of Ophthalmology, Copenhagen, Denmark

Purpose Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) for corneal endothelial dysfunction restores vision up to 5 years post-surgery, yet outcome exceeding this time span remains unknown. This study reports outcomes up to 7.8 years post-DSAEK in a prospective observational study.
Methods The cohort consists of the first 30 consecutive DSAEK-surgeries in 25 subjects at Rigshospitalet Copenhagen, in 2006-2007. Data are reported for 14 eyes of 10 subjects (median age 65.8 years, range 55-79 years) who completed more than 5 years of follow-up (mean 6.8 years, range 5.6-7.8). Best spectacle-corrected visual acuity (BSCVA) was obtained using Snellen charts and transformed to logMAR. Endothelial cell density (ECD) was calculated by a digital Topcon SP-3000P specular microscope camera. Central corneal thickness (CCT) was measured by OCULUS Pentacam.
Results BSCVA improved from -0.54 ±0.17 logMAR (mean ±SD; Snellen equivalent 6/18) pre-DSAEK to -0.29 ±0.32 logMAR (6/12) at 1 year (mean 1 year, range 0.6-1.4 years) and further improved to -0.17 ±0.09 logMAR (6/9) at 7 years (mean 6.8, range 5.6-7.8 years). The proportion of eyes with BSCVA better than Snellen 6/12 was 64% at 1 year and 93% at 7 years. All grafts had ECD above 2000 cells/mm2 pre-DSAEK. ECD decreased in most grafts from 1 to 7 years (mean loss 31%, range 10-43%), yet 5 grafts showed increased ECD (mean gain 39%, range 6-81%). CCT remained unchanged from 1 to 7 years post-DSAEK (p=0.39). 16 of the initial 30 eyes were lost to follow-up due to death (8 eyes), graft failure (3 eyes), or other circumstances (5 eyes).
Conclusions DSAEK provides continuous improvement of visual acuity up to 7.8 years post-surgery with stable corneal thickness, and decreasing endothelial cell density in most grafts, yet some grafts showed surprising increase.

• T065

Assessment of corneal layers thickness with spectral-domain optical coherence tomography

SEGURA F (1,2), López de la Fuente C (2,3), Sánchez-Cano A (2,3), Orduna E (4), Del Buey M (1,5), Pinilla I (1,2,5)
(1) University of Zaragoza, Department of Surgery- Gynecology and Obstetrics, Zaragoza, Spain
(2) Aragon Institute for Health Research, IIS Aragón, Zaragoza, Spain
(3) University of Zaragoza, Department of Applied Physics, Zaragoza, Spain
(4) University of Zaragoza, Department of Physiology and Pharmacology, Zaragoza, Spain
(5) Lozano Blesa University Hospital, Department of Ophthalmology, Zaragoza, Spain

Purpose To assess the corneal layers thickness in healthy young adults using spectral-domain anterior segment optical coherence tomography (AS-OCT).
Methods There were 86 eyes of 86 healthy volunteers, 55 females and 31 males, which were included in the study. The mean age ± standard deviation (SD) was 22.87 ± 3.90 years (range, 20-43). Spectral-domain AS-OCT was performed using Spectralis OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany). Measurements of central corneal thickness, and central thickness of epithelium, Bowman´s layer, stroma and the complex Descemet-endothelium were performed.
Results Mean central corneal thickness, epithelium, Bowman, stroma and Descemet-endothelium were 555.50 ± 29.64 µm (range 510-624), 54.60 ± 4.25 µm (range 45-63), 16.70 ± 1.73 µm (range 14-20), 467.51 ± 28.91 µm (range 420-533) and 16.74 ± 1.66 µm (range 14-20), respectively.
Conclusions Spectralis OCT can be easily used to non-invasive measurements of the anterior segment parameters and this study establishes a normal database for corneal thickness and all its layers in healthy young adults.

• T066

Immediate Effect of Ultraviolet-A Collagen CXL Therapy on Biomechanics and Histology of Human Cornea

DEL BUEY M A (1), Lanchares E (2), Calvo B (2), Lavilla L (1), Almenara C (1), Pérez I (1), Idoate A (1), Pinilla I (1), Ascaso J (1), Cristobal J (1)
(1) " LOZANO BLESA" CLINICAL UNIVERSITY HOSPITAL, OPHTHALMOLOGY, ZARAGOZA, Spain
(2) Universidad de Zaragoza, Engeniering, Zaragoza, Spain

Purpose To evaluate the immediate effect of the CXL treatment on the biomechanical properties and histological microstructure of healthy human corneal tissue. With this purpose, in vitro mechanical tests and histological observation of cross-linked and untreated human corneal tissue were performed.
Methods Mechanical tensile test and histological analysis were performed in de-epithelialized healthy human corneal tissue treated with riboflavin solution (0.01% riboflavin-5-phosphate and 20% dextranT-500) – 30 min UVA irradiation (treated sample TS). A similar study was performed to untreated de-epithelialized healthy human corneal tissue (control sample, CS). Both histological and mechanical analyses were performed immediately after treatment.
Results The analysis of the stress-strain curves showed a different corneal response between treated (TS) and untreated (CS) samples. TS showed a stiffer behaviour than CS. The treated corneal tissue (TS) resulted 1.8, 1.6, 1.7 and 1.5 fold stiffer than the untreated sample (CS) at 6, 8, 10 and 12% stretch, respectively.The histological analysis of TS showed an increased fibrillar density with decrease of interlamellar space in comparison with CS. Keratocyte apoptosis was observed in TS even at deep stromal level.
Conclusions The UVA-induced CXL has an immediate biomechanical and histological effect over the treated healthy human corneal tissue. Stiffening of the tissue, keratocyte apoptosis and stromal compacting were observed

• T067

Ocular Chronic Graft Versus Host Disease after Bone Marrow Transplantation

IEPPESEN H (1), Sengeloev H (2), Lindegaard J (1), Julian H (1), Prause J U (3), Heegaard S (4)

(1) Rigshospitalet Glostrup, Department of ophthalmology, Copenhagen, Denmark
(2) Rigshospitalet, Department of Hematology, Copenhagen, Denmark
(3) University of Copenhagen, Eye Pathology Section, Copenhagen, Denmark
(4) Rigshospitalet Glostrup and University of Copenhagen, Department of ophthalmology and Eye Pathology Section, Copenhagen, Denmark

Purpose Allogeneic bone marrow transplantation (BMT) is a curative therapy for a number of hematological diseases. Ocular chronic graft versus host disease (cGVHD) is a major contributor to long-term morbidity after BMT. The purpose of this study was to report the frequency of ocular cGVHD after BMT and onset in relation to systemic cGVHD.

Methods Retrospective examination of medical records of patients who underwent consecutive allogeneic BMT from 1980-2011 at Copenhagen University Hospital (Rigshospitalet). This study included adults (>16years) with no dry eye disease prior to BMT. The patients were seen by an ophthalmologist before BMT and annually after BMT. The ophthalmological examination included tear break-up time, Schirmers test, corneal fluorescein stain, slit lamp examination and ophthalmoscopy. The criteria proposed by the "International Chronic Ocular GVHD Consensus Group" was used to diagnose ocular cGVHD.

Results Out of the 939 patients included, 222 patients (23.6%) developed ocular cGVHD. We found no significant difference between gender and the development of ocular GVHD (p=0,67). Median age at time of BMT was 41 years (rage 16-73) and 46 years (17-68) in the group who developed ocular cGVHD. Median time of onset of ocular cGVHD was 20 months(0.4-196) after BMT. Diagnosis of ocular cGVHD preceded systemic cGVHD in 33 cases (15%). Twenty-seven patients (12%) had ocular cGVHD without systemic cGVHD. Ocular cGVHD was significantly higher in patients with systemic cGVHD involving the skin (p<0,001).

Conclusions Ocular cGVHD is common after BMT. It can occur at any age, but is more common in elder patients. Ocular cGVHD can occur in patients without systemic cGVHD. We recommend ophthalmological examinations in all patients before and after allogeneic BMT due to the high frequency of ocular cGVHD.

• T068

New insights into the proliferative capacities of rabbit corneal endothelial cells

CROUZET E (1), He Z (1), Forest F (2), Perrache C (1), Piselli S (1), Peoc'h M (2), Gain P (1), Thuret G (3)

(1) Jean Monnet University, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint-Etienne, France
(2) University Hospital, Dermatology, Saint-Etienne, France
(3) Jean Monnet University, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint-Etienne AND Institut Universitaire de France- Bd St Michel- Paris

Purpose Rabbits are known to have highly proliferative corneal endothelial cells (CECs) with excellent wound healing properties. Yet, little evidence of these capacities is available, except for 2 papers dating back to 1977 (PMID: 873721) and 1984 (PMID: 6511225). Aim: to better characterize the proliferative capacity of rabbit CECs using labelling of mitosis and DNA synthesis and to search for potential stem cells.

Methods Central corneal freezing (CF) was used on the right eye of young rabbits (4 weeks) with a brass bar soaked in liquid nitrogen. The thymidine analogue, 5-ethynyl-2'-deoxyuridine (EdU) was injected intraperitonealy at 0, 24 and 48 hours after CF. The corneal opacity was monitored using a slit lamp and corneal thickness using an AS-OCT. Rabbits were euthanatized 5 or 40 days after CF to label proliferating and slow cycling cells (presumed stem cells) using a Click-It EdU kit combined with Ki67 labeling. Both analyses were performed on flat mounted whole corneas to observe all CECs.

Results Corneal opacity and thickness increased within 24h after the CF. Both parameters returned to normal after 5 days. At 5 and 40 days the central endothelial cell density was normal. 266±17 (1.7%) EdU positive CECs and/or 1532±34 (5%) Ki67 positives CECs were observed, often grouped by pairs, in the endothelial periphery of the right eye as well as in the control eye. 14±4 Ki67 positive cells (0.3%) were observed grouped by pairs in the central endothelium of the right eye.

Conclusions In rabbit cornea, a few CECs are continuously spontaneously cycling at the periphery of the endothelium and all CECs may have the capacity to proliferate in response to injury, even in the centre.

• T069

Topical treatment with a new matrix therapy agent (RGTA, CACICOL) improves epithelial wound healing after penetrating keratoplasty in a rabbit model

CROUZET E (1), He Z (1), Olmiere C (2), Perrache C (1), Piselli S (1), Jullienne R (1), Gain P (1), Thuret G (3)

(1) Jean Monnet University, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint-Etienne, France
(2) Thea Laboratory, Development, Clermont Ferrand, France
(3) Jean Monnet University, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint-Etienne AND Institut Universitaire de France- Bd St Michel, Franc

Purpose Epithelial wound healing is a milestone in the early post-operative care after penetrating keratoplasty (PKP). It reduces the infectious risk, allows safe instillation of steroids, and conditions discharge from hospitalization. The present study assessed a new matrix therapy agent, for the management of post PKP epithelial defects in a preclinical rabbit model of PKP.

Methods New Zealand white rabbits received a 7.1/7mm PKP with a desepithelialized rabbit cornea from the same sibling. Immunosuppression was obtained thanks to subconjonctival corticosteroid. Rabbits were randomized to receive either CACICOL (n=3) or a placebo (n=3). Investigators were masked. Eyedrops were instilled immediately after graft and repeated on alternate day until complete reepithelilalization. The epithelial wound healing was monitored fluorescein staining. Corneal thickness was monitored using AS-OCT. Rabbits were euthanatized and corneas were analyzed using histological cross sections, confocal microscopy, scanning electron microscopy (SEM) and transmission electron microscopy (TEM).

Results Corneas receiving CACICOL healed in 6, 6 and 8 days versus 8, 8 and 10 days with the placebo (P=0,099). Epithelial thicknesses were 45, 32 et 23 µm with CACICOL and 25, 29 et 19 µm with the placebo. In SEM superficial cells of the CACICOL group were similar to normal corneas and had more numerous microvilli with the placebo. MET showed normal epithelial ultrastructure in the CACICOL group with more hemidesmosomes than with the placebo.

Conclusions RGTA seems a potentially useful, noninvasive therapeutic approach in PKP management.

• T070

Ex vivo porcine corneal storage using an innovative bioreactor

GUINDOLET D (1), HE Z (2), Bernard A (2), Rageade D (2), Piselli S (2), Perrache C (2), Forest F (2), Peoc'h M (3), Gain P (2), Gabison E (1), Thuret G (2)

(1) Fondation Ophtalmologique Rothshild, Cornea and External Diseases, PARIS, France
(2) Corneal Graft Biology- Engineering and Imaging Laboratory, EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine- Jean Monnet University, Saint Etienne, France
(3) Department of Pathology, University Hospital of Saint-Etienne, Saint Etienne, France

Purpose There is no animal model of medium-long-term corneal storage for easily available animals because, contrary to human, ex vivo, animal corneas rapidly and dramatically swell and loose their transparency. As intraocular pressure and optimal function of endothelial cells are critically important for corneal homeostasis, we suppose that the passive eye banking technique is not adapted for corneas of young animals with high stromal swelling pressure. We therefore reproduce physiological parameters to improve storage of animal corneas.

Methods We designed a bioreactor (BR) that restores a pressure equivalent to the intra ocular pressure in the endothelial chamber while allowing continuous renewing of media in both epithelial and endothelial chambers. Epithelial side underwent alternating air-lifting and medium immersion to reproduce blinking. Porcine eyeballs were obtained from a local slaughterhouse within 4 hours after death. Corneas were stored either in a BR or in conventional vials, both in standard organ culture medium. Transparency, thickness, histological structure and immunohistological staining (ABCB5, PAX6, 5-ethynyl-2'-deoxyuridine, K3-K12, Laminin-5) were compared to conventionally stored corneas after 2 weeks.

Results Porcine corneas stored in bioreactor were more transparent and thinner. Increased endothelial cell viability was observed in the BR and epithelial layer was preserved and mature. Epithelial stem cells also survived.

Conclusions The porcine version of our BR mimics physiological condition and improves corneal storage. It could be a new model of eye banking and a powerful experimental platform to study corneal physiopathology. Grant: UJM, ANSM

• T071

Comparison of corneal topographic indices of keratoconus versus normal eyes by using pentacam imaging

YEKTA A A (1), Khabazkhoob M (2), Hashemi H (3), Bakhshi S (4), Ostadimoghaddam H (4), Heravian J (4), Rezvan F (3), Yekta R (5)
(1) Mashhad University of Medical Sciences, Optometry, Mahhad, Iran
(2) Noor Eye Hospital, Noor Ophtalmology Research Center, Tehran, Iran
(3) Noor Eye Hospital, Noor Ophthalmology Research Center, Tehran, Iran
(4) Mashhad University of Medical Sciences, Optometry, Mashhad, Iran
(5) Fadak Clinic, Fadak Clinic, Mashhad, Iran

Purpose To compare the corneal topographic indices of keratoconus versus normal eyes by using pentacam imaging.
Methods One hundred and fifty patients (300 eyes) from keratoconus clinic based on inclusion criteria and 149 nominees (298 eyes) for refractive surgery with normal cornea were selected from the Noor Eye Hospital, Tehran, Iran. Pentacam scheimflug measurements were performed for both groups based on standard measurement factors. Pentacam topography indices were recorded for each case.
Results Average of topographic indices were evaluated and compared between two groups with T-test. The difference between two groups was significant. Effective indices in discrimination suspect from normal were evaluated by logistic regression. Sensitivity and specificity of indices were plotted by ROC curve. In order to diagnose suspect keratoconus, index of height decentration (IHD) and index of height asymmetry (IHA) had the most sensitivity and specificity values.
Conclusions The results of this study showed that the index of IHD and IHA were the most sensitive and specific criteria in the diagnosis and discrimination between keratoconus and normal eyes. Based on sensitivity and specificity criteria, the given cut-points for each indices play an important role in detecting subclinical keratoconus from normal eyes.

• T072

Ocular surface improvement after conjunctivochalasis (CCH) surgery.

CARAMELLO C M (1), Mateo Orobia A J (2), Peiro C (1), Del Buey M (1), Perez Navarro I (1), Almenara C (1), Esteban O (1), Ascaso J (1), Cristobal J (1)
(1) Hospital Clinico Universitario Lozano Blesa, Oftalmología, Zaragoza, Spain
(2) Hospital Universitario Miguel Servet, Oftalmología, Zaragoza, Spain

Purpose To evaluate symptomatology and ocular surface changes in patients with CCH grade III after excision surgery.
Methods Prospective, interventional study in which 15 patients with CCH grade III were enrolled.
Patients underwent CCH excision surgery: 8 patients underwent semiperitomy perilimbic with cauterization technique and 7 paste-pinch-cut conjunctivoplasty.
The following ocular surface properties were studied preoperatory and 6 weeks after surgical intervention:
– Symptoms by using Ocular Surface Disease Index questionnaires (OSDI)
– Tear Osmolarity by using Tearlab Osmolarity System®.
– Tear Break Up Time (BUT)
– Tear clearance and Tear Function Index by using fluorescein test measure by schirmer strip stain. (Vico and Benitez del Castillo technique)
– Corneal and conjunctival stain: Lissamin green (0-3 grades) and Fluorescein: (0-3 grades)
Results OSDI questionnaire confirm symptomatology improvement after surgery. Fluorescein Test measure by Schirmer strip stain reveal a better tear clearance. Fluorescein corneal stain and lissamine green corneal stain decrease. Osmolarity ocular surface values and tear BUT normalise after surgery. There was not significant difference between semiperitomy perilimbic with cauterization technique and paste-pinch-cut conjunctivoplasty.
Conclusions CCH patients have an increase proteolytic activitiy in ocular surface. Conjunctival excess interfere with appropriate meniscus tear formation and translate to a deficient corneal tear film. Inflammation control and conjunctival mechanical restore by surgery decrease ocular surface symptomps, improve tear clearance and tear stability and normalize osmolarity values.

• T073

Transfer of molecules into the endothelial cells of whole human corneas using carbon nanoparticles activated by femtosecond laser

JUMELLE C (1), Mauclair C (2), Houzet J (2), Barnard A (1), He Z (3), Piselli S (1), Perrache C (1), Gain P (1), Thuret G (4)
(1) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint-Etienne, France
(2) University Jean Monnet, Laboratory Hubert Curien- UMR-CNRS 5516, Saint-Etienne, France
(3) University Hospital, Ophthalmology, Saint-Etienne, France
(4) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine and Institut Universitaire de France- Bd St Michel-Paris, Saint-Etienne

Purpose The targeted delivery of drugs and genes represents a promising solution to modify human corneal endothelial cells (HCECs), however, it remains limited by the difficulty to efficiently cross cell membranes without altering their integrity. Aim: to adapt an innovative technique of macromolecules delivery in corneal endothelium using carbon nanoparticles (CNPs) activated by femtosecond laser (FsL).
Methods HCECs of 35 whole human corneas stored in organ culture were permeabilized by photo-acoustic reaction induced by irradiation of CNPs by FsL beam. The uptake of dextran AlexaFluor 488, a 3000-Da fluorescent macromolecule, was assessed using fluorescent microscopy. Three fluences (20, 30 and 40 mJ/cm^2) and protective additives (ROCK inh and Poloxamer 407) were tested in order to increase uptake efficiency while limiting cell mortality (ethidium +). Dextan uptake and cell mortality rates were quantified using the CorneaJ plugin for ImageJ.
Results Dextran delivery significantly increased with fluence, reaching a mean of 13% of HCECs for 40 mJ/cm^2. Induced mortality varied from 0 to 53 % and was more dependent of the cornea itself than on fluence. Treatment by either protective additive did significantly enhance the delivery rate, nor HCECs viability.
Conclusions For the first time, ex vivo HCECs of whole corneas were permeabilized by mediated-nanoparticles laser perforation. Even if the delivery rate was lower than for viral vectors, it remained high for a non-viral technique. Mortality was variable according to corneas tested even with the use of protective additives. GRANT: Fondation des Aveugles de France, Fondation de l'Avenir, Fondation Visaudio (ET1-638).

• T074

Pore size assessment during corneal endothelial cell permeabilization by femtosecond laser-activated carbon nanoparticles

JUMELLE C (1), Mauclair C (2), Houzet J (2), Bernard A (1), He Z (3), Piselli S (1), Perrache C (1), Gain P (1), Thuret G (4)
(1) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine, Saint Etienne, France
(2) University Jean Monnet, Laboratory Hubert Curien- UMR-CNRS 5516, Saint-Etienne, France
(3) University Hospital, Ophthalmology, Saint Etienne, France
(4) University Jean Monnet, Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine and Institut Universitaire de France- Bd St Michel-Paris, Saint-Etienne

Purpose Therapeutic molecules delivery represents a promising solution to maintain human corneal endothelial cells (HCECs) viability, but transport across cell membrane must be facilitated. A new delivery method consists in ephemerally permeabilizing cell membranes using a photo-acoustic reaction produced by carbon nanoparticles (CNPs) and femtosecond laser (FsL). The aim of this work is to investigate the size of pores formed at cell membrane by this technique.
Methods To induce cell permeabilization, HCECs (B4G12 cell line) were put in contact with CNPs and irradiated with a 500 µm diameter Ti:Sa FsL focalized spot. Four sizes of fluorescent reporter molecules were delivered into HCECs to investigate pore sizes: calcein (1.2 nm), FITC-Dextran 4kDa (2.8 nm) and FITC-Dextran 70kDa (12 nm) and FITC-Dextran 2MDa (50 nm). Uptake of each molecule was assessed by flow cytometry immediately after irradiation.
Results The delivery rate was dependent of their size. Calcein was delivered in 56±8% of HCECs, FITC-Dextran 4kDa in 42±4%, FITC-Dextran 70 kDa in 22±3% and finally FITC-Dextran 2MDa in 13±2%, suggesting that a large number of pores in the size ranging from 1.2 to 2.8 nm were formed. However, 12 nm and larger pores were almost half more infrequent.
Conclusions Pore sizes formed at cell membrane by the technique of cell permeabilization by FsL activated CNPs were investigated for the first time. This innovative non-viral method is characterized by pore sizes large enough for the efficient delivery of small, medium and big therapeutic molecules on HCECs. GRANT: Fondation des Aveugles de France, Fondation de l'Avenir, Fondation Visaudio (ET1-638).

• T075

Corneal Analysis before Cataract Surgery; Significance as the Clue for Unexplained Visual Complaint After Surgery

KIM J , Lee D , Lee J H , Choi J Y , Yeom J H
Ilsan Paik hospital- Inje University, ophthalmology, Goyang, South-Korea

Purpose We analyzed the corneal optics before cataract surgery to evaluate whether the corneal abnormalities are correlated with the unexplained visual complaints after successful surgery.
Methods Seventy-eight eyes of forty-seven patients who had undergone uncomplicated cataract surgery were enrolled in this retrospective study. The eyes were divided into group I which had visual complaint despite good visual acuity and group II without complaints after surgery. All included eyes had preoperative corneal data such as slit lamp bio-microscopy, automatic keratometer, corneal topography (Orbscan II, Bausch & Lomb, Germany), and aberrometer (KR-1W ®, Topcon, Japan). We investigated whether there are any correlations between the corneal abnormalities and unexplained visual complaint by comparing the corneal parameters of two groups.
Results The mean patient age was 67.9 years old. The mean preoperative topographic astigmatism in 78 eyes was 0.98 diopter (D); 19,23% of eyes had irregular astigmatism. Mean corneal spherical aberration measured by KR-1W was 0.31 ± 11.01 μm and corneal total higher order aberration (HOA) was 0.24 ± 0.17 μm. Total corneal HOA was correlated with irregularity index from topography. ($P<0.01$, $r=0.548$) No differences were shown between two groups in preoperative astigmatism. However, comparing the corneal parameters, irregularity index of 3mm, 5mm zone and corneal total HOA of group I were statistically significantly higher than those of group II respectively. ($p<0.05$, respectively)
Conclusions Unsatisfactory results associated with visual quality after cataract surgery might be originated from cornea irregularity and HOA. Evaluation of preoperative corneal optics is necessary to predict visual quality after surgery.

• T076

Long-term results orthokeratological therapy in patients with myopia

BUSHUYEVA N , Maliieva O
Filatov Institute of Eye Diseases, Laboratory of Binocular Vision Disorders, Odessa, Ukraine

Purpose The potential impact of the peripheral refraction on the refractogenesis and development of myopia is validating for using orthokeratological therapy to form a peripheral myopic defocus in patients with myopia.
The purpose of the research was to study the long-term results of orthokeratological therapy in patients with myopia
Methods 21 patients (42 eyes) with myopia from -0.75 D to -4.5 diopters σ = (-2,35±1,22) D, with average age (12,43±6,09),
used the night contact lenses Paragon CRT 100 were followed up for 3 years. Methods of examination included visometry, keratometry and refractometry after cycloplegy with Cyclomed 1% with using KR-8900, Topcon and HRK-7000, Huvitz; ultrasonic eye`s biometry with Desmin M (thickness of cornea and lens, depth of anterior chamber, length of vitreous) before and after 3 years using OK- therapy. We have used (patent Ukraine № 91371, 24.06.2014) coefficient K = ((AC+L/2) / (V+L/2)) x 100, AC - anterior chamber, L - thickness of lens, length of vitreous.
Results The long-term results of orthokeratological therapy showed the positive effect to slow of the myopic process. After 3 years OK- therapy myopia was stabilized in 27 eyes (64,29%). The date 31 and more of coefficient K showed the refractive type of myopia and less then 31 - showed axial type of myopia. The refractive type of myopia was in 22 eyes (52,38%) and axial type of myopia was in 20 eyes (47,62%).
Conclusions The most positive effect of orthokeratological therapy observed in patients with refractive component due to the curvature of the cornea. Coefficient have showed the type of axial or refractive myopia (Patent Ukraine № 83299U, 27.08.2013). The coefficient can be used for prognosis of progression myopia

• T077

The effect of trehalose 3% as adjuvant therapy on Lasik procedure.

MATEO OROBIA A J (1), Cristobal J (1), Casas Pascual P (1), Lafuente Ojeda N (2), Perez Garcia D (1), Peiro Embid C (1), Korobko Kulikova V (1), Del Buey M (1), Lavilla L (3)
(1) QUIRÓN HOSPITAL, OPHTHALMOLOGY, ZARAGOZA, Spain
(2) HOSPITAL UNIVERSITARIO MIGUEL SERVET, ANESTHESIOLOGY, ZARAGOZA, Spain
(3) HOSPITAL CLÍNICO UNIVERSITARIO LOZANO-BLESA, OPHTHALMOLOGY, ZARAGOZA, Spain

Purpose The majority of all Lasik patients experience dry eye. Usually temporary it also could last for months or years. Patients with no or mild dry eye symptoms but high risk factors have better post-LASIK outcomes when being preoperatively treated with lubricants. Surgical outcome of patients, with neither symptoms nor risk factors of having dry eye, could be maximized by optimizing the ocular surface before surgery. This study evaluated the effect of trehalose 3% eye drops (Thealoz), pre and post-surgery use, on the postoperative ocular surface status of the patient.
Methods Clinical study including 26 eyes from 13 patients, mean age of 35, having no dry eye signs or symptoms, who were scheduled for a LASIK procedure. Patients were randomly assigned to use trehalose 3% 48h before surgery (G1; 1 drop tid) or no treatment (G2). After LASIK surgery, G1 used trehalose 3% 1 drop q4h in association with artificial tears (hyaluronic acid -HA- 1 drop q4h) and G2 used only artificial tears (1 drop q4h) for 90 days, as corneal hydrating treatment.
Results OSDI score obtained during follow-up period showed a positive evolution in G1 compared to G2 (no statistical significance). Frequency and severity of the symptoms from first day after surgery were significantly lower in G1 ($p<0.05$). Other clinical test (osmolarity, TBUT, lissamine staining) also showed positive evolution in G1 but it was not observed statistical differences between treatments. Corneal staining (NIE and Oxford scales) showed lower scores in G1. Results were statistically significant at D30 and at D90 (NIE scale) and at D90 for Oxford scale.
Conclusions Addition of trehalose to the standard treatment using HA eye drops after LASIK surgery at pre and post-surgery period, it has been revealed as a positive therapeutic strategy to control and reduce dry eye symptoms and corneal staining score.

Commercial interest

• T078

Sterile corneal keratolysis in the rat at 300 nm

KRONSCHLAGER M (1), Talebizadeh N (2), Yu Z (2), Löfgren S (3), Findl O (1)
(1) Hanusch Hospital, Ophthalmology, Vienna, Austria
(2) Uppsala University, Gullstrand lab, Uppsala, Sweden
(3) Karolinska Institutet, Ophthalmology, Stockholm, Sweden

Purpose Ultraviolet radiation (UVR) today is widely used in anterior segment interventions. The purpose of the study was to evaluate toxicity of UVR at 3oo nm in the rat cornea.
Methods 16 Sprague Dawley rats were unilaterally exposed to 5 kJ/m2 UVR (λmax: 300 nm; λ0.5: 10 nm) for 15 min. Contralateral eyes were kept as control. The animals were divided into 4 latency groups and eyes were taken at 1, 5, 24 and 120 h post exposure. Apoptosis was detected with the TUNEL method and histopathological changes were visualized with H&E staining.
Results At 5 h post exposure all 3 exposed corneal cell layers displayed apoptotic cells with a peak at 24 h. Corneal stromal thinning and stromal neutrophil infiltration were found at 120 h in exposed corneas.
Conclusions In conclusion, sterile corneal keratolysis occurs in the post exposure time window 24 to 120 h and is probably induced by neutrophils. The potential danger of sterile corneal keratolysis is to be considered in the clinical applications of UVR.

• T079

Evaluation of the influence of corneal biomechanical properties on the central corneal curvature after a SUPRACOR procedure

DELBARRE M , Rambaud C , Berguiga M , Sendon D , Graber M , Froussart-Maille F
Hôpital d'Instruction des Armées Percy, Ophthalmology, CLAMART, France

Purpose SUPRACOR™, performed with the Technolas Excimer Workstation 217P (Bausch + Lomb Technolas), creates a small zone of high refractive power in the central cornea, the « bump », to facilitate near focus. The aim of this study is to evaluate the influence of corneal biomechanics on this « bump ».
Methods This retrospective study included 46 eyes of 23 patients. The Supracor ablation pattern was applied, to create hyperprolate shape resulting about 2 D near addition. The periphery was treated with hyperopic ablation in a 6 mm zone, using 9.5 mm suction ring, under 120 µm flap created by the IntraLase FS60 femtosecond laser (AMP, USA). Every patient underwent a corneal topography (Pentacam, Oculus, Germany) before and 1 month after surgery to evaluate the importance of the "bump", and a biomechanical evaluation with the Ocular Response Analyser (ORA, Reichert, NY). CH (Corneal Hysteresis) and CRF (Corneal Resistance Factor) were evaluated. Spearman's rank correlation coefficient was used to analyze the relationship between the parameters of the ORA and the « bump ».
Results The mean patient age was 55.5 ± 3.94, ranging from 50 to 62 years. Pre-operative spherical equivalent were 1.57±0.77 D. Mean corneal thickness was 548 ± 44 µm. CH and CRF were respectively 10.53 ± 1.63 mmHg and 10.90 ± 2.12 mmHg. Mean "bump" was 2.25 ± 0.98 D, ranging from 0.50 to 4.64 D. A correlation was found between the CH and the bump (r= 0.34; p= 0.022) and also between the pachymetry and the bump (r= 0.45; p= 0.004). A strong correlation was found between corneal thickness and the CH (r= 0.62; p= 0.001).
Conclusions In this study, the "bump" is correlated with the corneal thickness and the CH. The corneal thickness appears to be sufficient to predict the "bump" in hyperopic patients undergoing Supracor. These results should be confirmed in a larger sample of patients.

• T080

Intratarsal injection of kenacort in the treatment of severe cases of VKC

LAZREG S
Cabinet Lazreg, Cabinet d'ophtalmologie, Dar el Beida, Algeria

Purpose To treat refractory cases of Vkc with intratarsal injections of trialcinolone .
Methods We treated Severe cases of Vkc that have already experienced different anti allergic treatments and topical steroids with frequent relapses and dependancies to steroids with intratarsal injection of 40 mg of dexametasone , the follow up visits were performed at D0, D 3, D7 and D30 (slit lamp examination, corneal staining, ocular pressure)
Results 87 severe cases of Vkc 63 males , mean age 10,4+/- 3,5years , 90% bilateral , and 100% of corneal involvement . 70% mixed forms and 15% of tarsal forms, the mean follow up was 20+/-7 months . at D3 we had a decrease of all ocular signs(photophobia, redness and pruritis) at D7 decrease of corneal staining and trantas nods, and at d30 , total remission of the Vkc, the mean duration of the efficacy of the treatment was 10.4+/- 2.6 months , no adverse event was observed .
Conclusions Intratarsal injection of steroids is very effective in severe and resistant cases of Vkc , especially in our countries where this disease is very severe , frequent and when topical cyclosporine is not available .

• T081

3D model of pterygium and corneal limbus: Investigating histopathology and stem cell distribution.

BLOM N (1), Andreasen A (2), Heegaard S (3), Hjortdal J (1), Nielsen K (1)
(1) Aarhus University Hospital, Department of Opthalmology, Aarhus C, Denmark
(2) Aarhus University, Department of Biomedicine Anatomy, Aarhus, Denmark
(3) Glostrup Hospital- University of Copenhagen, Department of Ophthalmology, Copenhagen, Denmark

Purpose This study aims to create a complete histological 3D computer model of pterygium in situ, mapping the anatomy of the disease tissue, its relation to the corneal limbus and the distribution of limbal stem cells.
Methods One human eye affected with pterygium was obtained from a cornea donor post mortem. The anterior part of the eye was cut into 900 consecutive horizontal sections. Every other section was stained with HE to be digitized, aligned and 3D reconstructed using interactive 3D visualization software. Immunohistochemistry targeting CK19, MMP-1, p63 and VEGF was performed on the remaining sections alternating across the structure so as to create evenly distributed overlaying models.
Results Using the sections a high-resolution model of the pterygium and limbus was created, and in aligning the immunostained sections to the model, a spatial map of the staining was created.Analyzsing the model we found a mostly normal temporal limbus with intact architecture, however nasally the limbus was found to be buried under the pterygial mass and only partly intact, showing a number of pathological changes.
Conclusions The limbal degeneration underneath the pterygium appears to be a precondition for or a consequence of the pterygial growth.

• T082

Analysis of molecular mechanisms that predispose patients to develop post-PRK haze

RAJIV KUMAR N , Ghosh A , Shetty R , Pahuja N
NARAYANA NETHRALAYA FOUNDATION, GROW RESEARCH LABORATORY, BANGALORE, India

Purpose Factors that predispose certain patients to develop post-surgical haze remain unknown. We analyzed gene expression in corneal epithelium collected from patients prior to haze development following PRK. We further developed an in-vitro model to study haze using TGFβ that mimics pre-disposed and post haze conditions
Methods Corneal epithelium was collected intraoperatively from patients undergoing PRK. 4 eyes that developed haze postoperatively and 10 eyes of age matched controls without haze were analysed. Microarray analysis was followed by bioinformatics and validation. ***In vitro*** studies were performed on HCE cells on differential doses of TGFβ with or without wound for inflammatory markers, structural & pro-fibrotic genes and regulators of signaling cascades
Results Microarray analysis revealed 1100 up regulated and 1700 down regulated genes in haze patients. ECM- Receptor interactions were elevated in patients prior to haze induction while Wnt signaling genes and CXC motif chemokines were reduced. Structural genes (Col I, Col IV, MMP2 & 14, TIMP1) were reduced in haze patients which correlated with ***in-vitro*** model. Inflammatory factors TNFα, IL-11 were elevated, but IL6 and IL1 did not show appreciable changes. Regulators of signaling cascades EGFR and Wnt3a were reduced in haze patients & ***in vitro***. We propose a signal transduction network including few novel genes like PREX1, PXDN, SOX17, WNT3A, CXCL10 etc which can be factors that predispose patients to haze
Conclusions Our study shows that molecular factors poise the cornea in some patients to developing corneal haze after surgery

• T083

Corneal lenticules as an ex-vivo model to study keratocyte biology

SHROFF R (1), Shetty R (2), Kumar D (3), Ghosh A (3), Kumar S (3), Pahuja N (1), Ghosh A (3)
(1) NARAYANA NETHRALAYA, CATARACT - REFRACTIVE AND CORNEA, BANGALORE, India
(2) NARAYANA NETHRALAYA, CORNEA AND REFRACTIVE SERVICES, BANGALORE, India
(3) NARAYANA NETHRALAYA, GROW LAB, BANGALORE, India

Purpose Keratocytes show differential gene expression in culture media; and are extensively used to study wound healing, corneal disease biology and response to topical drugs. However, mono-layer culture cannot replicate the 3-dimensional biological environment of corneal stroma. Hence, we propose to establish corneal lenticule as an***ex-vivo*** model to study keratocyte biology for corneal diseases, drug response studies and in wound healing experiments.
Methods SMILE surgery was performed using the VisuMax femtosecond laser system (Carl Zeiss Meditec AG, Jena, Germany). After the refractive lenticule of intra-stromal corneal tissue was created using the femtosecond cutting procedure, it was dissected and separated through the side-cut opening and removed manually. SMILE lenticules from patients were obtained in MK media and were transferred to DMEM F12 with 10% FBS and 1% PSA. The media was replenished every 24h and lenticules were harvested at 0h, 24h, 48h, 78h and 96h. Gene Expression analysis was performed for pro-fibrotic genes (fibronectin, α-sma, vimentin, TGF-β and TGF-βR2), pro-inflammatory (IL-6 and TNF-α) and structural genes (Col1-A1, Col4-A1and Col5-A1).
Results Our results demonstrate that lenticules remain metabolically active in culture media for long periods of time as evident from the varying expression of different pro-fibrotic, pro-inflammatory and structural genes after 0h, 24h, 48h, 78h and 96h of culture. Furthermore, linear regression analyses show that clinical parameters like lenticule thickness do not affect the expression profile of the various genes by the keratocytes contained in the lenticule.
Conclusions In conclusion, lenticule can be used as an ex-vivo model to study keratocyte biology in various corneal diseases and for drug testing.

• T084

Novel role of PELI3 as a potential biomarker for Sjogren's syndrome related dry eyes

PILSON Q (1,2), Ni Gabhann J (1), Murphy C C (2)
(1) The Royal College of Surgeons in Ireland, Molecular and Cellular Therapeutics, Dublin, Ireland
(2) The Royal College of Surgeons in Ireland, Department of Ophthalmology, Dublin, Ireland

Purpose In Sjogren's syndrome (SS) related dry eyes (SS-KCS), reduced aqueous tear production and tear hyperosmolarity leads to inflammatory damage to the ocular surface. microRNAs (miR) are known to alter the expression of cytokines, which plays an important role in the pathogenesis and progression of SS. The aim of this study was to isolate miRs and mRNA from conjunctival epithelial cells (CEC) of patients with primary SS (pSS) to identify potential biomarkers that might aid diagnosis and future therapy in pSS.
Methods Confirmed SS-KCS and healthy controls were recruited to this study. mRNA isolated from conjunctival impression cytology was sent for miR and mRNA microarray. Bioinformatic analysis was performed to identify predicted targets and comparison was made with the mRNA microarray data. Validation experiments were performed in HeLa cells following transfection with selected miR mimics and predicted genes were detected using qPCR.
Results miR and mRNA microarray found 32 differentially expressed novel miRs and 136 differentially expressed genes in pSS patients compared to healthy controls. Following bioinformatic analysis, novel miR-A was chosen for further analysis. miR-A was significantly increased in pSS (p=0.0079) and bioinformatics suggested Pellino3 (PELI3), a negative regulator of inflammatory cytokines, as a predicted target. The mRNA microarray showed a decrease in PELI3 in pSS patients compared to healthy controls (p= 0.0731). Overexpression of miR-A mimic in HeLa cells resulted in decreased expression of PELI3, suggesting that it is a direct target for miR-A.
Conclusions We have identified differentially expressed miRs and gene targets from CEC in pSS. PELI3, a potential target of novel miR-A which is over expressed in pSS, is a negative regulator of cytokines that might have biomarker and therapeutic potential for pSS related dry eyes.

• T085

Randomised, controlled study of the efficacy and safety of a new eye-drop formulation for moderate to severe dry eye syndrome

DOAN S (1), Baudouin C (2), Khairallah M (3)
(1) Hopital Bichat, Ophtalmologie, PARIS, France
(2) CHNO des XV-XX, Service Ophtalmologie III, Paris, France
(3) Hôpital Fattouma Bourguiba, Service d'ophthalmologie, Monastir, Tunisia

Purpose The aim of this study was to compare the efficacy and safety in Dry Eye Disease (DED) of T2762, a new product containing an innovative bioprotective molecule trehalose (molecule finds in plants resistant to dissication with osmoprotectant properties) and hyaluronic acid, to Vismed®.
Methods Phase III, randomized, active-controlled, Investigator-masked, multicentric study in France and Tunisia. 105 Adult patients (≥18 years) with moderate to severe DED were included and received one drop of either T2762 (N=52) or Vismed® (N=53) 3-6 times per day for 84 days. The primary efficacy variable was the Oxford grading score at Day 35. Ocular Surface Disease Index (OSDI), dry eye symptoms, Schirmer test, TBUT, conjunctival hyperaemia, and global performance were assessed as secondary efficacy criteria at baseline, Day 35 and Day 84. Safety assessments were standard.
Results Non-inferiority of T2762 to Vismed® for Oxford grading score was demonstrated at Day 35. For secondary efficacy parameters, reductions in OSDI, dry eye symptoms and investigator/patient assessments of global performance were better for T2762. There were no clinically meaningful between-group differences for the other secondary criteria. Both treatments were well tolerated. Interestingly, there were fewer ocular symptoms upon instillation and fewer AEs with T2762.
Conclusions T2762 is effective and safe, with better patient satisfaction than existing hyaluronate-only eye drops, and offers a therapeutic advancement in the treatment of moderate to severe DED

• T086

Efficacy of Dry Eye Disease Treatment based on the 2007 Report of the International Dry Eye WorkShop (DEWS)

UTHEIM O (1), Ræder S (2), Utheim T P (3), Eidet J R (3), Badian R (4), Stojanovic A (5), Chen X (3)
(1) Oslo University Hospital, Ophthalmology Department, Oslo, Norway
(2) The Norwegian Dry Eye Clinic, Oslo, Norway
(3) Oslo University Hospital, Department of Medical Biochemistry, Oslo, Norway
(4) Elverum Hospital, Department of Ophthalmology, Oslo, Norway
(5) University Hospital of North Norway, Department of Ophthalmology, Tromsoe, Norway

Purpose Purpose: To assess the effect of dry eye disease (DED) treatment according to the guidelines reported by the International Dry Eye WorkShop (DEWS) in 2007.
Methods Methods: Dry eye disease patients with or without meibomian gland dysfunction (MGD), treated at the Norwegian Dry Eye Clinic, with at least 6 months follow-up time were consecutively included in the study. The choice of treatment for DED was based on the dry eye severity level (DESL), according to the 2007 Report of the International Dry Eye WorkShop (DEWS). The values of tear film break-up time (TBUT), Schirmer I test, ocular surface staining (Oxford scale), and dry eye severity level (DESL) on the right eye at 1, 3, 6, 12, and 24 months after the treatment were compared with those prior to treatment.
Results Results: A total of 237 eyes were included. At 6 months follow-up, TBUT increased from 5.07±3.63s to 8.54±5.12s (p<0.001); Schirmer I test did not show significant change; ocular surface staining decreased from 1.64±2.13 to 0.76±1.20; and DESL decreased from 2.08±0.47 to 1.72±0.54 (p<0.001). The improvement of TBUT, ocular surface staining, and DESL remained significant at 24 months follow-up.
Conclusions Conclusions: Treatment based on the 2007 Report of the International Dry Eye WorkShop (DEWS) was effective in a Norwegian cohort of DED patients with significant improvement in key parameters for assessing DED.

• T087

Systemic immunosuppression with mycophenolate mofetil to prevent corneal graft rejection after high risk penetrating keratoplasty: a 2-year follow-up study

SZAFLIK J P , Major J , Izdebska J , Lao M , Szaflik J
Medical University of Warsaw, Department of Ophthalmology, Warszawa, Poland

Purpose The study aimed to evaluate the efficacy and safety of systemic immunosuppression with mycophenolate mofetil (MMF) to prevent corneal graft rejection after high risk penetrating keratoplasty.
Methods One hundred ninety-six consecutive patients who underwent high risk penetrating keratoplasty defined as the presence of deep vascularization in more than two quadrants, keratouveitis, emergency keratoplasties, and retransplantations were enrolled in the study. Ninety-eight prospectively followed-up patients were treated with MMF (with dose adjustment based on mycophenolic acid [MPA] serum concentration), and 98 patients were in the non-MMF-treated retrospectively assessed control group.
Results During a mean of 24 months' observation, immune reactions occurred in 8 cases (8%) and graft rejection with subsequent graft failure occurred in 3 cases (3%) in the MMF group. In the control group, graft rejection occurred in 76 cases (78%) and failure due to graft rejection occurred in 30 cases (31%). Kaplan-Meier analysis showed that after a year 93% of the grafts in the MMF-treated group and 47% in the control group showed no immune rejection ($p < 0.01$, log-rank test). Cox regression analysis showed that MMF treatment decreased the risk of graft rejection 11 times (RR = 11, 95.0% CI 4.8-25, $p < 0.0001$). Among 98 MMF-treated patients, 13 had gastric discomfort, 3 developed leucopenia, and 2 had anemia that resolved after MMF dose reduction.
Conclusions MMF treatment after high risk penetrating keratoplasty is safe and reduces the incidence of immune graft rejection and graft failure. Side effects were rare and reversible in all but one case.

• T088

Differential molecular signature of ectatic and non-ectatic areas from Keratoconus patient corneas.

PAHUJA N (1), Rajiv Kumar N (2), Shetty R (1), Shroff R (1), Ghosh A (2)
(1) Narayana Nethralaya, Cornea, Bangalore, India
(2) Narayana Nethralaya, GROW lab, Bangalore, India

Purpose To evaluate if the gene expression profile of corneal epithelium from the cone area in Keratoconus (KC) differs from the peripheral non-ectatic areas Hypothesis: The ectasia in Keratoconic cornea is localized to the cone while the peripheral areas are apparently normal. Hence we hypothesized that within the cone of a KC patient cornea, the structural weakness may be a function of localized gene expression differences
Methods Study group contained 54 KC patients undergoing epithelium off corneal collagen crosslinking (CXL) and 9 non-ectatic subjects undergoing photo refractive keratectomy (PRK) as controls. The cone vs periphery distinction is based on keratometry and location of the cone based on elevation map. Using a 4.5 mm trephine centered on the cone, epithelium was scraped separately for cone and rest as periphery. In non-ectatic controls, the central 4.5 mm area was taken as cone. Gene expression profiling was performed for each pair of cone and periphery samples by quantitative PCR.
Results Lysyl oxidase levels were significantly reduced in the cone of KC patients ($p=0.002$). Structure related genes COL1($p=0.01$) and COL4($p=0.008$) were also reduced significantly in KC patient cones. The cytokines IL6, TGFβ and TNFα did show an increased trend; regulatory cytokine IL10 did not show significant trend. Matrix remodeler MMP9 showed an increasing trend at the cone while its inhibitor TIMP1 showed a reducing trend that was not significant($p=.09$).
Conclusions Ectasia in KC may be driven by local molecular factors at the cone that possibly spreads to other parts of cornea as disease progresses

• T089

Assessment of the performances of a handheld in vivo confocal microscope for the analysis of human corneal innervation

BREHON A (1), Perrot J L (2), Cinotti E (2), Labeille B (2), Grivet D (3), Crouzet E (1), Gain P (1), Thuret G (4)
(1) Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering, Faculty of Medicine- Jean Monnet University, Saint-Etienne, France
(2) University Hospital, Department of Dermatology, Saint-Etienne, France
(3) University Hospital, Department of Ophthalmology, Saint-Etienne, France
(4) Corneal Graft Biology- Engineering and Imaging Laboratory- EA2521- Federative Institute of Research in Sciences and Health Engineering- Faculty of Medicine- Jean Monnet University- Saint-Etienne- France- and Institut Universitaire de France, Bd St Mich,

Purpose We previously reported, for the first time, the use of a dermatological handheld in vivo confocal microscope (IVCM), VivaScope 3000 (Lucid, NY), for the imaging of the ocular surface and ocular adnexa (AmJOphthalmol2015;159:324). Aim: to further assess its performances for qualitative and quantitative analysis of corneal innervation.
Methods Clinical interventional prospective single-center study comparing the first version of the handy handheld VivaScope 3000 with the Heidelberg Retina Tomograph (HRTIII-RCM) as a reference. The right central subbasal plexus (SBP) of healthy corneas of non-diabetic patients, diabetic patients without peripheral neuropathy and diabetic patients with peripheral neuropathy was analyzed the same day with both IVCMs by the same observer. The three best images were selected for each device and the nerve density, the number of nerves by frame, the number of branch per frame, and tortuosity of the nerves of the central SBP were calculated using NeuronJ. Analyzes were done on similar areas, blind to the IVCM type, then on full fields.
Results The VivaScope provided 920 x 920 µm images versus 400 x 400 µm for the HRTIII-RCM. Images of the SBP were easily obtained but the 4 parameters were significantly lower in the 3 populations with the VivaScope despite a larger field of view. Comparisons between populations are ongoing.
Conclusions This handheld dermatological IVCM is able to image the SBP but is less informative than the static HRTIII-RCM. For SBP, the larger field is not an advantage because most of the field is out of focus. Improvements of the IVCM objective are proposed. GRANT: project INNOVEYE GIRCI RAA.

• T090

Contribution of Optical Coherence Tomography (OCT) with real-time OCT of the Femtosecond laser, and per operative OCT of the microscope in deep anterior lamellar keratoplasty (DALK) for keratoconus: a new technique

NGUYEN D T (1), Stephan S (1), Gleize S (2), Cochereau I (1), Gabison E (1)
(1) Hopital Fondation Rothschild, ophthalmology, Paris, France
(2) French Bank of Eyes, grafts, Paris, France

Purpose Deep anterior lamellar keratoplasty (DALK) is a treatment of choice for keratoconus. We evaluate the contribution of a new technique associating femtosecond laser with real-time OCT, and per-operative OCT on the microscope, in DALK surgeries forkeratoconus.
Methods After training on artificial anterior chambers of corneal grafts to evaluate the reproducibility of cuts, pre-cuts of human anterior corneal lamellae during DALK of keratoconus were realized using the femtosecond laser (Victus, Bausch and Lomb) with real-time OCT and a curved applanation's surface. The depth was caculated around 60% of the thinnest pachymetry. Surgeries were realized using the per-operative OCT with the Rescan system of the microscope (Lumera 700, Zeiss).
Results Curved applanation and visualization with real-time OCT of the cuts' depth enabled the realization of reproducible lamellar cuts on 200µ thick corneas, without modifying the laser-cornea interface neither using masking agents. Femtosecond laser cuts allowed the big-bubble formation on 10/10 ex-vivo corneas. In human surgeries, real-time OCT visualization allowed controlling non-penetrating cuts, and the curved applanation limited folds formation on the residual stroma. Each surgical step was controlled by per-operative OCT, with visibility of tissues' structure and thickness, and instruments in cross section. The Anwar-air dissection technique permitted the "big-bubble" formation in 7/7 case, clearly visible on OCT, with only 1 or 2 injections of air. Residual posterior stroma was resected realizing pre-descemetic lamellar grafts.
Conclusions This new technique, femtosecond laser associated with per-operative OCT, appears to be safe, effective, reproducible and time-saving in DALK surgeries, facilitating the "big-bubble"formation. It may be proposed for the management of keratoconus and other indications.

• T091

The P2X7 receptor is a potential therapeutic target for the treatment of Uveitis

TEMPEST-ROE S , Tam F , Taylor S
Imperial College London, Renal and Vascular Medicine, London, United Kingdom

Purpose Adenosine-5'-triphosphate (ATP) functions as an important extracellular messenger and plays a critical role as a danger signalling molecule during inflammation. In pathological conditions damaged cells leak high concentrations of ATP into the extracellular milieu, activating P2 Purinergic receptors which are highly expressed on immune cells. Pathological stimulation of the P2X7 receptor may be involved in the development of autoimmune disease, so we explored the impact of P2X7R antagonist treatment on the development of Experimental Autoimmune Uveitis (EAU) in mice.
Methods EAU was induced in P2X7-/- and wild-type mice using IRBP peptide 1-20(GPTHLFQPSLVLDMAKVLLD) with adjuvant Bordetella pertussis toxin. All procedures were performed under a Home Office License in accordance with the regulations of UK ASPA (1986). EAU was then induced in B10.rIII mice with RBP-3 161-180 (SGIPYIISYLHPGNTILHVD) and adjuvant Bordetella pertussis toxin. P2X7R antagonist A439079275 or vehicle were injected i.p. twice daily from day 12. p.i when clinical features of EAU manifested. Disease activity was observed through TEFI imaging and animals were treated until peak disease and termination at day 16 p.i.
Results P2X7R deficiency protected against the development of EAU, with disease scores significantly lower in P2X7-/- animals compared to control animals. P2X7R antagonist treatment with A439079 prevented development of severe EAU with disease scores in A439079 treated animals significantly lower than vehicle treated animals.
Conclusions P2X7R deficiency protects against the development of EAU in mice and P2X7R antagonist can ameliorate established disease. The P2X7R may represent a viable therapeutic target for ocular inflammatory disease.

Commercial interest

• T092

Role of macrophages in the course of an in vivo murine model of Anterior Ischemic Optic Neuropathy

KOKONA D , Häner N S , Ebneter A , Zinkernagel M S
Inselspital- University of Bern, Opthalmology, Bern, Switzerland

Purpose Anterior Ischemic Optic Neuropathy (AION) is a common cause of vision loss and is characterized by degeneration of the optic nerve and retinal ganglion cells. Recently, inflammation has been proposed to play a role in the course of AION, and we wanted to investigate the contribution of circulating and/or resident microglia.
Methods We examined the role of macrophages in the course of AION, employing an ***in vivo*** murine model of laser-induced AION. AION was induced in BALB/c mice and three and six days after, OCT was performed and the number of infiltrating cells in the vitreous body was quantified. Bone marrow chimeras were generated using bone marrow derived cells that express GFP under the promoter of CX3CR1, specifically labelling macrophages. Cells were injected intravenously in lethally irradiated BALB/c mice which were subjected to AION two weeks later. Three and seven days after the AION induction, the eyes were subjected to OCT. The mice were euthanized at day 7 and their eyes were prepared for immunohistochemical studies against GFP and Iba-1. FACS analysis of the retina was also performed in AION subjected BALB/c mice 3, 7 and 14 days after AION induction.
Results Three and six days after AION induction, quantification of the OCT data showed a statistically significant elevation of infiltrating cells in the vitreous of AION subjected eyes compared to control eyes. This finding was substantiated by FACS analysis. The chimeras experiments revealed infiltration of circulatory macrophages into the retina.
Conclusions Our data support a role of circulating and/or resident macrophages in the course of AION.

• T093

Contribution of virtual reality in clinical practice in ophthalmology

FLORES M (1), Mauris N (2), Anne Charlotte L (2), Thibaud M F (2), Saleh M (1)
(1) CHU Besançon, Ophthalmology, Besancon, France
(2) ISIFC, Bioengineering, Besancon, France

Purpose Feasibility study of a device allowing recording, transmission and viewing by another operator of a stereoscopic clinical examination at the slit lamp.
Methods Two medical cameras (CM900, Haag-Streit, Bern, Switzerland) were mounted on a slit lamp (BQ900, Haag-Streit, Bern, Switzerland) equipped with a beam splitter allowing to record stereoscopic videos. The video footage associated with the patient's clinical data were then remotely transmitted to another examiner located in another room via a secure server dedicated to telemedicine. The data was then visualized through augmented reality glasses type Oculus Rift DK2 (Oculus VR, California) for stereoscopic viewing of the recorded consultation.
Results Five patients consulting for diseases of the anterior and posterior segments were examined remotely and the diagnosis was consistent with that of the first examiner in all cases.
Conclusions The success of this experience of telemedicine and augmented reality offers significant opportunities in the fields of education and remote consultation.

• T094

Hyperreflective Dots in Spectral Domain Optical Coherence Tomography as Phenotypic Marker in Uveitis-Associated Cystoid Macular Edema

SELLAM A , Massamba N , Fel A , LeHoang P , Bodaghi B
Hôpital Pitié Salpétrière, Ophthalmology, Paris, France

Purpose To evaluate the agreement between hyperreflective dots (HRD) in retina layers by spectral domain optical coherence tomography (SD-OCT) and laser flare photometry associated with best-corrected visual acuity (BCVA) results in patients with uveitic cystoid macular edema (CME).
Methods All patients referred to our tertiary care center for posterior uveitis had full examination including: BCVA, laser flare photometry, SD-OCT, fluorescein and infracyanine angiography. §Causes of uveitis were multiple: infectious, inflammatory and unknown. The characteristics of the HRD were evaluated in all SD-OCT scans. HRD were defined as small focal hyperreflective material scattered mainly in outer retinal layers but also spreading to all retinal layers observed in at least one available scan. Two different ophthalmologists counted HRD using a horizontal B scan cross section through the fovea. They were classified on the basis of quantity (i.e. absent, few if less than 10, moderate if between 10 and 20, or numerous if more than 20). Central macular thickness (CMT) was also evaluated.
Results 24 eyes of 18 patients were included. 8 men and 10 women with posterior uveitis were examined. Mean flare measurement was 25.1 (3-62). Mean BCVA was 20/63. Mean central macular thickness was 463 µm. 2 subgroups were identified. 13 eyes presented decreased BCVA, normal or elevated Flare, numerous HRD and increased CMT, corresponding to active posterior uveitis. Other 11 eyes presented decreased BCVA, increased CMT, normal laser Flare photometry, those results corresponding to chronic posterior uveitis. The difference with the two groups was numerically significant.
Conclusions HRD are correlated to CMT and BCVA but not with anterior chamber flare in active posterior uveitis. A large prospective study is needed in order to confirm these results.

• T095

Therapeutics course of childhood noninfectious uveitis

TARFAOUI N (1), Lala E (1), Uettwiller F (2), Marot Y (1), Hoarau C (2), Lelez M L (1), Arsene S (1), Pisella P J (1)
(1) CHRU de Tours, Service d'ophtalmologie, Tours, France
(2) CHRU de Tours, Service d'immunologie pédiatrique, Tours, France

Purpose Childhood noninfectious uveitis is a relatively uncommon but severe disease. All cases seen at the Tours's Hospital were included in this study and were equally followed by the multidisciplinary consultation to evaluate our practice over time.
Methods 44 children followed from 2003 to 2013 were included. Demographic criteria (gender, age, type of uveitis, initial and final clinical description) and therapeutic outlines were recorded. A vision quality questionnaire Eye–Q associated with a tolerance questionnaire were sent to all patients.
Results 66% were girls, the average age of diagnosis is 6.5 years and 48% of cases were JIA. Average final visual acuity was approximately 20/20. The initial treatment was topical corticotherapy alone in 47% of cases, and 42 % associated with oral corticosteroids. Since the introduction of our multidisciplinary consultation, the delay in determining the change in treatment has been decreased (p = 0.001) without modifying neither the duration nor the dose of corticosteroid therapy. 16% developed new ocular complication during average follow-up of 39 months. 60% of the ocular complications ***de novo*** could be topical corticosteroid related. The response rate was 62% and 66% with preserved quality of vision. The Eye - Q score was correlated with the visual acuity but not with the duration or the doses of any treatments.
Conclusions Our population showed similarity to that of the literature, except for the early support. Our Visual and inflammatory results were satisfactory, which could be explained by the introduction of our multidisciplinary consultation allowing a faster adaptability of therapeutics.

• T096

Efficacity and safety of TOXO KO vaccine to prevent ocular toxoplasmosis in congenital murine model

TARFAOUI N (1), Morisse S (2), Lemee G (1), Dimier-Poisson I (3), Seche E (2), Pisella P J (1)
(1) CHRU de Tours, Service d'Ophtalmologie, Tours, France
(2) Vitamfero, Service de Recherche et développement, Tours, France
(3) Faculté de Pharmacie de Tours, Service d'immunologie/vaccinologie, Tours, France

Purpose Toxoplasmosis is a worldwide zoonotic disease caused by the protozoa ***Toxoplasma gondii*** and is a major cause of abortions but also of ocular lesions. Thus, ocular toxoplasmosis is a major health issue in certain parts of the world, especially in South America and Africa.
Methods We have studied the efficacy of a live attenuated strain of ***T. gondii*** (***i.e.*** Toxo mic1-3 KO mutant) as a vaccine against ocular toxoplasmosis in a congenital toxoplasmosis model in mice. Mice were vaccinated with Toxo ***mic1-3*** KO strain, mated and infected during pregnancy. Nonvaccinated mice infected at mid gestation with ***T. gondii*** were used as control. One month after delivery, pups were sacrificed and ocular fundus, cytokine production in intra-camerular tissue and cysts formation in eye and in brain were analysed.
Results We have demonstrated that: Retinal ***T. gondii*** cysts were detected in 71% of pups born to nonvaccinated dams (2.54 ± 4.10). A significantly smaller number of cysts in retinal tissue was seen in pups born to vaccinated dams 0.56 ± 1.18 (>86% reduction in cysts in ocular tissue).Clinical signs of ocular infection were detected in 73,2% of pups born to non vaccinated dams against 19% of pups born to vaccinated dams.
Conclusions In conclusion, Toxo mic1-3 KO is an effective vaccine against ocular toxoplasmosis in a congenital mice model. This strain could be a promizing vaccine.

• T097

Occult non-metallic intraocular foreign body causing recurrent anterior uveitis

MORREALE BUBELLA R
Section of Ophthalmology, Department of Exsperimental Biomedicine and Clinical Neuroscience BioNeC- University of Palermo, Agrigento, Italy

Purpose To describe the case of textile worker with recurrent anterior uveitis following the traumatic penetration of nylon thread into the anterior segment of the eye.
Methods Examination by slit-lamp of the affected eye
B-scan ultrasonography during the inflammatory episode and after the resolution of the uveitis.
Visual Acuity Measurement during the inflammatory episode and after the resolution of the uveitis.
Results The use of topical therapy together with antibiotic systemic therapy led to the regression of the inflammatory symptoms (intense epibulbar and tarsal hyperemia with perikeratic reaction, corneal sub-oedema with some folds in the Descemet's membrane, Tyndall 2+ and a layer of lower hypopyon associated with a filamentous foreign body with a spiral shape at the base of the lower chamber. In miosis the pupil did not react to a light stimulus) and pain. Removal of the foreign body allowed the rapid resolution of the recurrent uveitis.
Conclusions This case underlines the need for an accurate search for possible foreign bodies in cases of ocular traumas, even apparently slight ones, once penetration into the posterior chamber has been excluded.

• T098

Changes in lamina cribrosa and prelaminar tissue in anterior ischemic optic neuropathy

MUNOZ - NEGRETE F J , Rebolleda G , García-Montesinos J , Oblanca-Llamazares N , De Juan V , De Dompablo E
Hospital Ramón y Cajal. IRYCIS, Ophthalmology, Madrid, Spain

Purpose To determine changes in lamina cribrosa (LC) and prelaminar tissue in patients with unilateral non-arteritic anterior ischemic optic neurophaty (NAION) using enhanced depth imaging (EDI) spectral domain optical coherence tomography (SD-OCT).
Methods Seventeen eyes of 17 patients with NAION were prospectively studied. SD-OCT scans using EDI technology were obtained at the acute episode and at two and six months after the ischemic event. The OCT device was set to image a 15x10 degree vertical rectangle centered on the optic disc. The scan in LC was seen clearliest was selected for analysis. The vertical distances from three equidistant points on the reference line (Bruch's membrane opening-BMO) to the anterior prelaminar tissue surface, and to the anterior and posterior surfaces of the LC were measured.
Results At diagnosis, mean prelaminar tissue was significantly thicker and anterior LC surface more posteriorly placed in NAION eyes than in non-involved eyes. During the follow-up, in NAION eyes there was a significant prelaminar thinning and an anterior LCreversal (P=0.001 and P=0.002 at 2 and 6 months respectively). BMO significantly reduced during follow-up (P=0.008 and P=0.034 at 2 and 6 months respectively). Both prelaminar tissue thickness and BMO changes correlated with retinal nerve fiber layer thickness measurements.
Conclusions OHN is a dynamic structure that undergoes biomechanical changes in eyes suffering NAION. A significant prelaminar tissue thickening and posterior lamina cribrosa displacement occurred during the acute ischemic optic neuropathy, that reverse as the edema resolves.

• T099

The added value of undiluted vitreous biopsy samples processed by the Cellient® tissue processor (Hologic) in unsolved uveitis.

VAN CALSTER J , Van Ginderdeuren R
University Hospitals Leuven, Dept. of Ophthalmology, Leuven, Belgium

Purpose In this prospective study, the added value of undiluted vitreous biopsy samples in the diagnosis of unsolved uveitis was evaluated. Vitreous biopsies are difficult to handle because of the paucity of cells and the gelatinous structure of the vitreous. Histopathological analysis of the vitreous is useful in challenging cases to differentiate uveitis from lymphoma or infection and to define the type of cellular reaction.
Methods 97 consecutive undiluted vitreous samples were isolated in patients with unsolved intermediate or posterior uveitis. A 1.5-2.5cc sample was taken through a single 23G or 27G port using the EVA vitrectomy platform (DORC) with a twin duty cycle high speed cutter. The samples were analysed with the Cellient® tissue processor (Hologic). This machine is a fully automated processor starting from a specified container with PreservCyt® (fixative fluid) with cells to paraffin. Routine histochemical and immunostainings were evaluated.
Results In 94.8% of the cases, sufficient material was found to provide an added value in the diagnostic workup. In 34%, a Cytolyt® mucolytic wash was necessary to prevent clotting of the tubes in the Cellient® tissue processor due to the viscosity of the sample. In 7% the diagnosis was an acute inflammation (presence of granulocytes), in 42% chronic active inflammation (presence of T-lymphocytes), in 36% low-grade inflammation (presence of CD68 cells, with <5% T-lymphocytes); and in 9% a malignant process (lymphoma). In 5% no diagnosis was found. In the chronic active inflammation group 39% was a granulomatous inflammatory process.
Conclusions This standardized protocol for sampling and handling undiluted vitreous biopsies gives a superior result in morphology, number of cells, and possibility of immuno-histochemical stainings. The diagnosis can be established or confirmed in 94.8% of cases.

• T100

APMPPE as a window on systemic granulomatous inflammation

LABALETTE P (1), Bouabane I (1), Maurage C A (2)
(1) CHRU de Lille, Ophtalmologie, Lille, France
(2) CHRU de Lille, Anatomo-Pathologie, Lille, France

Purpose Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) an unfrequent posterior uveitis presumed to be caused by a general hypersensitivity vasculitis.
Methods Eight patients aged from 12 to 33 years presented with AMPPE were studied. For each patient a systemic work-up for systemic granulomatous disease was performed, including pathologic analysis of accessory salivary glands biopsies.
Results A granulomatous infiltration of the accessory salivary glands biopsies was found in six cases, a feature consistent with a systemic involvement rather than an isolated eye disease. In addition two patients were diagnosed for systemic sarcoidosis.
Conclusions In numerous cases, AMPPE seems to be the eye expression of a systemic granulomatous reaction

Commercial interest

• T101

Relapsing Polychondritis and its Orbital Manifestations

TEO L (1,2,3), Choo C T (1,2,3)
(1) Singapore National Eye Centre, Oculoplastics, Singapore, Singapore
(2) Duke- NUS Graduate Medical School, Ophthalmology, Singapore, Singapore
(3) Singapore Eye Research Institute, Oculoplastics, Singapore, Singapore

Purpose We describe a 73 year old Chinese Gentleman with bilateral relapsing, remitting orbital inflammatory disease associated with Relapsing Polychondritis (RP).
Methods We reviewed the current literature available on the diagnosis and management of orbital inflamamtory disease in RP.
Results Our patient first presented with right orbital inflammation that did not improve despite antibiotic treatment. Computer tomography (CT) of the orbits showed a soft tissue mass along the roof of the orbit, which was biopsied, revealing acute on chronic inflammation. There was complete resolution of his orbital inflammation within 2 weeks of initiating systemic steroid treatment. He subsequently developed recurrent bouts of left orbital inflammation. One year later, he was diagnosed with relapsing polychondritis and subsequently developed multiple myeloma seven years later.
Conclusions In summary, recurrent orbital inflammatory disease should prompt the Oculoplastics surgeon to exclude a systemic autoimmune disease and hematological malignancy. The course of orbital inflammation in RP can be relapsing and remitting. Co–managementwith a rheumatologist will be helpful to achieve control of the disease with judicious use of immunosuppression. Long-term follow-up of the patient will be necessary to monitor for malignant transformation of the orbital lesion, as well as the development of hematologic malignancies.

• F001

Receptor-targeted liposome-peptide-siRNA nanoparticles represent a novel and efficient siRNA delivery system to prevent conjunctival fibrosis

YU-WAI-MAN C (1), Tagalakis A (2), Manunta M (2), Hart S L (2), Khaw P T (1)
(1) NIHR BRC at Moorfields Eye Hospital and UCL Institute of Ophthalmology, Cell Biology & Ocular Biology and Therapeutics, London, United Kingdom
(2) Wolfson Centre for Gene Therapy of Childhood Disease, Gene Therapy, London, United Kingdom

Purpose Glaucoma is the leading cause of irreversible blindness worldwide and fibrosis is the main cause of failure of glaucoma surgery. We have previously described how the Myocardin-related transcription factor/ Serum response factor (MRTF/ SRF) pathway is intricately linked to all the key pathways in ocular fibrosis. Our aim was to develop a novel liposome-peptide-siRNA (LYR) nanoparticle as an efficient delivery system for MRTF siRNA in conjunctival fibrosis.
Methods The LYR nanoparticles were characterised with regard to particle size and zeta potential. Real-time qPCR and western blotting were used to compare the silencing efficiency in human Tenon's fibroblasts using different MRTF siRNA concentrations, targeting peptides, and liposomes. The cytotoxicity of the LYR nanoparticles was assessed using the MTT cell assay. Three-dimensional fibroblast-populated collagen matrices were also used as a functional assay to measure contraction in vitro.
Results All LYR nanoparticles were strongly cationic with sizes around 100 nm and PDIs < 0.4. The LYR nanoparticles efficiently silenced the MRTF gene by 76% and 84% using 50 nM and 100 nM siRNA respectively. The MRTF gene was also efficiently silenced by 76% and 75% using the targeting peptides Y and ME27 respectively. The MRTF protein expression was significantly decreased by the LYR nanoparticles. The non-PEGylated liposome formulations showed higher silencing efficiency than the cationic PEGylated formulations. The MRTF nanoparticles were also not cytotoxic at 50 nM siRNA concentration and prevented matrix contraction after a single transfection treatment.
Conclusions This is the first study to show that receptor-targeted liposome-peptide-siRNA nanoparticles represent an efficient and safe siRNA delivery system that could be used to prevent fibrosis after glaucoma surgery.

• F002

Leuven Eye Study - Baseline and methods

ABEGAO PINTO L (1), Willekens K (2), Van Keer K (2), Shibesh A (3), Vandewalle E (2), Molenberghs G (3), Stalmans I (2)
(1) Centro Hospitalar Lisboa Norte / Faculty of Medicine of Lisbon University, Department of Ophthalmology, Lisbon, Portugal
(2) University Hospitals Leuven, Ophthalmology, Leuven, Belgium
(3) University Hospitals Leuven, Bio-Statistics, Leuven, Belgium

Purpose Glaucoma is known to be associated with vascular dysfunction. However, integrating this knowledge in the clinical setting has been limited, considering the majority of vascular oriented studies have been either underpowered or only addressed a small segment of the vascular parameters in strictly selected patients. The Leuven Eye Study aims at bridging this gap by prospectively collecting the largest amount of vascular oriented data in a large real-life glaucoma clinic setting.
Methods Prospective, cross-sectional, case-control hospital-based study. Patients with primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), glaucoma suspect or ocular hypertension (OHT) and healthy volunteers were recruited. In addition to an ophthalmological examination, a vascular-oriented questionnaire was completed and ocular blood flow assessment (color Doppler imaging of retrobulbar vessels, retinal oximetry, dynamic contour tonometry, optical coherent tomography enhanced depth imaging of the choroid) was performed in each subject.
Results 620 subjects (297 male) were recruited between March and December 2013 (POAG: 214, NTG: 192; glaucoma suspect: 41; OHT: 27; healthy controls: 146). Mean age was 68,4±12,9 years. Other than IOP, there was no difference in demographic variables between glaucoma groups and healthy volunteers. Values for the ocular blood flow parameters are in line with the current literature.
Conclusions the Leuven Eye study stands as the largest clinical trial on ocular blood flow in glaucoma. The creation of this vast database may help integrate the vascular aspects of glaucoma into the clinical practice of glaucoma.

• F003

Biomechanical properties of eyes with asymmetrical glaucoma defect

CELLINI M , GIZZI C , Finzi A , Campos E C
Ophthalmology Service, 1.Department of Specialized- Diagnostic and Experimental Medicine, Bologna, Italy

Purpose To evaluate biomechanical properties in eyes of patients affected by primary open angle glaucoma (POAG) with marked asymmetrical defects by means of Ocular Response Analyzer (ORA) and Spectral Domain OCT with Enhanced Depth Imaging (EDI SD-OCT) function.
Methods We studied 20 patients (mean age: 56±12) with asymmetrical POAG. One eye was classified as mild glaucoma (MG) and the sound eye as severe glaucoma (SG) by visual field indexes: MD -4.21±1.51 vs -16.56±5.76 dB; p=0.011 and PSD 3.54±0.87 vs 10.95±3.51 dB; p=0.007. An EDI SD-OCT centered on the optic nerve head and an ORA examination were performed on each eye of every subject before and during a IOP increase of 12.5±2.1 mm/Hg induced by a compression of the globe with an ophthalmodinamometer. Corneal histeresis (CH), corneal resistence factor (CRF) and laminar displacement (LD) were statistically analyzed by Wilcoxon's rank sum test and Spearman's correlation test considering significant a p<0.05.
Results After IOP increase we found a decrease of CH: 9.3±3.66 vs 6.92±3.04 mm/Hg; p=0.012 in SG and 8.62±2.16 vs 7.23±2.29 mm/Hg; p=0.176 in MG. CRF instead increase: 8.61±2.31 vs 12.38±3.65 mm/Hg; p=0.016 in SG and 9.02±1.48 vs 12.22±5.68 mm/Hg; p=0.041 in MG. LD was positive in MD: 29.08±19.28 um and negative in AG-

6.58±16.09 um. In AG eyes we found a correlation between LD and CRF (r=-0.658; p=0.019) and between LD and Scleral Rigidity (r=-0.693; p=0.012).
Conclusions This study demonstrates that in asymmetrical glaucoma the IOP increase changes the eye biomechanics with stiffening of the eye structures that involves not only the lamina cribrosa but also the corneal tissue.

• F004

Multicenter clinical trial of high-intensity focused ultrasound treatment in glaucoma patients without previous filtering surgery

APTEL F (1), Denis P (2), Rouland J F (3), Renard J P (4), Bron A M (5)
(1) University Hospital of Grenoble, Department of Ophthalmology, Grenoble, France
(2) Hospices Civils de Lyon, Department of Ophthalmology, Lyon, France
(3) Hôpital Claude Huriez- CHRU de Lille, Department of Ophthalmology, Lille, France
(4) HIA du Val de Grace, Department of Ophthalmology, Paris, France
(5) CHU Dijon, Department of Ophthalmology, Dijon, France

Purpose To evaluate the efficacy and safety of the ultrasonic circular cyclocoagulation procedure in patients with open-angle glaucoma naïve of previous filtering surgery.
Methods Prospective non-comparative interventional clinical study conducted in five French University Hospitals. Thirty eyes of 30 patients with open-angle glaucoma, intraocular pressure (IOP) > 21 mmHg and with no previous filtering glaucoma surgeries were sonicated with a probe comprising six piezoelectric transducers. The six transducers were activated with a 6-s exposure time. Complete ophthalmic examinations were performed before the procedure and at 1 day, 1 week, 1, 2, 3, 6 and 12 months after the procedure. Primary outcomes were surgical success (defined as IOP reduction from baseline ≥ 20% and IOP > 5 mmHg with possible retreatment and without hypotensive medication adjunction) at the last follow-up visit and vision-threatening complications. Secondary outcomes were mean IOP at each follow-up visit compared to baseline, medication use, complications and retreatments.
Results IOP was significantly reduced (p<0.05) from a mean preoperative value of 28.2 ± 7.2 mmHg (n = 3.6 hypotensive medications) to 19.6 ± 7.9 mmHg at 12 months (n = 3.1 hypotensive medications and n = 1.1 procedures) (mean IOP reduction of 30%). Success was achieved in 63% of eyes (19/30) at 12 months (mean IOP reduction of 37% in these eyes). No major intra- or postoperative complications occurred.
Conclusions The ultrasonic circular cyclocoagulation procedure seems to be an effective and well-tolerated method to reduce IOP in patients with open-angle glaucoma without previous filtering surgery.

Commercial interest

• F005

Comparison of preservative-free latanoprost and bimatoprost in a multicenter, randomized, investigator-masked cross-over clinical trial

STALMANS I (1), Cordeiro F (2), Hommer A (3), Oddone F (4), Ribeiro L (5), Sunaric Mégevand G (6), Rossetti L (7)
(1) UZ St. Rafael, Ophthalmology, Leuven, Belgium
(2) ICORG – Imperial College Ophthalmologic Research Group, Imperial College Healthcare NHS Trust, London, United Kingdom
(3) Hommer Ophthalmology Institute, Vienna, Austria
(4) G.B.Bietti Eye Foundation – IRCCS, Rome, Italy
(5) AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal
(6) Clinical Research Centre - Mèmorial A de Rothschild, Geneva, Switzerland
(7) Centre for Clinical Trials at San Paolo Hospital, University of Milan, Milano, Italy

Purpose To investigate the efficacy and safety of Bimatoprost Unit Dose Preservative Free (BUDPF) and Latanoprost Unit Dose Preservative Free (LUDPF) in a clinical setting.
Methods Prospective, randomized, investigator-masked, cross-over comparison. Patients with ocular hypertension or open angle glaucoma (OAG) with an IOP less than or equal to 21 mmHg with a preserved prostaglandin monotherapy at screening were washed out and randomized to receive BUDPF or LUDPF for 3 months and were then switched to the other respective treatment for another 3 months. IOP curves were performed at baseline and after each treatment period, and safety and tolerability were assessed at the two latter timepoints.
Results Both drugs were effective in lowering IOP, both at 3 and at 6 months (estimated differences compared to baseline pressures: -4,0±0.5 for both BUDPF and LUDPF, p<0.01 at 3 months; -5.2±0.5 for BUDPF, -3.4±0.5 for LUDPF, both p<0.01 at 6 months). Analysis at 6 months (primary endpoint) showed a difference of 1.6±0.5 mmHg between the two groups, favoring BUDPF (p<0.01). An intra-subject IOP difference of 0.9±0.2 mmHg in favor of BUDPF was observed (p<0.01).
Conclusions This study demonstrate a superior efficacy of BUDPF over LUDPF in lowering IOP.

Commercial interest

• F006

Double-hump sign on gonioscopy: definitive plateau iris? A cross-sectional study using ultrasound biomicroscopy

CORDEIRO SOUSA D (1,2), Leal I (1,2), Caiado F (1), Goncalves I (1), Reina M (3), Marques-Neves C (1,2,4), Prior Filipe H (5), Abegao Pinto L (2)
(1) Hospital Santa Maria - Lisbon Academic Medical Center, Ophthalmology, Lisboa, Portugal
(2) Faculty of Medicine, Lisbon Academic Medical Center, Lisboa, Portugal
(3) Centro Hospitalar Lisboa Central, Ophthalmology, Lisbon, Portugal
(4) Centro de Estudos Ciencias Visao, Ophthalmology, Lisbon, Portugal
(5) ALM - Ofialmolaser Clinic, Ophthalmology, Lisbon, Portugal

Purpose Plateau iris configuration (PIC) is a rare condition involving an angle closure unrelated to pupillary block. It may be defined by a narrow angle and a double-hump configuration on gonioscopy. Plateau iris syndrome (PIS) may lead to acute angle-closure glaucoma due to an anterior displacement and rotation of the ciliary body. It has been proposed that ultrasound biomicroscopy (UBM) is helpful in PIC/PIS diagnosis. Our work aims to describe UBM quantitative and qualitative findings in patients whose gonioscopy suggested a PIC/PIS.
Methods Cross-sectional study involving patients with a double hump gonioscopic finding. UBM was then performed by a blinded observer and evaluated for the presence of following ultrasonographic (US) criteria: 1) a thick and flat iris, 2) a sharp, square root angulation on its insertion, 3) an anterior rotation of the ciliary body, 4) irido-ciliary sulcus narrowing, 5) iris-trabecular apposition and 6) a relatively normal anterior chamber (AC) depth. Only high-quality images were accepted.
Results From Sep/14-May/15, 35 patients (59 eyes) were recruited. Only 3 eyes presented the six US criteria, 23 eyes filled five of the criteria, 13 satisfied four criteria, 16 presented three criteria and 4 two criteria. The most commonly verified criteria (over 95% of them) were a thick and flat iris and a square root insertion. There was no association between any of these criteria and sex nor age (p>0.10). Furthermore, the presence/absence of these criteria did not correlate with either anterior chamber depth, lens vault and lens length (p>0.10).
Conclusions The majority of patients presenting with clinical iris plateau syndrome do not fulfill the entire US criteria for this condition. However, the US-based iris morphological parameters seem to be present in nearly all iris plateau patients.

• F007

How accurate are optometrist referrals for glaucoma in the NICE era?

BOBAT H, Begum S, Lockwood A, Kirwan J F
Queen Alexandra Hospital, Eye Department, Portsmouth, United Kingdom

Purpose To determine if the reason(s) stated by the optometrist affect the positive predictive value (PPV) of referrals for suspected glaucoma.
Methods Optometrist referrals in Portsmouth are streamlined though the Glaucoma Referral Refinement Scheme (GRRS). We retrospectively analysed 100 'positive' and 100 'negative' referrals to the GRRS. Positives: those referred on to a secondary care glaucoma clinic; negatives: those discharged from the GRRS. Reason(s) for referral were determined and classified: intraocular pressure (IOP) optic disc changes (OD), visual field defect (VF), shallow anterior chamber depth (ACD). Since negative referrals to GRRS are four times more prevalent than positives, we calculated a 'corrected' PPV for each reason by multiplying the number of negatives by 4.
Results The overall PPV was 0.16. 70.4% cases were referred for a single reason (47.2% IOP, 12.2% OD, 8.8% VF, 2.4% ACD); the PPV was 0.11 for IOP and for OD, 0.05 for VF, 0.17 for ACD. 26.2% were referred for two reasons; the PPV was 0.47 for IOP + OD, 0.21 for OD + VF and 0.14 for IOP + VF. 4.2% were referred for IOP + OD + VF with a PPV of 0.62. Positive family history of glaucoma (21.4% referrals) did not increase PPV. The GRRS increased the PPV to 0.8.
Conclusions The majority of patients are referred for a single reason, yet the chance of a positive diagnosis is low. Accuracy is increased when IOP is reported in combination with OD, but VF adds little value as a second parameter. The highest PPV is found when all three reasons are stated (IOP+OD+VF). The proportion of referrals for IOP alone is similar to that found prior to the NICE guidelines. However, the PPV is considerably lower; 0.11 compared to 0.3 - 0.4 found in previous studies. In the NICE era, refinement schemes play an important role in reducing false positive referrals.

• F008

A pilot study of survey on patient satisfaction and its meaning in an Glaucoma outpatient

POURJAVAN S (1), Vanhaecht K (2)
(1) Cliniques Universitaires St. Luc, Ophthalmology, Brussels, Belgium
(2) KULeuven, Public Health & Primary care, Leuven, Belgium

Purpose To assess the degree of patient satisfaction and its correlation with the subjective satisfactory score of the ophthalmologist.
Outcomes:
- The % of satisfied patients.
- The correlation between doctor-patient perception of care.
- The impact of the interpersonal chemistry and the mood of care provider.

Methods A prospective, blind study. A simple and short questionnaire is given to the patients. Patients were asked to fill in the questionnaire including 4 questions with a 1 (lowest) to 5 (highest satisfaction) scores.
1. The score the "care"?
2. the ophthalmologist?
3. Recommend of the outpatient?
4. Recommend of the specialist?

The ophthalmologist gives her subjective score in three fields:
1. The quality of consultation (QoC).
2. The interpersonal "click" with the patient.
3. Her "mood".

The consented patients will be called for more spontaneous explanation.
Results Patient's score: 98% gave high scores >3.
Ophthalmologists score: neg. click with 15%, natural: 48% and good click: 36%, her mood was 33% each in 3 scores (bad, natural and hyper), Her objective QoC was 95% high scores. The click was significantly related with her mood and her mood was significantly related with QoC. The only correlation was between click & the high score on Q3. On telephonic enquete were good outcome of the surgery, optimal care, location and their "like" for the specialist, important.
Conclusions All patients had a high satisfaction score & not influenced "Mood" or "QoC". Upon spontaneously explaining of the patients, the most important factors for their satisfaction were; good operation outcome, optimal care, correct diagnosis but the geographical location (nearby, parking space) and their affection for the specialist were also very important reason for their satisfaction.

• F009

Corneal and optic nerve head biomechanical changes after deep sclerectomy

MUNOZ - NEGRETE F J, Rebolleda G, Díez L, Oblanca-Llamazares N, De Juan V, Casas-Llera P
Hospital Ramón y Cajal. IRYCIS, Ophthalmology, Madrid, Spain

Purpose To evaluate corneal and optic nerve head (ONH) biomechanical changes following nonpenetrating deep sclerectomy (DS).
Methods Forty-nine eyes undergoing DS were prospectively studied. Changes in corneal hysteresis (CH) and corneal resistance factor (CRF) using the Ocular Response Analyzer, as well as changes in prelaminar thickness, cupping and lamina cribrosa (LC) position using EDI technology before surgery and 3 months postoperatively were obtained. Simple and multiple linear regression models were used to determine predictors of ONH changes including age, corneal central thickness (CCT) and axial length (AL).
Results Mean corneal compensated IOP significantly decreased by 27.9 % (P<0.001). Mean CH increased and CRF decreased by 18.4% and 10.1% respectively (P<0.001) and both were significantly correlated with IOP reduction (P<0.001). There was a significant reversal of ONH cupping mainly due to a prelaminar tissue thickening (P<0.001). Mean preoperative AL correlated with the preoperative LC thickness (-0.459, P=0.012) and a further anterior displacement of LC postoperatively (0.377, P=0.044). A significant association was found between ONH cupping reversal and both preoperative IOP (P=0.046) and preoperative CRF (P=0.002).
Conclusions CH increased and CRF decreased significantly 3 months after NPDS and these changes correlated with IOP reduction. A significant cupping reversal mainly due to changes in prelaminar tissue thickness was observed. The magnitude of IOP reduction was the most significant factor in both corneal and ONH biomechanical changes.

• F010

Selective laser trabeculoplasty: Results on intraocular pressure and number of topical antiglaucoma medications

BONNEL S, Fenolland J R, Marill A F, Gaillard R, Rosenberg R, Theillac V, Mazharian A, Mouinga A, Giraud J M, Renard J P
HIA Val de Grace, Ophtalmologie, Paris, France

Purpose To evaluate results at one year of selective laser trabeculoplasty (SLT) on intraocular pressure (IOP) and assess if differences are related to number of topical treatments in ocular hypertension (OHT) and open angle glaucoma (OAG) patients.
Methods We performed a retrospective chart review of 106 eyes treated by SLT. Indications for SLT treatment were insufficient IOP control, allergy, discomfort or non-compliance to antiglaucoma treatment. Only patients with at least 1 year of follow-up after SLT were included. IOP was measured before and at 1, 6 and 12 months after SLT. All IOP measurements were performed with Goldmann applanation tonometry.
Results 106 eyes of 68 patients untreated (n=13), or treated with one (n=25), two (n=39) or three (n=28) topical antiglaucoma medications were included. Mean preoperative IOP was 19.4±3.6mmHg (respectively 21.1±2.7, 19.8±3.1, 19.1±4.2 and 18.9±3.4mmHg corresponding to the group without, one, two or three treatments) and 15.7±3.1mmHg at 12 months (respectively 16.2±3.5, 15.6±2.6, 15.6±3.4 and 15.5±2.8mmHg for each groups) which corresponds to an average decrease of 18.3% (respectively 23.7%, 19.7%, 17.2% and 16.1% for each groups). At 1 year, 62.2% (n=66) were responders (≥3mmHg reduction from baseline IOP =15,5% of IOP baseline) : 92.3% without treatment (n=12), 68% with one (n=17), 59% with two (n=23) and 50% with three treatments (n=14). The average IOP of responders decreased from 20.7±3.4 to 15.2±2.9mmHg (26.6%), respectively from 20.8±2.6 to 15.8±3.2 (25%) without treatment, from 20.6±3.2 to 14.9±3.7 (27.3%) with one, from 20.8±4.1 to 15.5±3.3 (25.1%) with two and from 20.7±3.2 to 14.4±2.4mmHg (29.7%) with three treatments.
Conclusions Lowering of IOP and number of responders after SLT appears to be more important un OHT and OAG patients with less topical antiglaucoma treatment.

• F011

Primary open angle glaucoma treated by high intensity focused ultrasound (HIFU) with the 2nd generation probe

ROULAND J F (1), Aptel F (2)
(1) Université de Lille, Ophtalmologie, Lille, France
(2) Grenoble University Hospital, Department of Ophthalmology, Grenoble, France

Purpose To assess the safety and efficacy of Ultrasound Ciliary Plasty (UCP procedure) using HIFU (high intensity focused ultrasound) with a second-generation probe which increases the treatment surface area and the firing duration in patients with primary open angle glaucoma.

Methods Prospective clinical series performed in two University Hospitals, on eighteen eyes of eighteen patients with primary open-angle glaucoma, treated with the EyeOP1 medical device equipped with six miniaturized cylindrical piezoelectric transducers of a new generation with an increased lesion volume. All eyes were treated with an 8-second exposure time per transducer. The main assessment criteria were safety and efficacy measured by the incidence of complications and IOP reduction. Ophthalmic examination and ultrasound biomicroscopy were performed before treatment and during clinical follow-up at D7, M1, M3, M6 and M12.
Results The mean intraocular pressure was significantly reduced from 28.4 ± 5.4 mmHg before treatment to 17.4 ± 3.8 mmHg at last follow-up. Complete success rate, as defined by an IOP reduction >20% and IOP> 5 mmHg after one UCP procedure was 84%. The mean IOP reduction achieved in responding patients was 42%. No major intra- or post-operative complications were observed. Clinical examination showed no lesions of ocular structures other than the ciliary body and no or few signs of intraocular inflammation after treatment.
Conclusions Coagulation of the ciliary body using high intensity focused ultrasound carried out with the new-generation of miniaturized transducers is a simple, well-tolerated procedure which enables to significantly reduce the intraocular pressure in patients with Open Angle Glaucoma.

Commercial interest

• F012

Glaucoma patient satisfaction after switching from preserved treatment to preservative-free latanoprost; results from the PASSY survey in three European countries

MUNOZ - NEGRETE F J (1), Lemij H (2), Erb C (3)
(1) Ramon y Cajal Hospital, Department of Ophthalmology, Madrid, Spain
(2) Rotterdam Eye Hospital, Glaucoma Service, Rotterdam, The Netherlands
(3) Augenklinik Berlin, Ophthalmology, Berlin, Germany

Purpose An European survey was implemented to evaluate patient satisfaction especially after the switch from a preserved prostaglandin to the preservative-free (PF) latanoprost (Monoprost®)
Methods Multicentre, epidemiological, retrospective survey. OHT/glaucoma patients treated with Monoprost® for 3 months were included. The following data were collected: glaucoma history, previous treatment, reasons for change, tolerance, patient satisfaction, ocular signs and surface disease.
Results 1541 patients were included (213 from Germany, 25 from the Netherlands and 1303 from Spain). These results focus on the patients who previously received a preserved treatment (n=1058; 69.4% of patients). Regarding tolerance, 94.8% of the patients were satisfied or very satisfied with PF latanoprost. In comparison to the previous preserved treatment, 75.1% of the patients considered that PF latanoprost was better or much better tolerated, and for 21% of them was the same. The tolerance evaluated with a Visual Analog Scale (VAS: 0 mm: very bad tolerance – 100 mm: very good) was 82.4 ± 17.08 for PF latanoprost and 56.1 ± 27.30 for the previous preserved treatment (mean difference: 26.3 mm; 47% of increase). Switching to PF latanoprost increased the VAS value whatever the previous preserved treatment: +31.1 switching from travoprost, +23.7 from latanoprost, +37.7 from bimatoprost 0.03%, +33.2 from bimatoprost 0.01% and +23.5 from beta-blockers (p<0.0001) In relation with previous preserved treatment, Monoprost® unidoses was considered as easier or much easier to use by 38.8% of the patients and as the same by 50.6%. The use of artificial tears decreased for 28.4% after switching to PF Latanoprost.
Conclusions After 3 months of Monoprost® treatment, patients that had switched from a preserved treatment were more satisfied concerning tolerance and needed fewer artificial tears.

• F013

Intraocular pressure in Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

PINNA A (1), Blasetti F (2), Campesi I (3), Scanu B (4), Carru C (3)
(1) University of Sassari, Department of Surgical- Microsurgical and Medical Sciences- Unit of Ophthalmology, Sassari, Italy
(2) University of Sassari, Department of Surgical- Microsurgical- and Medical Sciences- Unit of Ophthalmology, Sassari, Italy
(3) University of Sassari, Department of Biomedical Sciences, Sassari, Italy
(4) University of Sassari, Department of Surgical- Microsurgical- and Medical Sciences, Sassari, Italy

Purpose Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is one of the most common human genetic abnormalities, with a high prevalence in Sardinia, Italy, where the reported rates range from 10% to 15%. Hemizygous males have totally deficient erythrocytes. We are unaware of any previous report investigating intraocular pressure (IOP) in G6PD deficiency. The purpose of this study was to assess IOP in G6PD-deficient and G6PD-normal Sardinian men and ascertain whether there are significant differences between the two groups.
Methods IOP was measured by applanation tonometry in 104 G6PD-deficient and 104 age-matched G6PD-normal men. The Student t test was used to assess differences in IOP values between the two groups.
Results Mean IOP was 13.94±2.62 mm Hg in G6PD-deficient men and 14.29±2.84 mm Hg in G6PD-normal men, a not statistically significant result (P = 0.096).
Conclusions Results suggest that men with G6PD deficiency do not have a higher risk of increased IOP.

• F014

Normal tension glaucoma associated with lamina cribrosa defects and complicated of maculopathy: A case report

BESOMBES G, Bachetti P, Labalette P, Rouland J F
University Hospital of Lille, Ophthalmology, LILLE, France

Purpose Eyes with glaucoma often present modification of the lamina cribrosa, including posterior displacement, thinning, defects and pore deformities.
Methods A 40-year-old woman with no past medical history have been seen for an acute blurred vision of her left eye 5 days ago. Anamnesis didn't find any family history of glaucoma, but she described a Raynaud phenomenon. Complete ophthalmoscopic examination was performed, with biomicroscopy, fundus imaging, visual field test (Humphrey field analysis 30-2), optical coherence tomography (OCT) assessment with both Spectralis (Heidelberg) and Cirrus OCT (Carl Zeiss), ultrasonography and fluorescein/infracyanin angiography.
Results The maculopathy was characterized by schisis-like thickening and serous detachment. The presence of lamina cribrosa defects permits anomalous communications between intraocular and extraocular spaces. OCT showed a schisis cavity between the inner and outer retina and a larger outer-layer retinal detachment. The two were connected by a hole in the outer layer near the fovea. The associated subretinal and intraretinal fluid may derive from cerebrospinal fluid that passes through the opening created by the discontinuity of the lamina cribrosa into the subarachnoidal space. This complication usually occurs in case of congenital optic pit.
Conclusions We describe the case of a patient with a recent diagnosis of normal tension glaucoma, showing a pit-like structure within the ONH. We observed focal areas of laminar holes in the superior pole of the optic disc. This location differs from the congenital and acquired optic pits mostly temporally or inferiorly located. Enhanced Depth Imaging OCT of the ONH enables microstructural evaluation of lamina cribrosa defects, especially helpful in case of normal tension glaucoma.

• F015

A high oxygen demand in normal tension glaucoma

TURKSEVER C (1), Todorova M (2), Orguel S (2)
(1) Vista Klinik, Ophthalmology, Baselland, Switzerland
(2) University Eye Clinic Basel, Ophthalmology, Basel, Switzerland

Purpose To evaluate relationship between vascular dysregulation and retinal oxygen demand in normal tension glaucoma (NTG).
Methods Retinal vascular responses of 27 eyes of 18 Caucasian (10♀:8♂) individuals with NTG were measured. Subjects were grouped based on their median vascular responsiveness. In each group, retinal vessel oxygen saturation was measured in arterioles (A-SO2) and in venules (V-SO2) within the peri-papillary annulus with the oximetry tool of Retinal Vessel Analyser (IMEDOS Systems UG, Jena, Germany).Retinal nerve fiber layer thickness (RNFL) was measured with spectral domain optical coherence tomography (Carl Zeiss Meditec, Dublin, CA, USA) and visual field (VF) with Octopus perimeter (Haag-Streit International, Switzerland). Retinal oxygen concentration per micron of nerve fiber layer thickness (O2-C) was calculated as follows; the difference of aretrio-venous oxygen saturation (A-V SO2) was divided to the mean RNFL thickness. A linear mixed-effects model was applied (IBM SPSS®)
Results The eyes were grouped based on their vascular responsiveness (group1≤ 2.90%; n=13, group2> 2.90%; n=14). In group1 and in group2, mean A- SO2, V–SO2 and A-V SO2 were 96.50%(± 4.38); 97.77% (± 3.03)(p=0.517), 62.89%(± 6.23); 60.71%(± 6.28)(p=0.391), 34.64%(± 4.51); 36.68%(± 5.27)(p=0.294), respectively. Subjects in group1 showed higher O2-C 0.488%/µ(±0.0848) than in group2 0.434%/µ(± 0.0551)(p=0.027). Mean age (65.45y (± 11.7)) and VF(dB) defect (4.7dB(± 3.6), 3.4dB(± 5.2) were not statistically different between groups (p=0>141). In group1, RNFL thickness was significantly less than in group2 (72.23µm(± 12.1); 85.31 µm(±13.67)(p=0.014)
Conclusions Oxygen demand was increased in patients with excessive vascular dysregulation, while mean SO2 values were not related to age and/or flicker responses. This conclusion remains to be confirmed in further studies

• F016

Estimated cerebrospinal fluid pressure and trans-lamina cribrosa pressure difference in open angle glaucoma. The Korea National Health and Nutrition Examination Survey 2009-2012

LEE S H (1), Kwak S W (2), Kang E M (1), Hong S (1), Seong G J (1), Kim C Y (1)
(1) Yonsei Univ- College of Medicine, Department of Ophthalmology, Seoul, South-Korea
(2) University of Georgia, Department of Statistics, Athens- Georgia, United States

Purpose To investigate associations of estimated cerebrospinal fluid pressure (CSFP) and trans-lamina cribrosa pressure difference (TLCPD) with glaucomatous optic neuropathy in a population-based setting.
Methods A total of 6,656 adults (≥40 years) who participated in the Korea National Health and Nutrition Examination Survey (KNHANES) from 2009 to 2012 were included. Subjects were divided into non-glaucomatous and glaucomatous group, and glaucomatous subjects were further divided into normal tension glaucoma (NTG) group and high tension glaucoma (HTG) group. Based on a previous study with lumbar CSFP measurements, CSFP was estimated as CSFP(mmHg)= 0.55 Body Mass Index(kg/m2)+0.16 Diastolic Blood Pressure(mmHg)-0.18xAge(years)-1.91. TLCPD was calculated as intraocular pressure (IOP)-CSFP. Differences in estimated CSFP and TLCPD were assessed between the non-glaucomatous and glaucomatous groups.
Results In the non-glaucomatous population (n= 6016), mean estimated CSFP was 11.38±3.11mmHg and mean TLCPD was 2.54±3.83mmHg. When compared to the glaucoma group (n= 640), lower IOP (p<0.001), higher CSFP (p<0.001), and lower TLCPD (p<0.001) were observed in the non-glaucomatous group. Differences between glaucomatous subjects and non-glaucomatous subjects in estimated CSFP, TLCPD, and IOP were greater for the HTG subjects than for the NTG subjects.
Conclusions Estimated CSFP and TLCPD may play a significant role in pathogenesis of NTG and HTG.

• F017

Comparison of Humphrey visual field perimetry and new invented PC-based visual field testing system in healthy people and glaucoma patients.

KIM Y G (1), Lee J (2), Lee B (2), Kim S (2), Lee N (2), Kim S (2), Park J (2), You H (2), Kang J H (1)
(1) Kyung Hee University Medical School, Department of Ophthalmology, Seoul, South-Korea
(2) Pohang University of Science and Technology, Department of Industrial and Management Engineering, Pohang, South-Korea

Purpose The aim of this study was to compare the visual field test in healthy people and glaucoma patients with Humphrey visual field perimetry (HFA) and new invented PC-based visual field testing system (PCVF).
Methods This prospective study included 48 healthy people and 37 glaucoma patients who underwent both HFA and PCVF. Pattern standard deviation (PSD), mean deviation (MD) were compared between the 2 tests using Pearson correlation. Areas under receiver operating characteristics curve (AUCs) for discriminating healthy from glaucoma, sensitivity and cut-off value at 80% and 90% specificity of MD and PSD were determined in HFA and PCVF.
Results MD and PSD were correlated in glaucomatous eyes (r =0.48, 0.50 p<0.002, <0.002). The AUCs of MD and PSD from HFA were 0.882, 0.903 and those from PCVF were 0.676, 0.813. The sensitivity at 80% specificity of MD was 81.1% in HFA, 43.2% in PCVF, with the cut off value of PSD at 80% specificity at -2.86dB in HFA and -4.40dB in PCVF.
Conclusions MD and PSD data from HFA and PCVF significantly correlated in glaucomatous eyes. PCVF can be comparable to HAF for visual field testing system.

• F018

Glaucoma patient satisfaction regarding tolerance to their prostaglandin treatment: results from the GOAL (Glaucoma patients treated with prOstaglandins; sAtisfaction evaLuation) survey in Europe.

CLARKE J (1), Stalmans I (2), Lemij H (3), Baudouin C (4)
(1) Moorfields Eye Hospital, NIHR Biomedical Research Centre NHS Foundation Trust and UCL Institute of Ophthalmology, London, United Kingdom
(2) University Hospitals Leuven, Ophthalmology Department, Leuven, Belgium
(3) Rotterdam Eye Hospital, Glaucoma Service, Rotterdam, The Netherlands
(4) Quinze-vingts National Hospital and Vision Institute- University Paris 6, Ophthalmology, Paris, France

Purpose The high prevalence of ocular surface diseases (OSD) in patients treated for OHT/glaucoma is expected to displease them. To evaluate this, a survey was conducted in three European countries: the Netherlands, Belgium and United Kingdom.
Methods In this multicentre epidemiological survey, the following data were recorded during a visit to the ophthalmologist: glaucoma history, previous treatments and reasons for any change, tolerance, patient satisfaction, ocular signs and the presence of OSD.
Results The data of 793 patients treated with prostaglandins were analysed (168 from the Netherlands, 253 from Belgium and 372 from England). Only 9% of the treatments were preservative-free.
A very large number (93.7%) of patients declared to be satisfied or very satisfied with their current glaucoma treatment. The mean score of tolerance evaluated on a Visual Analog Scale (VAS) was 82.7±16.1mm (range from 0mm: very bad tolerance to 100mm: very good tolerance).
At the same time, the survey revealed (displayed in percentage of all patients):
• OSD was diagnosed in 42.5%
• symptoms upon instillation in 31.4%
• symptoms between instillations in 57.3%
• a conjunctival hyperaemia in 32%
• frequent use of artificial tears in 25.1%
The presence of hyperaemia, ocular signs, and symptoms upon or between instillations, positive conjunctival staining and frequent use of tear substitutes was statistically significantly linked to patient satisfaction (p≤0.006).
Conclusions A high percentage of satisfied patients (94%) was found in this survey, despite OSD signs and symptoms. Tear film substitutes are commonly prescribed to treat these side effects. Alternative treatment regimes such as preservative free treatments may reduce local side effects and encourage ophthalmologists to convince their patients that local intolerance is no longer inevitable.

• F019

Tarsal inflammatory response after topical prostaglandin analogues treatment - pilot study.

TRZECIECKA A (1), Paterno J J (1,2), Toropainen E (1), Wylegala E (3), Kaarniranta K (1,2), Smedowski A (1,2,3)
(1) University of Eastern Finland, Department of Ophthalmology, Kuopio, Finland
(2) Kuopio University Hospital, Department of Ophthalmology, Kuopio, Finland
(3) Medical University of Silesia, Clinical Department of Ophthalmology, Katowice, Poland

Purpose To describe impact of topical preservative-free (PF) prostaglandin analogues on inflammatory response within eyelid tarsus.
Methods New Zealand rabbits' eyes (n=12 animals) were exposed to topical PF prostaglandins for 8 weeks daily. Each right eye was treated and each left eye kept as a control – topical PBS application. As eye drops we used PF tafluprost (Taflotan, Santen), PF latanoprost (Monoprost, Thea) and PF bimatoprost (Lumigan, Allergan). After 8 weeks animals were sacrificed, eyelids were post-fixed in 4% paraformaldehyde and embedded in paraffin. Tarsal sections were immunostained for macrophage-specific Iba-1 and mucin. Tissue histology was evaluated by Masson trichrome staining. Quantitative analysis of macrophages (MFs) infiltration within tarsal: conjunctiva, stroma and glands was performed.
Results PF prostaglandin treatment for 8 weeks did not affect mucin expression within analyzed tissues. Total number of MFs forming infiltration in tarsal conjunctiva of PF tafluprost group was 3.5±2.5 vs 2.2±1.5 cells (p>0.05, respectively for treated vs control eye), in PF latanoprost group was 11.6±9.8 vs 3.8±1.8 cells (p<0.05) and in PF bimatoprost group was 6.8±5.1 vs 3.9±2.5 (p=0.05). There was significantly different intensity of MFs infiltration within tarsal conjunctiva between groups: PF latanoprost>PF bimatoprost>PF tafluprost (p<0.05, Kruskal-Wallis test). MFs infiltration within tarsal stroma and glands was slightly increased in PF latanoprost group when compared with control (p<0.05), however it was not significantly different from other prostaglandins (p>0.05).
Conclusions Applied PF prostaglandin analogues affected MFs infiltration within tarsus. The strongest macrophage-associated inflammatory reaction was related to PF latanoprost application, however there is a need for further analyses of other inflammatory response pathways.

• F020

Glaucomatocyclitic crisis, a rare cause of unilateral ocular hypertension

OZCAN A A , Sariyeva A
CUKUROVA UNIVERSITY, OPHTHALMOLOGY DEPT, ADANA, Turkey

Purpose To report a case of glaucomatocyclitic crisis which is a rare cause of ocular hypertension.
Methods A 40 -year- old immunocompetent male patient admited, with the complaints of blurry vision, photophobia,red eye, and severe pain in the left eye for the last 2 days.Examination revealed mild anterior chamber reaction, corneal oedema, appearance of keratic precipitates and a very high intraocular pressure (52 mmHg) with an unresponsive, semi-dilated pupil in the same eye. Gonioscopy revealed open angles in both eyes.
Results He was treated with topical steroids and topical pressure-lowering agents with oral acetazolamide. The patient was also evaluated for systemic causes of red eye. Investigations carried out included routine blood tests and ESR, the results of which were all within normal limits. In the following 24 month period, the patient had two further episodes of unilateral IOP spikes associated with cyclitis.
Conclusions This is an interesting and a rare uveitic condition. Although the list of differential diagnoses is long, the condition is relatively quickly identifiable by the presence of remarkable signs and symptoms. Medical and surgical treatments are indicated to reduce inflammation and to prevent long-term glaucomatous optic nerve damage related to the high intraocular pressure.

• F021

Risk of glaucoma and treatment with systemic antihypertensive treatment - A nationwide study

HORWITZ A (1,2), Jeppesen J (3), Torp-Pedersen C (4), Kolko M (5,6,7)
(1) University of Copenhagen, Dep. of Neuroscience and Pharmacology, Copenhagen N, Denmark
(2) Glostrup Hospital, Dep. of Neruophysiology, Glostrup, Denmark
(3) Copenhagen University Hospital, Dep. of Cardiology, Copenhagen, Denmark
(4) Aalborg University Hospital, Dep. of Health- Science & Technology, Aalborg, Denmark
(5) University of Copenhagen, Dep. of Neuroscience & Pharmacology, Copenhagen, Denmark
(6) Roskilde University Hospital, Dep. of Ophthalmology, Roskilde, Denmark
(7) University of Copenhagen, Center for Healthy Aging, Copenhagen, Denmark

Purpose The aim of the study was to investigate the co-morbidity of antihypertensive treatment and glaucoma in the Danish population throughout 16 years.
Methods The study population comprised of all individuals living in Denmark in the period 1996-2012. The National Prescription Registry was used to identify all claimed prescriptions for glaucoma medication and antihypertensive drugs. Duration analysis models were employed to investigate the associations between antihypertensive treatments and the risk of development of glaucoma. A total of 26,596 observations were used in the estimated risk of developing glaucoma when treated with Calcium channel blockers (CCB), Angiotensin-converting-enzyme inhibitors (ACEI), Angiotensin II receptor blockers (ARB), Beta blockers (BB) or Diuretics (DR).
Results An average age at onset for hypertension was 60.3 years (range: 0–109 years; 55.6 % female). A total of 3.2 % of all patients treated with antihypertensive drugs were diagnosed with glaucoma. The study found that antihypertensive treatment are associated with the risk of developing glaucoma. The risk of glaucoma increased significantly with age and was most strongly associated with ACEI, ARB, and CCB treatment.
Conclusions Antihypertensive drugs are strongly associated with glaucoma.

• F022

Dexamethasone induced glaucoma as part of chemotherapy for T cell lymphoblastic lymphoma.

LOCKWOOD A J (1,2), Mitchell A (3), Gray J (3), May K (1)
(1) Southampton General Hospital, Ophthalmology, Southampton, United Kingdom
(2) Queen Alexandra Hospital, Ophthalmology, Portsmouth, United Kingdom
(3) Southampton General Hospital, Oncology, Southampton, United Kingdom

Purpose To describe glaucoma after high dose corticosteroid chemotherapy in an eleven-year-old girl.
Methods Topical steroids are well known to induce a rise in intraocular pressure, but responses to oral steroids are rare. We report a significant elevation in an eleven-year-old girl following high dose dexamethasone treatment as part of her chemotherapy for T cell lymphoblastic lymphoma.
Results Six days after initiation of her first cycle of chemotherapy including oral dexamethasone 4.5 mg bd she presented with headaches, photophobia and blurring of vision. Intraocular pressures IOP were 48 and 52 mm Hg in the right and left eye respectively. Control of IOP was achieved medically, although systemic carbonic anhydrase inhibitor use necessitated admission to intensive care for renal support.
Conclusions Vision threatening IOP rise may be a complication of high dose oral dexamethasone treatment. Routine screening of children undergoing this type of chemotherapy may be indicated.

• F023

Reproducibility of intraocular pressure self-measurement by ICare Home rebound tonometer and comparison with Goldman applanation tonometer

GAILLARD R , Fenolland J R , Bonnel S , Rosenberg R , Marill A F , Bostanci K , Giraud J M , Renard J P
Hôpital du Val de Grâce, Paris, Paris, France

Purpose To compare the intraocular pressure (IOP) measurements and reproducibility of the new ICare Home® rebound tonometer (RT) with Goldman applanation tonometer.
Methods 36 healthy eyes of 36 patients were enrolled. Three IOP measurements were performed with ICare Home by an ophthalmologist (RT-O) then by the patient (RT-P), and with GAT and non-contact tonometry (AIR). All of the subjects underwent an examination including: slit lamp examination, keratometry, and optical measurements of ocular axial length and central corneal thickness.
Results Results of mean IOPs were 16.3 ± 4.8 mmHg (RT-O), 16.2 ± 4.7 mmHg (RT-P), 15.1 ± 2.6 mmHg (GAT) and 16.0 ± 2.9 mmHg (AIR). There was no statistically difference between the 4 methods with random one-way ANOVA or repeated measures (P=0.09) and no difference between each couple of methods after Bonferroni correction for multiple comparisons. Correlation between the tonometers were : r=87.4% between RT-O and RT-P, r=63.4% between RT-O and GAT and r=65.0% between RT-P and GAT. The intraclass correlation coefficients (ICC) were 0,924 for RT-O, 0,854 for RT-P and 0,887 for GAT. Bland Altman plots showed a good agreement between the different methods.
Conclusions IOP measurements with ICare Home by the patient or the ophthalmologist were well correlated to GAT without statistically significant differences . Reproducibility was good and with a good agreement between the differents methods of measures.

• F024

Generic Drugs- are they as good as brand-names?

KOLKO M (1,2), Ali N (2), Jensen P K (1)
(1) Roskilde University Hospital, Ophthalmology, Roskilde, Denmark
(2) University of Copenhagen, Neuroscience and Pharmacology, Copenhagen, Denmark

Purpose The aim of the present study was to investigate different characteristics of six Latanoprost generics.
Methods Prize, drop size and volume in each generic were determined. The hardness of each bottle was further evaluated using a fish weight and a hook. Finally, pH was measured and the buffer capacity evaluated by addition of NaOH.
Results Price, drop size and volume varied significantly between the brand version (xalatan) and the generic latanoprost products. Hence, drops sized were in the range 40 – 47 µl and the number of drops in each generic bottle varied between 95 and 111 drops. The embalages of each latanoprost product were different in both size and hardness. The control value of pH in the brand version (Xalatan) was 5.99 ± 0.01 (mean ± SD), whereas the generic latanoprost products had significantly higher values within the range 6.70 – 6.82. Hence, titration of 2.5µl Xalatan to neutrality required 70.4 ± 0.4 nmol NaOH compared to the generic latanoprost products which required within the range 28.1 – 33.7 nmol NaOH.
Conclusions The present study identifies differences among latanoprost generics such as different pH values and different buffer capacities. Moreover, the emballages varies significantly, thereby leading to critical variations in the handling of the generics. Finally, the number and size of drops in each generic were different, not to mention the prize variations between the brand version and the generics. Over all, generic eye drops should not be considered identical. Therefore, re-evaluation of the requirements for introducing generic drugs seems reasonable.

• F025

Cystic macular edema induced by Latanoprost

PEREZ I, Ascaso F J, Caramello C M, Almenara C, Esteban O, Martinez M, Sánchez J I, Idoate A, Nuñez E
Hospital Clinico Universitario "Lozano Blesa", Ophthalmology, Zaragoza, Spain

Purpose Prostaglandin analogues are powerful ocular hypotensives that can change the blood-aqueous barrier, developing an CME in patients with some risk factor associated such as previous ocular surgery, aphakia, rupture of the posterior capsule, uveitis history, diabetic retinopathy. We present a case of CME after the administration of Latanoprost
Methods OCT-SD were used in the diagnosis and follow-up of the patient
Results A 32 years old patient, with surgery of congenital cataratas at 9 months, and treated with Latanoprost due to a open-angle glaucoma. After one month of treatment, the patient referred decreased visual acuity on his left eye, being the exploration compatible with the development of a CME which had decreased the visual acuity to 0,4. The diagnose was confirmed by OCT. Latanoprost was suspended; It was prescribed nepafenac eyedrops each 8 hours and brimodine each 12 hours. One month later, the AV had improved to 0.7 and showed a decrease OCT macular thickness, with disappearance of cysts and recovery foveal depression
Conclusions Although in healthy eyes it has not been posible to establish a causal relationship between the prostaglandin analogues and the development of a CME, it looks obvious that could favor its appearance in eyes with a blood-aqueous barrier alteration especially with previous surgery and rupture of the posterior capsule. In our case, the patient had been previously operated of congenital cataract with no IOL implantation. The OCT appears as a useful non-invasive method for the diagnosis and follow-up of this complication.

• F026

The pathophysiology of pseudoexfoliation syndrome is affected by interaction of TGF-ß1 and LOXL1

LIRAVI P, Zenkel M, Kruse F E, Schlötzer-Schrehardt U
University of Erlangen-Nürnberg, Department of Ophthalmology, Erlangen, Germany

Purpose The cross-linking enzyme lysyl oxidase-like 1 (LOXL1) and profibrotic transforming growth factor (TGF)-ß1 play key roles in pathophysiology of pseudoexfoliation (PEX) syndrome/glaucoma. The purpose of this study was to investigate the interaction between LOXL1 and TGF-ß1 with respect to the PEX-specific disordered matrix metabolism.
Methods Primary human Tenon's capsule fibroblasts (hTCF) obtained from patients were treated with TGF-ß1 (0-10 ng/ml) for 12-72 hours without or with preincubation with inhibitors of TGF-ß signalling pathways. Expression of LOXL1 and PEX-specific extracellular matrix components was examined by using quantitative RT-PCR and Western immunoblot analysis. Direct binding of LOXL1 to TGF-ß1 was analyzed by blot overlay assay and solid phase ELISA using purified LOXL1, recombinant human TGF-ß1, TGFß1-LAP. The effect of LOXL1 on TGF-ß1 signaling was analyzed using TGF-ß receptor signaling real time PCR assays (BioRad) after transient transfection of hTCF with a full-length pCMV6-LOXL1 vector construct/with empty vector .
Results TGFß1 significantly increased LOXL1 expression, secretion and enzymatic activity and correlated with enhanced expression of BMP-1, elastin, fibrillin-1, fibulin-4 and fibulin-5 with peak effects at 10 ng/ml for 48 hours. This induction was blocked by TGF-ß receptor inhibitors and inhibitors of the canonical Smad and non-canonical signaling pathways. Direct binding between LOXL1 and TGFß1-LAP was demonstrated by Blot overlay assays and ELISA. LOXL1 overexpression temporarily upregulates different transcriptional regulators and some protein kinases of p38-MAPK signalling pathway after 12 to 24 hours post-transfection.
Conclusions The results of this study indicate that the interaction of LOXL1 and TGF-ß1 plays an important role in the PEX-associated abnormal matrix metabolism and fibrosis.

• F027

Effects of recurring intraocular pressure elevations on the retina and the autoimmune component

TEISTER J, Gramlich O, Neumann M, Tao X, Pfeiffer N, Grus F
Experimental Ophthamology, Department of Ophthalmology, Mainz, Germany

Purpose In glaucoma, complex changes of IgG serum autoantibody (Aab) repertoire highlight the possible contribution of an autoimmune component in the pathogenesis of this neurodegenerative disease. An elevated intraocular pressure (IOP) and its fluctuations are considered as major risk factors. The aim of the study was to identify the systemic influence of fluctuations using recurring pressure peaks and drops in a glaucoma animal model.
Methods Sedated male Long Evans rats experienced a unilateral, intermittent IOP manipulation using a silicone loop adjusted around the eye globe for 1 hour during 27 treatments. The pressure profile included pressure peaks to 35 and 45 mmHg and drops to a physiologic value of 8 mmHg. Contralateral (n=12) and untreated eyes (n=14) served as controls. Neurodegeneration was determined after paraphenylenediamine staining and Brn3a staining. Microglia activation was identified after Iba1 staining in retinal cross-sections. Changes of serum immunoreactivities were identified using a microarray approach with a glaucoma-specific antigen Setup.
Results A loss of axon density (as axons/0.05 mm2) of treated eyes (19624±1709) compared to contralateral (21943±1510; $p<0.01$) and untreated eyes (22267±1408; $p<0.01$) occured, which was confirmed by retinal ganglion cell count. Next to an activation of microglia, upregulated Aab reactivities for GST, transferrin, and NSE were identified in serum of treated animals in comparison to control serum.
Conclusions This animal model including pressure peaks and drops allows the establishment of individual IOP profiles. The retina and the optic nerve sustained a significant damage and an altered autoimmune repertoire could be induced. A significant influence of recurring pressure fluctuations could be demonstrated using this sophisticated glaucoma animal model.

• F028

Association of microRNA DGCR8 and XPO5 gene polymorphisms with the risk of primary open angle glaucoma occurrence

SZAFLIK J P (2), Majsterek I (1), Molasy M (1), Walczak A (1), Przybylowska-Sygut K (1), Szymanek K (2), Szaflik J (2)
(1) *Medical University of Lodz, Department of Clinical Chemistry and Biochemistry, Lodz, Poland*
(2) *Medical University of Warsaw, Department of Ophthalmology, Warszawa, Poland*

Purpose Many reports suggest the correlation between altered microRNA level and the pathogenesis of glaucoma. It is suspected that disruption in microRNA processing machinery may influence microRNAs action. The single nucleotide polymorphisms in genes *DGCR8* and *XPO5*, which are involved in microRNA biogenesis may be the key factor in this process.
Methods The blood samples of 80 patients affected by primary open angle glaucoma and 250 age matched controls were enrolled to this study. The DNA was isolated from the peripheral blood lymphocytes. The polymorphic variant frequencies of *DGCR8* (rs 3757) and *XPO5* (rs 1107) genes were determined using TaqMan® SNP Genotyping Assays.
Results The statistical analysis revealed that the polymorphism of *DGCR8* gene did not affect to the risk of primary open angle glaucoma. While, the TT genotype of *XPO5* was found to be present mainly in patients not affected by glaucoma (P=0.049746).
Conclusions In conclusion, it was evaluated that the TT genotype of *XPO5* gene might have protective effect on the risk of primary open angle glaucoma. Therefore, future analysis of polymorphic variants of genes involved in microRNA biogenesis could be used for patient's diagnosis according to glaucoma occurence.

• F029

Angle evaluation after cataract operation using Swept-Source OCT in elder Asian

LEE W, Bae H, Kim C Y, Seong G J
Severance hospital- Yonsei University, Department of Ophthalmology, Seoul, South-Korea

Purpose To investigate the change of anterior angle morphology after phacoemulsification with intraocular lens implantation in eyes with cataract using Swept-Source optical tomography(SS-OCT) in elder Asian people
Methods One eye of 31 patients with cataract was performed phacoemulsification with intraocular lens implantation. Before and after the operation, the postop 1 day and 1 month, the anterior chamber angles were evaluated by SS-OCT(CASIA®, Tomey) under dark conditions using three-dimensional angle analysis scan protocol. In order not to indent eyes, in naturally eye opening status, we obtained SS-OCT scans and analyzed with nasal and temporal quadrant of eyes. AOD, TISA, TIA were calculated automatically by SS-OCT after an observer marked the scleral spurs.(AOD : Angle Open Distance, TISA : Trabecular-Iris Space Area, TIA : Trabecular-Iris Angle)
Results Enrolled 31 patients were 18 men and 13 women. The mean age was 68.71±9.82 years. Preoperative means of AOD, TISA, TIA were 0.51±0.27(mm), 0.21±0.11(mm), 28.83±11.51(°). Postop 1day and 1month, the means of AOD, TISA, TIA were 0.63±0.19(mm), 0.24±0.08(mm), 32.05±7.54(°), and 0.67±0.24(mm), 0.26±0.1(mm), 36.78±8.4(°). Longitudinal data analysis was conducted based on multilevel model framework. The changes of AOD, TISA, TIA were significantly increased linearly or quadradically after adjusting age and gender.(p=0.004, p=0.002, p=0.000)
Conclusions The eyes that were performed cataract operation have greater improved anterior chamber angle parameters. It means that cataract surgery can improve aqueous humor dynamic in angle closure suspect or glaucoma patients.

• F030

Repeatability of retinal nerve fiber layer reflectance intensity measurement in glaucoma

GARDINER S, Demirel S, Reynaud J, Fortune B
Devers Eye Institute, Discoveries In Sight Laboratories, Portland, United States

Purpose Decreased reflectance within the retinal nerve fiber layer (RNFL), observable using optical coherence tomography (OCT), appears to be related to functional loss in glaucoma. In order to investigate this in a quantitative manner, reliable measurements of reflectance intensity are needed. However, reflectance may not only be affected by pathophysiological changes in tissue properties but also confounded by other effects of ocular media and image quality. This study assesses the repeatability of intensity measurements, before and after normalization aimed to reduce test-retest variability.
Methods Data were taken from participants with glaucoma in a test-retest study. Each had peripapillary circle scans acquired from both eyes 5 times within 10 weeks. For each scan, the following were extracted: average RNFL thickness; RNFL intensity, defined as the mean reflectance intensity of pixels within the delineated RNFL; sub-RNFL intensity, defined as the mean intensity of pixels between the outer boundary of the RNFL and Bruch's Membrane; and intensity ratio, defined as RNFL intensity divided by sub-RNFL intensity. For each parameter, deviations from the per-eye mean were calculated. The intra-eye standard deviations (SD) were expressed as percentage of the width of the range of observed measurements.
Results The intra-eye SD of RNFL intensity was 12.5% of the range. Normalization reduced the intra-eye SD of intensity ratio to 4.9% of the range, representing a significant reduction in absolute deviations with $p<0.0001$ (Wilcoxon signed rank test). RNFL thickness was more repeatable, with intra-eye SD 0.8% of its range.
Conclusions RNFL reflectance intensity varies substantially between scans. However, dividing by the intensity of sub-RNFL tissue greatly reduces this variability. Such normalization allows useful measurements to be obtained.

• F031

Comparison of Optical Coherence Tomography Measurement Reproducibility between Children and Adults

KIM S H (1), Chung H K (1), Han Y G (1), Oh S (2)
(1) Boramae Medical Center, Ophthalmology, Seoul, South-Korea
(2) Boramae Medical Center, Biostatistics, Seoul, South-Korea

Purpose To compare the reproducibility of SD-OCT (spectral-domain optical coherence tomography) measurements of RNFL (retinal nerve fiber layer) and macular thickness between children and adults.
Methods Seventy-one eyes of 71 healthy myopic children and 71 eyes of 71 normal adults were enrolled. RNFL and macular thicknesses were measured by one operator, with a brief rest between measurements. The two measurements were obtained using the eye tracking and retest function of Spectralis SD-OCT. Reproducibility was evaluated with reference to COVs (coefficients of variation) and ICCs (intraclass correlation coefficients). The ICC values of the RNFL and macular thicknesses were compared, respectively between the two groups, by Fisher's z-test.

Results The RNFL and macular thicknesses did not differ between the two groups. The COVs of the RNFL measurements ranged from 0.945 to 4.531% in the children group and from 0.496 to 1.391% in the adults group. In most of the RNFL sectors, the ICCs of the children group (range: 0.784 – 0.987) were significantly lower than those of the adults group (range: 0.986 – 0.993). The COVs of the macular measurements ranged from 0.496 to 1.157% in the children group and from 0.275 to 0.656% in the adults group. The ICCs (range: 0.859 – 0.973) in the children group, significantly lower than for the adults (range: 0.989 – 0.995), in all of the macular sectors.
Conclusions The reproducibility of SD-OCT RNFL and macular measurements for healthy myopic children was excellent, albeit statistically lower than that for adults.

• F032

Surgical outcomes of Ahmed gluacoma valve implantation in pseudoexfoliative glaucoma.

KIM G A (1), Ko J (2), Bae H (1), Hong S (1), Kim C Y (1)
(1) Yonsei university college of medicine, ophthalmology, Seoul, South-Korea
(2) Changnyeong-gun public health center, ophthalmology, Seoul, South-Korea

Purpose Pseudoexfoliation is considered to be the most common identifiable cause of open angle glaucoma worldwide and pseudoexfoliative glaucoma(PEXG) patients often require surgical intervention. But no studies are available reporting surgical outcomes of Ahmed glaucoma valve (AGV) implantation in PEXG. This study aims to evaluate the efficacy and safety of AGV implantation in PEXG patients.
Methods A retrospective chart review of 27 eyes of PEXG patients who underwent AGV implantation (n=14) or trabeculectomy (n=13) and 13 eyes of primary open angle glaucoma(POAG) patients who underwent AGV implantation as a primary surgical option was conducted. Postoperative intraocular pressure, number of medications and complications were compared between 3 groups.
Results At postoperative 1,3,6,9,12 month, intraocular pressure and number of medications were similar between 3 groups. Rates of transient hypotony were significantly lower in PEXG eyes with AGV implantation (14.3%) in comparison with those with trabeculectomy (61.5%, p=0.018).
Conclusions AGV implantation as a primary surgical treatment in PEXG patients produced similar intraocular pressure reduction and numbers of medications compared with AGV implantation in POAG patients and trabeculectomy in PEXG patients. And It offers advantage of reduced rate of transient hypotony over trabeculectomy in PEXG. Therefore, AGV implantation may be promising alternative in surgical management of this type of glaucoma.

• F033

Complementary effects of PlGF inhibition and MMC in the improvement of surgical outcome after glaucoma filtration surgery

VAN BERGEN T (1,2), Jonckx B (1), Moons L (2,3), Feyen J (1), Stalmans I (2)
(1) ThromboGenics NV, Ophthalmology, Heverlee, Belgium
(2) KU Leuven, Lab of Ophthalmology, Leuven, Belgium
(3) KU Leuven, Department of Biology- Zoological Institute, Leuven, Belgium

Purpose We previously showed that inhibition of placental growth factor (PlGF) was more effective than anti-VEGF-R2 treatment in improving surgical ouctome of glaucoma filtration surgery (GFS). In this study, we investigated the complementary effects of mitomycin-C (MMC) and anti-PlGF therapy and compared it to the combined administration of MMC with aflibercept.
Methods The effect of PlGF inhibitor (5D11D4; ThromboGenics NV) and MMC on surgical outcome was investigated in a mouse model of GFS. The 1st group was treated during surgery with MMC 0.02% for 2 minutes; the 2nd group received a combination of MMC and an intracameral (IC) injection of 5D11D4 (1 µl; 5.4 µg). MMC together with IC administration of aflibercept (1µl; 3.4 µg) was given to the 3rd group. Treatment outcome was studied by clinical investigation of the bleb every other day. Fibrosis was investigated on postoperative day 52 by performing a Sirius Red staining.
Results The combination of MMC and 5D11D4 was able to significantly improve bleb area as compared to MMC (n=20; p<0.001) by an additional reduction of fibrosis with 10 % at day 52 (n=6; p<0.001). Moreover, all blebs from the combination group survived until day 52, whereas blebs treated with MMC were failed at postoperative day 34 (n=20; p<0.001). As compared to MMC together with aflibercept, the combined administration of MMC and 5D11D4 was equally effective in improving surgical outcome (n=15; p=0.88) and reducing the postoperative fibrotic process in the bleb (n=15; p=0.49).
Conclusions We know that inhibition of PlGF is more effective that anti-VEGF treatment. These data suggest that MMC together with PlGF inhibition may even have complementary effects in the improvement of surgical outcome and might be equally effective as the combined treatment of MMC and aflibercept.

Commercial interest

• F034

Longterm outcomes of cyclodiode treatment for patients with neovascular glaucoma

WESTON K, Lockwood A , Penwarden A , Kirwan J
Queen Alexandra Hospital, Eye department, Portsmouth, United Kingdom

Purpose To investigate the outcomes following cyclodiode treatment for patients with refractory neovascular glaucoma.
Outcome measures were sustained IOP reduction, symptom relief, number of medications and progression to pthysis, over a 10 year period. Visual acuity data was also collected.
Methods A consecutive retrospective series of 15 eyes of 14 patients in a single eye unit, undergoing cyclodiode treatment between May 1999 to July 2005. Case notes were reviewed.
Results Four patients died before completion of 10 year follow up but are included in the 5 year follow up data.

Symptomatic relief was achieved in all eyes. Four eyes required a single further treatment with cyclodiode at 2 months to 3 years.
Mean IOP prior to treatment was 42 mmHg. Following treatment, mean IOP was 18.5 mmHg at 1 month, 19.6 mmHg at 6 months, 15.33 mmHg at 1 year, 15.07 mmHg at 2 years, 12.92 mmHg at 3 years, 14.38 mmHg at 5 years and 10.1 mm/Hg at 10 years (75.95% reduction). 88% of eyes did not require any medication at 10 years. The mean reduction in number of medications used was 2 (2.8 to 0.8).
Pthysis occurred in 5 eyes. In 3 eyes this occurred within 1 year of cyclodiode and in the remaining 2 eyes by 4 years. No patients progressed to evisceration or enucleation. 60% of eyes were NPL at 10 years, with pre-cyclodiode acuities in this group of HMs to PL. One eye remained the same, with PL vision, and one eye improved from CF to 1/60. The vision in 2 eyes dropped from CF to HMs.
Conclusions Cyclodiode laser treatment is effective for both pain control and maintaining IOP in the long term. It allowed a reduction in the number of topical treatments required.

• F035

Surgically induced corneal astigmatism after fornix-based trabeculectomy

VAN KEER K (1), Willekens K (1), Abegão Pinto L (2), Delbeke H (1), Vandewalle E (1), Stalmans I (1)
(1) University Hospitals Leuven, Department of Ophthalmology, Leuven, Belgium
(2) Centro Hospitalar Lisboa Norte, Department of Ophthalmology, Lisbon, Portugal

Purpose To evaluate the degree of surgically induced corneal astigmatism (SIA) following trabeculectomy and to investigate the relation of SIA with long-term reduction of intraocular pressure (IOP).
Methods Fourty-four eyes of 44 patients undergoing fornix-based trabeculectomy were included in this single center, prospective trial. IOP, visual acuity (VA), corneal astigmatism, medication use and adverse events were recorded preoperatively and at 1, 3, 6 and 18 months postoperatively. Changes in corneal astigmatism were analysed using vector analysis. Pre- and postoperative parameters were compaired using one-sample t-test. Correlation between SIA and IOP were assessed using Pearson correlation coefficients.
Results Vector analysis of corneal astigmatism revealed a significant increase in with-the-rule corneal astigmatism, reaching a maximum at 1 month postoperatively (1.15 ± 0.8 D, P<0.001) followed by a gradual decline (0.87 ± 0.8 D, P <0.001 at month 18). SIA at 1 month showed a borderline significant correlation with IOP reduction at 3 months (r=0.315, P = 0.051). SIA at 3,6 and 18 months did not correlate with reduction in IOP (P>0.05). After a transient decline at 1 month after surgery, VA recovered to preoperative values at month 3 without need for adjustment of the optical correction.
Conclusions Fornix-based trabeculectomy induces statistically significant with-the-rule astigmatism without affecting long term VA. In our population, maximum SIA, measured at 1 month postoperatively, showed a borderline significant correlation with reduction of IOP at 3 months.

• F036

Changes in choroidal thickness after intraocular pressure reduction following trabeculectomy

KADZIAUSKIENE A , Kuoliene K , Galgauskas S , Asoklis R
Vilnius University, Centre of Eye Diseases, Vilnius, Lithuania

Purpose To evaluate changes of choroidal thickness (CT) after an acute reduction in intraocular pressure (IOP) following trabeculectomy.
Methods Subfoveal and peripapillary CT and IOP were measured in 40 glaucomatous eyes (40 patients) 1 day before, 1 week and 1 month after the trabeculectomy. The choroid was evaluated using spectral domain optical coherence tomography enhanced depth imaging at the fovea and 1.7mm superior, temporal, inferior and nasal to a optic nerve head centre. Biometry was performed preoperatively.
Results The mean IOP was significantly reduced after trabeculectomy at both follow-up visits (P<0.001). The mean subfoveal CT (±SD) increased from 216.1 (±86.1) µm at baseline to 260.3 (±86.9) µm after one week and 243.1 (±87.1) µm after one month postoperatively (P<0.001). The mean CT significantly increased one week after trabeculectomy at all peripapillary locations (P<0.01), however, the thickening of choroid was significant only temporally after one month. There was positive correlation between the magnitude of change in subfoveal CT and the IOP reduction (r=0.518, P<0.001 for the 1-week follow-up; r=0.290, P=0.034 for the 1- month follow-up). The preoperative axial length correlated positively with the magnitude of thickening of subfoveal CT after one week (r=0.451, P=0.002).
Conclusions The subfoveal and peripapillary CT increased with the IOP reduction following trabeculectomy, however, choroidal thickening around the optic nerve disc appeared to be short-term. The thickening of subfoveal CT was found to be related to the greater IOP reduction and longer axial length.

• F037

Nanomedicine and Ophthalmology: looking forward

CORDEIRO SOUSA D (1,2), Ferreira Q (3), Araujo M (4), Morgado J (3,5), Ferreira J (6), Leal I (1,2), Abegao Pinto L (2), Marques-Neves C (1,2,7)

(1) Hospital Santa Maria - Lisbon Academic Medical Center, Ophthalmology, Lisboa, Portugal
(2) Faculty of Medicine, Lisbon Academic Medical Center, Lisboa, Portugal
(3) Instituto Superior Técnico, Instituto de Telecomunicacoes, Lisbon, Portugal
(4) Instituto Superior Técnico, Biomedical engineering, Lisbon, Portugal
(5) Instituto Superior Técnico, Bioengineering, Lisbon, Portugal
(6) Centro Hospitalar Lisboa Central, Ophthalmology, Lisbon, Portugal
(7) Centro de Estudos Ciencias da Visao, Ophthalmology, Lisbon, Portugal

Purpose Nanomedicine has been receiving greater attention in recent years due to the ability to use materials and devices at the size of intracellular structures and molecules, involving systems in the order of less than 100 nm. In particular, nanosized materials can provide substantial advantages when compared to current therapeutics that are used in the treatment of ocular diseases. Nanotechnology-based approaches are being explored in order to enhance drug permeation, to control mechanisms of drug release and to improve the action of nanocarriers with specific targeting moieties. From biopharmaceuticals to continuous intraocular pressure biosensors and tissue regeneration, nanotechnology provides an impressive range of possibilities to explore and improve patient care.
Methods Herein, we review the most recent literature regarding nanotechnology applications in ophthalmology, highlighting their advantages and challenges to overcome, prospecting them in terms of clinical utility.
Results Nanocarriers, nanodevices and nanostructured biocoatings with applications in the treatment of ocular diseases are resumed and their impact in the evolution of ophthalmology is discussed. We present a recent study about nanostructured films composed of drugs encapsulated in nanocarriers with applications in glaucoma treatment. Our results suggest that nanocarriers improve drug delivery and that specific drug amounts can be released during controlled periods of time.
Conclusions Our research emphasizes new trends and applications of nanodevices in ophthalmology. Nanomedicine is definitely part of a paradigm shift in healthcare providing, making it possible to reach excellence in ophthalmological diagnosis and therapeutics.
Acknowledgements: The authors thank FCT–Portugal for financial support under the project UID/EEA/50008/2013 and Post-Doc grant to QF.

• F038

Quantification of total retinal blood flow via dual-beam bidirectional Doppler optical coherence tomography for the assessment of neurovascular coupling

ASCHINGER G (1), Werkmeister R (1), Garhöfer G (2), Schmetterer L (1)

(1) Medical University of Vienna, Center for Medical Physics and Biomedical Engineering, Vienna, Austria
(2) Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria

Purpose In recent years, the reliability of dual-beam Doppler optical coherence tomography (DOCT), a method for measuring absolute retinal blood flow velocities, has been proven. A simultaneous determination of retinal vessel diameters allows calculating total retinal blood flow. The combined measurement of both parameters also offers the ability to quantify perfusion of the retina under different stimuli conditions and by this getting insight into the mechanisms of neurovascular coupling.
Methods Total retinal blood flow was measured in four healthy subjects at baseline condition (constant illumination of the fundus) and 20 min after this during stimulation with diffuse luminance flicker light at 12 Hz.
Results The average increase in total retinal blood flow during flicker stimulation was about 40%, which is assumed to be caused by an increased firing rate of the retinal ganglion cells. However, when comparing the blood flow in single retinal vessels under both baseline condition and flicker stimulus, the individual increase varied vastly.
Conclusions We think the observed phenomena are caused by resistance changes of the vasodilated vascular network which cause non-linear flow changes in single vessels. Our results show that the measurement of a single retinal vessel alone is not adequate for assessing neurovascular coupling in the retina. To conclude, for gaining insight into the mechanisms and functioning of neurovascular coupling, total retinal blood flow must be assessed.

• F039

Combination of Resveratrol with omega-3 fatty acids synergize to counteract VEGF-R pathway in sick retinal pigment epithelium cells mimicking AMD

CHALONS P (1), Scagliarini A (1), Courtaut F (1), Olmière C (2), Delmas D (1)

(1) Université de Bourgogne- INSERM U866, Equipe Chimiothérapie- Métabolisme Lipidique et Réponse Immunitaire Antitumorale, Dijon, France
(2) Laboratoire Théa, R&D, Clermont Ferrand, France

Purpose The aim of this work is to assess whether RSV (Resveratrol) can act synergistically with omega-3 fatty acids to modulate VEGF (Vascular Endothelial Growth Factor) signaling pathway in order to identify a new and more effective therapy for the treatment of AMD (Age-Related Macular Degeneration).
Methods In this study, undifferentiated and differentiated human retinal pigment epithelial cells (ARPE-19) were used. The cells were treated with an omega-3/RSV preparation (Resvega®), or a RSV-free formulation or RSV alone for 24h. The expression of key proteins in VEGF signaling pathway was evaluated by Western Blotting.
Results We observed that the combination omega-3/RSV preparation (Resvega®) induces a stronger inhibition of the VEGF-R pathway activation than the RSV-free formulation or RSV alone in sick retinal cells. Surprisingly, Resvega® maintains and increases the functional VEGF-R pathway in normal retinal cells.
Conclusions This work brings a new insight into the mechanism by which omega-3/RSV could counteract AMD and could protect the other eye when AMD is already present.
Financial Support: This work is supported by Théa laboratory.

• F040

Inhibition of micro-fibrillar associated protein 4 as a potential therapy targeting choroidal neovascularisation in age related macular degeneration

BLACKLEY Z (1), Ved N (1), Schlosser A (2), Holmskov U (2), Bates D (1), Sorensen G L (2)

(1) University of Nottingham, Cancer Biology- Division of Cancer and Stem Cells- School of Medicine, Nottingham, United Kingdom
(2) University of Southern Denmark, Department of Cancer and Inflammation- Institute of Molecular Medicine, Odense, Denmark

Purpose To evaluate inhibition of Micro-Fibrillar Associated Protein 4 (MFAP4) on choroidal neovascularization (CNV) in a mouse model of age-related macular degeneration (AMD).
Methods All experiments complied with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Female C57BL/6J mice were subjected to laser-induced CNV, and intravitreally injected with either 1µg αMFAP4, 5µg αMFAP4, 1µg mouse IgG or 1µg αVEGF-A on day 0 and day 7. Fluorescein angiography (FA) was undertaken at day 7 and day 14, and choroids stained for inflammation (CD45) and vasculature (isolectin B4, IB4).
Results FA showed that injection of αMFAP4 reduced average lesion size and density on day 7 compared to IgG ($p<0.01$) and αVEGF-A positive controls ($p<0.05$) and both αMFAP4 and αVEGF-A reduced average lesion size and density by day 14 compared to IgG ($p<0.001$ and $p<0.05$ respectively). IB4 staining indicated that both αMFAP4 and αVEGF-A reduced lesion fluorescence intensity ($p<0.05$). Both αMFAP4 and αVEGF-A treatments also reduced infiltration of macrophages into the lesion site ($p<0.01$ and $p<0.05$).
Conclusions These results show that inhibition of MFAP4 results in a significant decrease in neovascular lesions in an animal model of AMD. The reduction in macrophage infiltration suggests a potential mechanism of action for anti-MFAP4 treatment. Together, this suggests that inhibition of MFAP4 could be a potential novel AMD therapeutic.

• F041

Rescue of photoreceptor degeneration by progesterone in an animal model of retinitis pigmentosa

MIRANDA M, Benlloch-Navarro S, Trachsel-Moncho L C, Ramírez D T, López-Pedrajas R, Almansa I, Silvestre D
Universidad CEU Cardenal Herrera, Ciencias Biomédicas, Moncada, Spain

Purpose Retinitis Pigmentosa (RP) is a neurodegenerative disease, resulting in progressive death of photoreceptors. rd10 mice are a model of RP that have a mutation on the cGMP phosphodiesterase codifying gene. The aim of this study is to evidence the neuroprotective role on photoreceptors of progesterone.
Methods Progesterone was orally administered (150 mg/kg at postnatal days 15, 17, 19 and 21). The last day, eyes were enucleated and sectioned or homogenized. Sections were stained with hematoxilyn-eosin and TUNEL assay was performed. Alterations of different proteins (pCREB, CREB, BDNF, TNFα and LC3) were determined by western blot (WB). Oxidative stress markers (glutathione (GSH) and malondialdehyde (MDA)) were determined by HPLC. To explore PG mechanism, ARPE-19 PG treated cells were exposed to H2O2 and cell viability was measured. Tissue homogenates were also exposed to a biochemical induction of lipid peroxidation, and the effect of PG was studied.
Results Hematoxilyn-eosin and TUNEL assays revealed that histological degeneration decreased with PG. No differences were obesrved in WB analyzed proteins between control and rd10 retinas. Retinal GSH/GSSG ratio was decreased and MDA increased in rd10 mice, and PG restored these alterations. After H2O2 stress, major viability was detected on ARPE-19 PG treated cells and inhibiton of lipid peroxidation was observed in tissue when PG was added.
Conclusions Results suggest that progesterone protection could be related with its antioxidant ability.

• F042

Neuroprotection as a therapeutic target in diabetic retinopathy: a basic approach

DAL MONTE M, Amato R, Biagioni M, Cammalleri M, Casini G
University of Pisa, department of Biology, Pisa, Italy

Purpose To test the hypothesis that protecting retinal neurons from apoptosis elicited by diabetic stress may prevent the increase of vascular endothelial growth factor (VEGF) in the retina.
Methods *Ex vivo* mouse retinal explants were exposed to stressors similar to those characterizing diabetic retinopathy (DR), i.e. high glucose (HG), oxidative stress (OS) or advanced glycation end-products (AGE). Retinal cell death was antagonized with octreotide (OCT), a somatostatin analog, and pituitary adenylate cyclase activating peptide (PACAP), two well-documented neuroprotectants. Data were obtained with real time RT-PCR, Western blot, ELISA and immunohistochemistry.
Results Control explants remained viable up to 10 days. Increased apoptosis was observed after HG, OS or AGE, and it was paralleled by increases in VEGF expression and release. Both OCT and PACAP reduced retinal apoptosis. At the same time, they also reduced VEGF expression and release. To get indications about the biological significance of VEGF release by stressed retinal cells, a VEGF trap (VT) was administered to HG, OS or AGE treated retinal explants. The effect of the VT was to further increase cell death induced by treatments.
Conclusions Protecting retinal neurons from diabetic stress also reduces VEGF expression and release, while inhibiting VEGF leads to exacerbation of apoptosis. This suggests that the retina in early DR releases VEGF as a pro-survival factor. Neuroprotective agents may decrease the need of VEGF production by the retina, therefore limiting the risk, in the long term, of pathologic angiogenesis.

• F043

Suprachoroidal pocket to collect drugs for treatment of ocular diseases

RODRIGO M J, Prieto E, Idiope M, García-Martín E, Otin S, Polo V
Miguel Servet Hospital, Oftalmología, Zaragoza, Spain

Purpose We present the progressive improvement of a surgical procedure for suprachoroidal (sc) administration of drug, as an alternative route for drug administration to the posterior segment of the eye.
Methods 25 New Zealand albino rabbit eyes were used in the study. 50 microliters volume of different increasing viscosity formulations were tested: balanced saline solution (BSS), 0.5% sodium hyaluronate solution (SH) and a formulation with patent to be register. Catheters of several gauges (25Gs, 27 Gs and 22 Gs) and different matherials: metal cannula or flexible intravenous catheter were tested. Different architecture of the scleral-sc pocket were assayed: large quadrangular area with sutures, rectangular area with small port wihtout stitch and conic with small entrance without stitch.
Results Following items were analyzed: 1) Reflux post-administration: depending on the formulation; BSS and SH 0.5% (100%) versus Formulation (73.33%), on the surgical instrument for administration; 25G and 27G (100%) vs 22G (20%), and on different pocket architecture; quadrangular and rectangular (100%) vs conic pockets (73.33%). 2) Signs of ocular irritation: higher grades of hiperemia and secretion were observed in pockets with stitches 3) Ocular perforation: 1 eye in quadrangular pocket wiht stitch. 4) Surgical time: longer in sutured pockets.
Conclusions The possibility of perform a sc pocket with a large conic area, small port and without stitches, permits us to use it as a receptacle for high viscosity formulations or implants for sustained drug delivery, avoiding the risks of intravitreal devices and allowing an easier removal of the implant in case of adverse reactions.

• F044

In-vivo microdialysis as a new technique to assess ocular pharmacokinetics of topically applied drugs in a rabbit model

GARHOFER G (1), Klaus R (2), Jäger W (3), Zeitlinger M (1), Richter-Müksch S (4), Schmetterer L (2)
(1) Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria
(2) Medical University of Vienna, Center of Medical Physics and Biomedical Engineering, Vienna, Austria
(3) University of Vienna, Department of Clinical Pharmacy and Diagnostics, Vienna, Austria
(4) Hietzing Hospital, Department of Ophthalmology, Vienna, Austria

Purpose Although topical drug delivery is the most widely used ocular drug administration route, the in-vivo pharmacokinetic profile of topically applied drugs is only inadequately described. This is mainly caused by the fact that in the eye the assessment of in-vivo pharmacokinetics is difficult and technically demanding. Here, we propose a new technique for the in-vivo assessment of pharmacokinetic parameters of topically applied drugs using in-vivo microdialysis in a rabbit model.
Methods 8 Female New Zealand White rabbits were included in the experiments. A linear microdialysis probe (30 kDa molecular weight cut off [MWCO]) was implanted in the anterior chamber, a concentric probe (20 kDa MWCO) in the posterior segment of the same eye . After a run-in period to obtain stabile conditions, a single drop of ciprofloxacin eye drops was administered on the cornea. Microdialysis samples were collected every 30 min for 6h. Probes were analyzed using HPCL.
Results In the anterior chamber, the maximum total drug concentration was reached after 116±36 minutes (Tmax) and amounted to 0.373±0.281 µg/ml (Cmax). AUC (0-n) for ciprofloxacin in the anterior chamber was 78.8±47 µg min/ml. In the vitreous, drug concentration was considerably lower. A Cmax of 0.02±0.03 µg/ml was reached after 106±60min. AUC (0-n) for ciprofloxacin in the vitreous was 0.286±370 µg min/ml.
Conclusions Here, we present in-vivo microdialysis as a new method for the in-vivo assessment of pharmacokinetic profiles. Maximum drug concentration in the anterior chamber was reached approximately 2 hours after single drug administration. Although the drug concentration in the vitreous was considerably lower, time course of drug concentration was comparable. In summary, our data show that microdialysis is an excellent method to assess in-vivo pharmacokinetics with a high temporal resolution.

• F045

Angiotensin Receptor Blockade in Retinopathy of Prematurity: An Experimental Study

NATH M (1), Kumar A (1), Chandra P (1), Singh B (2), Deorari A K (3), Velpandian T (4)
(1) All India Institute of Medical Sciences, Ophthalmology- Dr. Rajendra Prasad Centre for Ophthalmic Sciences, new delhi, India
(2) All India Institute of Medical Sciences, Biophysics, new delhi, India
(3) All India Institute of Medical Sciences, Pediatrics, new delhi, India
(4) All India Institute of Medical Sciences, Ocular Pharmacology- Dr. Rajendra Prasad Centre for Ophthalmic Sciences, new delhi, India

Purpose Retinal renin angiotensin (RRAS) system has been reported to play a vital role in the retinal angiogenesis pathway.Present study was conducted to evaluate the modulation of RRAS components by quantitative gene expression studies in retina and to evaluate the effect of angiotensin receptor1 (AT1) blockade in the oxygen induced retinopathy (OIR) experimental model.
Methods Neonatal Wistar rat pups were exposed to high oxygen saturation (75%±2%) chamber, from postnatal day (PD) 7th to postnatal day 12th. On PD 12th the pups were randomised into four groups (n=9) viz. disease control (saline treated), AT1 receptor blocker (ARB) treated (telmisartan), antibody against VEGF (AAV) treated positive control (bevacizumab) and pups grew up in normoxia. On Day 17th Rat pup retina was assessed through fundus imaging and electroretinogram (ERG) by MICRON III. Rat pups were then sacrificed and retinas were extracted to study the gene expression of RAS components (renin, angiotensinogen, AT1 receptor & ACE), VEGF and HIF 1α in various test groups. Flat mounted ADPase stained retinas were subjected for light microscopy. Rat pups plasma, vitreous and retina were subjected for LC-MS/MS.
Results Examination of rat pup retina through fundus imaging, ADPase staining and ERG showed the reduction in tortousity index,vessel density of the retinal vasculature and improved "b" wave. Gene expression analysis revealed that treatment with ARB was able to normalise the expression of all the genes to a significant level except renin levels. ARB concentration in the retina was found to be therapeutically effective.
Conclusions Present study shows Intervening in the over activated RRA system through angiotensin receptor 1 blockade was able to regulate this system in experimental model of ROP. Further studies are in progress to understand the RRAS mechanisms involved in ROP.

• F046

Ghrelin inhibits choroid-retinal cell migration, proliferation and in vitro angiogenesis, under a high glucose environment

ROCHA DE SOUSA A (1,2), Silva-Gomes R (2), Conceição G (2), Moleiro A (2), Santos C (2), Leite-Moreira A (2)
(1) Department of Senses Organs- faculty of Medicine- University of Porto, Ophthalmology, Porto, Portugal
(2) Faculty of Medicine- University of Porto, Department of Physiology and Thoracic Surgery, Porto, Portugal

Purpose Ghrelin is a peptide expressed in many organs and tissues. Recently, ghrelin has been implicated in the pathophysiology of proliferative retinopathy, although its true involvement remains unclear. The aim of this study is to test the effect of ghrelin in the migration, proliferation, apoptosis and ***in vitro*** angiogenesis of primate choroid retinal endothelial cells (RF/6A), cultured under high glucose conditions.
Methods RF/6A cells were incubated for 24 hours with different glucose concentrations (0-300mM). Cell migration was assessed using wound-healing assay. Colorimetric immunoassay was used for the quantification of cell proliferation, based on the measurement of BrdU incorporation. Cell apoptosis was assessed by TUNEL technique. For each glucose concentration, the effect of ghrelin (10-10 to 10-5nM) was determined after 24 hours of incubation. The ***in vitro*** angiogenesis was assessed by tube formation assay after exposure to the same glucose concentrations and ghrelin (10-7nM) for 4 hours.
Results Ghrelin significantly inhibited RF/6A cell migration at every glucose concentrations, although this effect is more consistent under low glucose environment. Ghrelin, at the concentration of 10-7nM, significantly reduces cell proliferation at every glucose concentration. ***In vitro*** angiogenesis is decreased by ghrelin under a high glucose environment. No differences on the apoptosis assay were seen.
Conclusions In conclusion, ghrelin significantly inhibits RF/6A cells migration, proliferation and in vitro angiogenesis, under high glucose environment.

• F047

The diameter regulation of retinal arterioles during systemic hypoxia is impaired in diabetic patients without retinopathy

PETERSEN L, Bek T
Aarhus University Hospital, Department of Ophthalmology, Aarhus, Denmark

Purpose Diabetic retinopathy (DR) is characterized by retinal lesions related to disturbances in retinal vascular supply that may lead to retinal hypoxia. Additionally, the metabolic activity of cyclooxygenase (COX) and nitric oxide synthase (NOS) have been found to be changed in patients with diabetes mellitus. Therefore, the purpose of the present study was to investigate the effects of inhibiting the COX and the NOS enzymes during hypoxia.
Methods Twenty patients with type 1 diabetes mellitus and no visible diabetic retinopathy were studied. Using the Dynamic Vessel Analyzer the diameters of retinal arterioles at rest and during isometric exercise and flicker stimulation were studied before and during systemic hypoxia induced by breathing a hypoxic gas mixture. The examinations were performed before and during i.v. infusion of the NOS inhibitor L-NMMA and all examinations were repeated on a second day after topical administration of the COX-inhibitor diclofenac.
Results Hypoxia reduced the vasodilatation induced by flicker stimulation (p=0.0003) and the vasocontraction induced by both isometric exercise (p=0.001) and NO synthesis inhibition (p<0.0001), whereas COX inhibition had no significant effects on the diameter responses.
Conclusions In diabetic patients, hypoxia reduces the diameter response of retinal arterioles secondary to changes in blood pressure and retinal metabolism, and the response depends on nitric oxide synthesis. This may potentially point to targets for intervention on retinal flow disturbances in patients with diabetic retinopathy.

• F048

Clinical evaluation of Nidek autorefractometer AR-360A

STOOR K, Karvonen E, Liinamaa J, Saarela V
Oulu University Hospital, Ophthalmology, Oulu, Finland

Purpose A clinical evaluation of the Nidek AR-360A autorefractometer was performed to examine its accuracy in measuring refraction and visual acuity, in a pilot study for a clinical screening trial (the Northern Finland Birth Cohort Eye Study).
Methods Measurements of the refractive error were obtained from 160 eyes of 80 subjects (mean age 48.9), first objectively with the AR-360A and then subjectively by an optometrist. Agreement with the subjective refraction was calculated for sphere, cylinder, mean spherical equivalent (MSE), cylindrical vectors J45 and J0, and presbyopic correction (add). Visual acuity was measured using an ETDRS chart and the autorefractometer. The central corneal thickness (CCT) was measured with pachymetry.
Results The refractive error measured with the AR-360A was lower than the subjective refraction performed by the optometrist for sphere (-0.13D ±0.31D p<0.0005), and higher for cylinder (0.11D ±0.18D p<0.0005). The bias between the measurements of MSE, J45 and J0 was very low; -0.08D ±0.31D p=0.002, 0.00D ±0.43D p=0.89, and 0.19D ±0.36D p=0.51, respectively. The amount of add measured by the autorefractometer was slightly higher at 0.16D±0.23D p<0.0005. There was no statistically significant correlation with either visual acuity (p=0.650) or CCT (p=0.054) and the difference between the subjective and objective refraction. In 99.4% of the measurements of visual acuity using the ETDRS chart and the autorefractometer, values were within one Snellen line of each other.
Conclusions The Nidek AR-360A autorefractometer is a reliable tool for determining the refraction and visual acuity in a clinical screening trial.

• F049

Assessment of deviation angle and oblique muscle function in strabismus patients using analysis of two-dimensional eye globe pictures in diagnostic gaze positions

BUSHUYEVA N, Romanenko D
Filatov Institute of Eye Diseases, Laboratory of Binocular Vision Disorders, Odessa, Ukraine

Purpose To develop simple and fast method of deviation angle and extraocular muscle (EOM) function examination in strabismus patients
Methods Pictures of eye globes in 12 diagnostic gaze positions were taken. They were analyzed using developed software: for both eyes the program calculated pupil center shift relative to pupil center position in primary gaze for each gaze position in millimeters. 140 volunteers (70 adults and 70 children) without EOM pathology and refraction anomalies were examined to create reference interval database for each gaze position. 148 strabismus patients were examined using developed method and conventional ones: Hirschberg and Fresnel prism tests for deviation measurement, 0-4 scale was used to assess oblique muscle function
Results Eye globe shifts in healthy adults and children mainly ranged from 3 to 4,5 mm, maximal shifts equaled 6,5 mm in adults and 5,5 mm in children. Correlation coefficient between deviation angle measured with the method and Hirschberg test was 0,797, mean difference between measurements was 1,1°. Correlation coefficient between the method and Fresnel prism test was 0,881, mean difference between measurements was 3,8 PD. Cluster analysis sorted out 3 degrees of oblique muscle disfunction measured with the developed method. They in 80% correlated with conventional scale
Conclusions Developed automated method of deviation angle and EOM function assessment simplifies and objectifies examination of strabismus patients

• F050

Testing of an automated tablet-based method for the determination of low contrast near visual acuity in ophthalmic patients

MIRZA N (1), Tahir H J (1,2), Wang Y (2), Parry N R A (2,3), Murray I J (2,3), Aslam T M (2,4)
(1) *Faculty of Medical and Human Sciences, Manchester University, Manchester, United Kingdom*
(2) *Vision Science Centre, Manchester Royal Eye Hospital- Central Manchester University Hospitals NHS Foundation Trust- Manchester Academic Health Science Centre, Manchester, United Kingdom*
(3) *Centre for Hearing and Vision Research- Institute of Human Development, University of Manchester, Manchester, United Kingdom*
(4) *Heriot-Watt University, Visual Science and Interface Technologies, Edinburgh, United Kingdom*

Purpose To test an automated, tablet-based self-testing method for the determination of low contrast near visual acuity in ophthalmic patients.
Methods The Mobile Assessment of Vision by intERactIve Computer (MAVERIC) system consists of a calibrated tablet computer (Samsung Galaxy Tab S 8.4) running purpose-built software housed in a bespoke physical booth. Near low contrast (25%) visual acuity was measured in one eye using the MAVERIC system and a near ETDRS chart at a distance of 40cm on a population of ophthalmic patients with various retinal conditions. Patients independently completed testing using the MAVERIC system once an explanation of its use had been given. Repeat measures of near acuity were also conducted using the MAVERIC system.
Results The MAVERIC system displayed excellent repeatability. Bland Altman analysis of data showed reasonable agreement between measurements obtained using MAVERIC and the near ETDRS chart. The degree of difference between data sets was consistent.
Conclusions This study demonstrates the potential viability of the MAVERIC self-testing system as a means to test low contrast near visual acuity in ophthalmic patients with a high degree of reliability and thus a potential method of both initial assessment and monitoring of near visual acuity in such patients.

• F051

Assessment of interlinked double staircase acuity test

GIULVEZAN S (1), Gallagher K (2), Davies N (1)
(1) *CHELSEA AND WESTMINSTER HOSPITAL, OPHTHALMOLOGY, lONDON, United Kingdom*
(2) *Moorfields Eye Hospital, Education, London, United Kingdom*

Purpose To compare a novel visual acuity threshold algorithm using a predictive double staircase method with standard ETDRS logMAR chart.
Methods Software was written in MATLAB to generate a computerised visualacuity test. The algorithm uses a randomly presented double staircasemethod, the staircases are interlinked using a prediction of thresholdbased on each prior response. This reduces test duration and increasesaccuracy. The screen was calibrated using a Vernier scale and theresolution of the test was 0.02 log units. Ten threshold measurementswere made for each test, the results expressed as the mean and standarddeviation. The test was performed by three observers each with aninduced range of refractive errors and compared with the result ofETDRS logMAR acuity using a chart generated with the same screencalibration.
Results Mean staircased acuities were -0.13, 0.02, 0.22, 0.36, 0.56 log unitsfor 0, 0.5, 1, 1.5 and 2 dioptres of defocus respectively. The mean single letterscore logMAR acuities were -0.08, 0.01, 0.17, 0.38, 0.58 log units.The mean error in the staircased test was 0.02 (SD 0.01) log units forall defocus values. The mean difference between the two tests was-0.01 log units (SD 0.09). Bland-Altmann plots showed no systematicdifference. The mean time to perform the staircased test was 93seconds (SD 19s).
Conclusions The interlinked double staircase method gives a fast and accurateassessment of visual acuity which compares well with ETDRS logMAR. Ten threshold measures allow error estimation which is not available in a logMAR test. Otheradvantages over logMAR include a true resolution of 0.02 log units rather thaninterpolation and random letter generation with no memory effect.

• F052

Significance of Camouflage, Chromatic Acuity and Contour in the Design of Pseudoisochromatic Plates

KRASTEL H (1), Schultze-Lutter S (2), Mothes N (2), Udodov E (3), Kahlert C (4), Jonas J B (5)
(1) Mannheim Medical Faculty- University of Heidelberg, Dept. of Ophthalmology, Neckargemünd, Germany
(2) OCULUS Optik Geräte GmbH, R & V, Wetzlar, Germany
(3) Medical center "Novoye zrenie", Ophthalmology, Minsk, Belarus
(4) Klinikum Chemnitz, Ophthalmology, Chemnitz, Germany
(5) Mannheim Medical Faculty- University of Heidelberg, Ophthalmology, Mannheim, Germany

Purpose Pseudoisochromatic plates use a pseudo-chaotic pattern of image dots to conceal the contour of colour optotypes. By our study we want to improve the understanding of functional principles of pseudoisochromatic plates.
Methods The circular elements of red / green pseudoisochromatic plates were varied in size and degree of pseudo-chaotic arrangement. Illuminated by standard white D 65, colour optotypes were presented to daltonians and to normal observers, and the rates of failure and success in recognition were recorded.

Results Recognition of pseudoisochromatic optotypes is related to the size of elements in a non- linear way. Towards small visual angles, colour optotype recognition may improve due to fusion of the perceived colour of adjacent small elements. Towards large visual angles, colour optotype recognition may again improve due to detection of the individual colours of elements. Weakening of contours by defocus may improve the recognition of colour optotypes due to loss of camouflage. Loss of camouflage also occurs with a more regular, less pseudo-chaotic arrangement of image dots, thus facilitating the recognition of colour optotypes
Conclusions Besides the colours themselves, arrangement and size of coloured elements need careful consideration in designing pseudoisochromatic plates. In application of the plates defocusing has to be avoided.

Commercial interest

• F053

Comparability and reproducibility of four wavefront aberrometers for measuring lower and higher order aberrations in pseudophakic eyes

NGUYEN P M , Hirnschall N , Doeller B , Schuschitz S , Varsits R , Findl O
Vienna Institute for Research in Ocular Surgery, Hanusch Krankenhaus Wien-Department of Ophthalmology, Vienna, Austria

Purpose To compare measurements of lower and higher order aberrations (HOA) obtained with four different wavefront aberrometers and to assess their reproducibility
Methods This prospective study included pseudophakic otherwise healthy patients. Four wavefront aberrometers were compared. Three of the aberrometers in this study are combined with coneal topographers. Two of the devices use a Hartmann-Shack sensor (WASCA, Carl Zeiss Meditec AG; iDesign Advanced WaveSan aberrometer, Abbott Medical Optics), one device works on the basis of ray tracing (iTrace, Tracey Technologies), one device utilizes automated retinoscopy (OPD-ScanIII; NIDEK Co. Ltd.). All patients are measured with an autorefractometer (Topcon, Japan) and also a subjective refraction has been performed. In addition a Purkinjemeter measurement has been done.
Results In total, 51 eyes of 51 patients were included. No patient was lost to follow-up. Mean difference concerning root mean square of all higher order aberrations was 0.013 µm between Wasca and iDesign and 0.113 µm between Wasca and OPD, respectively. Reproducibility was found to be between 0.09 µm (SD:0.06) (iDesign) and 0.41µm (SD: 0.12) (iTrace). Details for higher order aberrations will be presented at the meeting.
Conclusions Feasibility was found to be excellent for Wasca and iDesign and was high for iTrace but for the OPD Scan there was a flat learning curve. Reproducibility was found to be good for all devices but slightly weaker for the iTrace device.

• F054

The Repeatability of straylight measurements using the C-Quant in young and older adults

PUELL M , Barrio A R , Antona B
Complutense University of Madrid, Applied Vision Research Group- Faculty of Optics and Optometry, Madrid, Spain

Purpose To assess the repeatability of retinal straylight measurements using the C-Quant straylight-meter and to evaluate the effect of age on repeatability.
Methods Twenty nine young (35.6 ± 9.6 years old) and twenty three older (61.8 ± 8.7 years old) subjects participated in the study. They were examined with the C-Quant straylight-meter. Two readings were taken in two different sessions with a time interval between them from 1 to 3 weeks. Inclusion criteria were distance best-corrected VA of at least 0.8 decimal and without manifest ocular diseases. The repeatability of the straylight was estimated by the Bland-Altman method whereby the mean difference (MD) and the 95% limits of agreement were determined as the coefficient of repeatability (COR).
Results Mean retinal straylight was 0.97 ± 0.12 log units and 1.21 ± 0.21 in the young and the older group, respectively. Repeatability of straylight measurements in the entire sample was high (MD: - 0.003 log units, COR= ± 0.21 log units). The repeatability was better in the younger group (MD: +0.024 log units, COR= ± 0.15 log units) than in the older group (MD: - 0.021 log units, COR= ± 0.24 log units). There were not any significant differences between the two repeated measurements in each group and also in the entire sample.
Conclusions The measurement of retinal straylight using the C-Quant showed a good repeatability, although was worse in the older group. The impact of changes in straylight caused by intraocular scatter in the older eye should be considered when measuring straylight in age-related diseases such as cataract.

• F055

Mesopic Visual Acuity in Type2 Diabetes without Retinopathy

ALDAHAM S (1), Martín-Ridura M D C (2), Barrio A R (1), Antona B (1), Carballo-Álvarez J (1), Puell M (1)
(1) Complutense University of Madrid, Applied Vision Research group- Faculty of Optics and Optometry, Madrid, Spain
(2) Madrid City Hall, Diabetes Unit- Health promotion and prevention services, Madrid, Spain

Purpose Today, the information about the extent to which mesopic visual acuity (VA) is altered in diabetics without retinopathy is lacking. The purpose of this study was to evaluate distance high contrast VA (HC-VA) and low contrast VA (LC-VA) under mesopic luminance conditions in type 2 diabetics without any signs of retinopathy.
Methods Thirty-six control subjects and twenty-three diabetics (well controlled glucose level) without retinopathy (mean onset duration 8.5±4.42 yrs) were tested. All subjects had best corrected VA of 20/20 or better. VA was measured using the HC (96% contrast) and LC (10% contrast) Baily-Lovie charts under photopic (85 cd/m2) and mesopic (0.10 cd/m2) luminance conditions with best distance correction worn. The subject was left to dark adapt for 10 minutes in the dark before testing mesopic VA.
Results Mean photopic VA's (logMAR) were significantly worse in diabetics than controls (HC-VA 0.03±0.08 and -0.03±0.08, $p<0.01$; LC-VA 0.17±0.08 and 0.11±0.11, $p<0.05$, respectively). Mean mesopic HC-VA was also worse in diabetics than controls (0.56±0.11 and 0.48±0.09, $p<0.05$, respectively), but with less extent than photopic VA. Mesopic LC-VA was not significantly different between diabetics and controls (0.94±0.11 and 0.91±0.06).
Conclusions Distance photopic high contrast and low contrast VA, and mesopic HC-VA were able to detect the worsening of VA in type 2 diabetics before any signs of retinopathy can be detected.

• F056

Analysis of Mp-1 audio-biofeedback impact on fixation in low vision patient with maculopathy.

SATO G (1), RIZZO R (1), Villani G M (2), Camerucci C (2)
(1) Low Vison Center, Low Vision Center Padova, Padova, Italy
(2) Low Vision Center Verona, Low Vision Center Verona, Verona, Italy

Purpose To study the impact of a low vision rehabilitation strategy based on Nidek MP-1 auditory biofeedback (BFB).
Methods Retrospective study of 39 eyes/26 consecutive patients referred for low vision rehabilitation. Patients received 8 monocular training sessions of BFB, each of 10 minutes duration, 7-14 days apart. Microperimetry, ETDRS VA and Pelli-Robson was performed at the beginning and at the end of the sequence. BFB employs a sound to train the patient to keep a specific gaze position.
Results Age median was 70. Pre-BFB logMAR VA was 1, logCS 0.60. Post-BFB logMAR VA was 1, logCS 0.75. Dense central scotomas and eccentric fixation locations were detected in 35 eyes/24 patients, and relative scotomas with central fixations in 4 eyes/2 patients. Mean sensitivity was 7.60 dB pre-BFB, and 8 db post-BFB. Pre-BFB fixation stability was 24% within 2°, and 67% within 4°; post-BFB, it was 25% within 2°, and 64% within 4°. BCEA analysis showed pre-BFB values for 68.2% BCEA to be 3.6 , and 4.46 post-BFB. After BFB, no significant difference was found for any of the above-mentioned parameters in the sample as a whole. Nevertheless, grouping cases by change in pre-vs post-BFB BCEA (group A: decrease in BCEA, n= 21; group B: increase in BCEA, n= 18) showed a significant difference in terms of BCEA itself, and in the related fixation stability ($p<0.05$).
Conclusions Although no significant difference in VA, CS, mean sensitivity, fixation stability at 2° and 4°, and BCEA was found after BFB in the sample as a whole, still there was an improvement in 21 eyes (53,8%) in terms of BCEA and fixation stability. Grouping analysis demonstrated that, while other tested outcome measures were not affected, some cases did respond significantly to BFB improving their fixation stability

• F057

Frequency-Doubling Perimetry in Type2 Diabetes without Retinopathy

ALDAHAM S (1), Martin-Ridura M D C (2), Pérez-Carrasco M J (1), Palomo-Álvarez C (1), Carballo-Álvarez J (1), Puell M (1)
(1) Complutense University of Madrid, Applied Vision Research group- Faculty of Optics and Optometry, Madrid, Spain
(2) Madrid City Hall, Diabetes Unit- Health promotion and prevention services, Madrid, Spain

Purpose: Frequency Doubling Technology (FDT) perimetry has been utilized to detect visual field (VF) changes in type 1 diabetics with no retinopathy. However, it has not been tested in type 2 diabetes. The purpose was to assess FDT perimetry and its diagnostic capacity in type 2 diabetics without retinopathy.
Methods : This comparative cross-sectional study included thirty-one controls and nineteen age-matched patients with type 2 diabetes without retinopathy, well controlled glucose level and onset duration >4 years. Full threshold C-20 program was used for VF testing in the FDT perimeter. Mean sensitivities for each VF location, mean deviation (MD), pattern standard deviation (PSD), and test duration were compared. Area under the curve (AUC) of a Receiver Operating Characteristic (ROC) was calculated to assess the diagnostic value of the FDT perimetry.
Results : Mean sensitivities for some VF locations were significantly lower in the diabetic group. The mean MD was worse in diabetics (-3.35±2.02 dB) than controls (-1.95±1.70 dB) ($p<0.05$). Neither the mean PSD nor the testing time was significantly different between the two groups. AUC values for MD and PSD were 0.29 and 0.69, respectively, (standard error=0.076, p=0.024).
Conclusions : FDT perimetry has a diagnostic capacity as a clinical tool for the detection of early retinal dysfunction in Type 2 diabetics before the onset of retinopathy.

• F058

Presbyopia compensation: looking for cortical predictors

IMBEAU L (1), Majzoub S (1), Thillay A (2), Bonnet-Brilhault F (2), Pisella P J (1), Batty M (2)
(1) Hôpital Bretonneau CHU TOURS, Ophtalmologie, Tours, France
(2) Inserm- Imagerie et Cerveau UMR U 930-, Centre Universitaire de PédoPsychiatrie-, Tours, France

Purpose New surgical techniques have recently been developed in order to compensate for visual impairment for presbyopic patients. However, the follow-up results are still variable, depending on the correction modality used and/or the patient. The main purpose of this study was to identify predictive electrophysiological markers of post-correction visual comfort for presbyopic patients.
Methods Thirteen presbyopic patients received randomized presbyopia compensation with contact lenses successively by monovision, and by multifocality, for 3 weeks with a break of two weeks without any presbyopia compensation in between. Follow-up examinations were performed at entry (T0) and after each correction modality (Tmono and Tmulti). They included testing for near and distance visual acuity, stereoacuity (TNO test), binocular contrast sensitivity and electrophysiological recordings (monocular and binocular patterns Visual Evoked Potentials).
Results A significant correlation was found between the TNO score difference (monovision-multifocallity) and the P100 latency evoked by the binocular pattern at T0, suggesting that late P100 latency could be associated with a lesser decrease in stereoacuity with monovision.
Conclusions While our findings do not permit decisions regarding the superiority of f one type compensation over another, these preliminary results support using the P100 latency evoked by binocular patterns as a predictor of post-compensation stereoacuity.

• F059

Three family cases with Retinitis pigmentosa rod-cone dystrophy with autosomal dominant inheritance

KOEV K
MEDICAL UNIVERSITY SOFIA, OF OPHTHALMOLOGY, SOFIA, Bulgaria

Purpose Three family cases with Retinitis pigmentosa (RP) rod-cone dystrophy with autosomal dominant inheritance according to American Academy of Ophthalmology classification were diagnosed and studied: the grandmother G. D., 83 years old; the son A.D., 61 years old and granddaughter A.B., 27 years old.
Methods The diagnosis was confirmed clinically, ERG, OCT, Angiography, (with colour tests) ATL, Ishihara table and Rabkin chart, All color Anomaloscope IF-2 TOMEY, Test 28 HUE de Roth Farnsworth-Munsell, with kinetic Kugel perimeter and automated Humphrey perimeter using the SITA-Fast computerized perimetric threshold strategy.
Results During the photopic test with ERG, there was observed retinogram with normal morphology and polarity but with drastic decline of the amplitude by 50 mV on average. In the process of dark adaptation, a decline of bioelectric activity was detected: from subnormal to non-recording ERG during white and blue flashes at 30 Hz. In all of the three different generations' cases, there was established reduction in residual bioelectric activity with the advancing of age of the patients with progressive degenerative RP disease. During the colour test, the grandmother and the father could read only ATL, which proves there was no acquired colour vision disorder. This is in confirmation to the autosomal dominant inheritance. In the process of anomaloscopic test and the colour tables and charts of Ishihara and Rabkin, as well as Test 28 HUE de Roth Farnsworth-Munsell, the grandmother and the father were found to be with deuteranomaly. The granddaughter had a normal trichromacy. The perimetric tests showed concentric narrowing of the visual field to tubular vision.
Conclusions Serum for genetic tests was taken from the three family cases in order to confirm the diagnosis and administer a gene therapy.

• F060

Aplication of low-level Laser therapy (LLLT) in patients with Retinitis Pigmentosa (RP)

KOEV K
MEDICAL UNIVERSITY SOFIA, DEPARTMENT OF OPHTHALMOLOGY, SOFIA, Bulgaria

Purpose Retinitis pigmentosa (RP) is a group of rare, genetic disorders that involve a breakdown and loss of cells in the retina. The objective of this study is to examine long-term effects of low-level laser therapy (LLLT) in patients with **(RP).**
Methods The research was implemented for a period of 3 years. For LLLT, a He-Ne Laser with continuous emission at 633 nm (01 mW/cm2) was used in patients with RP. In total, 14 patients (7 men and 6 women - 28 eyes) with RP of 56.5 ±3.2 years were included in the study. Laser radiation was applied transpupillary 10 times for 3 min once in two days to the macula. Visual acuity was followed for a 3-year period. The ERG, Anomaloscope IF-2 TOMEY, Test 28 HUE de Roth Farnsworth-Munsell, Kugel perimeter, Humphrey perimetry , Fluorescein angiogram and Amsler test was used.
Results The patients had complained of nyctalopia and decreasing vision. Biomicroscopy showed optic nerve atrophy, and narrow retinal vessels with a typical pattern of retinal pigmentation. Visual fields were reduced to a central residual of 10 degrees. Visual acuity remained unchanged in all patients with RP. There was a statistically significant increase in visual acuity ($p<0.001$, end of study versus baseline) for RP patients for the period of 3 years after the LLLT. The mid-peripheral absolute concentric scotoma in RP was reduced after LLLT. No side effects were observed during the therapy.
Conclusions This study shows that LLLT may be a novel long-lasting therapeutic option for RP. This is highly effective treatment that improves visual acuity for a long time.
References:
1.Ivandic BT1, Ivandic T. Low-level laser therapy improves vision in a patient with retinitis pigmentosa. Photomed Laser Surg. 2014 ;32(3):181-4.
2.E. Mitschischek: "Retinale Laser-Stimulation- Ein neues Therapiekonzept beiTrockener AMD. der Augenspiegel 3/2003, pp. 20-24

• F061

Female heterozygotes of X-linked ocular disease in the era of molecular diagnostics

KREPS E O (1), De Zaeytijd J (1), De Baere E (2), Leroy B P (1,2)
(1) Ghent University Hospital, Ophthalmology, Ghent, Belgium
(2) Ghent University Hospital, Center for Medical Genetics, Ghent, Belgium

Purpose To investigate the accuracy of recognizing female heterozygotes for X-linked retinitis pigmentosa (XLRP) and choroideraemia (CHM) using fundoscopy and blue-light fundus autofluorescence (FAF).
Methods Retrospective analysis revealed 26 female XLRP heterozygotes from 17 different families (age 3-77 years) and 8 CHM heterozygotes from 5 families (age 14-65 years). Molecular diagnosis has been obtained for all subjects.
Results In XLRP, 17 of 26 patients (65.4%) mentioned nyctalopia. RPGR mutations were identified in 18 subjects – 9 of which in ORF15 - whereas a causative mutation was found in RP2 in the remaining 8 subjects. Dilated fundoscopy showed no abnormalities in 8 subjects, a tapetoid reflex in 2, regional pigmentary changes in 16 and full-blown RP features in 2 patients. An abnormal FAF pattern was found in 18 of 26 patients (69.2%). Of the 26 molecularly proven heterozygotes, 23 (88.5%) showed abnormalities on fundoscopy and/or FAF. In CHM, only 1 of 8 patients - aged 40 - mentioned visual difficulties at night. In each of the 8 subjects, equatorial mottled pigmentary changes were evident. FAF revealed multiple hyper- and hypoautofluorescent flecks in all 8 patients. In both XLRP and CHM, clinical findings were independent of age or specific mutation.
Conclusions Female heterozygotes of XLRP show abnormalities on dilated fundoscopy and/or blue-light fundus autofluorescence in 88.5% of cases with a molecularly proven diagnosis. The most characteristic feature is a radial pattern of alternating areas of hyper- and hypoautofluorescence. In CHM, all carriers exhibit pigmentary changes in the retinal midperiphery and scattered autofluorescence changes, despite a lack of visual symptoms.

• F062

Multifocal electroretinogram and en-face OCT in patients who underwent retinal detachment surgery

RICOUARD F, Bigan G , Tumahai P , Flores M , Castelbou M , Delbosc B , Saleh M
CHU Jean Minjoz, Ophtalmology, Besancon, France

Purpose To study the anatomical and functional recovery after retinal detachment surgery (RD) by studying the reflectivity of the ellipsoid band (ISe) measured in en-face OCT and multifocal electroretinography (M-ERG) and investigate the factors involved in the results.
Methods Prospective study of 39 patients operated successfully of RD and examined at baseline and at 3 (M3) and 6 months (M6). SD-OCT and M-ERG were performed at each visit. A coronal view of the ganglion cell layer (GCL) and the cone inner segment ellipsoid (ISe) band were reconstructed on en-face OCT. The mean reflectivity in the 2 central degrees was calculated using image J and expressed as a gray level ranging from 0 (black) to 256 (white).
Results M-ERG waves amplitudes were reduced in RD involving the macula ($p<0.05$). Best corrected visual acuity (BCVA) was correlated to the M-ERG amplitudes at 6 months ($p<0.01$). CGL and ISe reflectivity were lower in the group with macular involvement ($p<0.05$). ISe reflectivity was correlated with the BCVA at M3 and M6 ($p<0.001$). ISe reflectivity was also related to the duration of the macular detachment ($p=0.01$). However, we did not observe any correlation between GCL reflectivity and BCVA. While, the GCL reflectivity was correlated with the RMS amplitudes ($p=0.03$), there was no correlation between M-ERG amplitudes and ISe reflectivity.
Conclusions M-ERG represents a valuable tool in the assessment of visual function after RD. En-face OCT brings new insight on the integrity of the retinal structures after surgery, and shows that both inner and outer retinal layers are impaired after RD reattachment.

• F063

The STZ-induced diabetic rat as a model for studying neuronal pathologies of diabetic retinopathy

HERRMANN R , Zippel N , Haller J , Streicher R
Boehringer Ingelheim Pharma GmbH & Co. KG, CardioMetabolic Diseases Research Germany, Biberach an der Riss, Germany

Purpose Diabetic retinopathy (DR) is a sight-threatening complication of diabetes and a leading cause of blindness in adults. Current therapies target late-stage vascular dysfunction of DR. However, DR is not a vascular disease per se, but is also characterized by chronic neurodegeneration. To identify neuroprotective treatments, it is critical to utilize appropriate animal models reflecting a hyperglycemia-dependent loss of retinal function. Here we report a comprehensive characterization of the STZ-induced diabetic rat as a model for neuronal dysfunction in DR.
Methods Hyperglycemia was induced in Brown Norway rats upon STZ treatment. Blood glucose levels were monitored regularly and insulin levels were measured at study termination. To investigate different aspects of retinal function, dark- and light-adapted flash and flicker electroretinograms were recorded at 4 and 7 weeks post STZ application, respectively. One group of animals received insulin treatment for antagonizing the effects of hyperglycemia.
Results STZ treatment led to decreased insulin and increased blood glucose levels. Hyperglycemia caused functional impairments of both rod- and cone-driven pathways on the level of the outer as well as the inner retina, which could be partially rescued by insulin treatment. Overall, the degree of functional impairments correlated with increasing blood glucose levels.
Conclusions The STZ-induced diabetic rat model is characterized by a hyperglycemia-dependent dysfunction of retinal neurons. Thus, this model is an attractive tool for investigating novel mechanisms underlying DR.

• F064

Evidence for a new model of the human eye - a holographic laser system, biophotonics. The holographic view

MANU M D (1), Plesu G (2)
(1) Cabinet Oberon Iasi, Research and Development- in BioPhotonic and bionics, Iasi, Romania
(2) Gheorghe Asachi University Iasi, Iasi, Romania

Purpose The authors proposed to verify the eyes structure and function as laser system, position of the image on retina, and properties of bio-luminescence (BL) of the eye, with help of multidisciplinary studies, biophotonic and bionic tests.
Methods Methods demonstrated that the eyes are laser bifocal systems, with nonlinear medium, through multidisciplinary studies up to date in medicine, biochemistry and physics, original biophotonic tests, delayed luminescence DL, self-emission SE tests, and two original models of bionic eye.
Results We detected: errors of the photographic mechanism of human vision; other properties of human eye as holographic laser system, a laser bifocal system; the eye is initiating BL tract as laser phenomenon, due to internal source of light as phosphate - water; a right position of the images on retina; the amplification of BL along nervous tract, from the eye till to bones and muscles; the BL sense of propagation is reverse nighttime, from brain-retina-cornea, show a right position too, as dream; BL properties are: monochromatic, coherent, directionality, rotary polarization, amplified power and information along the nervous system; every color has oscillation plans; nonlinear medium of the cells and organs apply Stokes and anti-Stokes rule; so it was done the first step for psychic processes (vision, memory, thinking, speech) and bionics.
Conclusions The eye is a bifocal laser system that initiates a biological laser phenomenon, BL, a coherent monochromatic, polarized and amplified radiation, and renders holograms in right position on retina, due to eye itself, not to brain. Important applications are in medicine, physics, teaching, bionics etc. Keywords: eye, nonlinear medium, laser bifocal system, BL, biophotonic tests, holography, bionics, view.

• F065

Bioluminescence - Biological Laser Phenomenon initiated by eye. Biophotonic tests.

MANU M D
Cabinet Oberon Iasi, Research and Development- in BioPhotonic and bionics, Iasi, Romania

Purpose The study of the characteristics of bio-luminescence (BL) in eyes, optic nerves, brain, spinal cord, muscles, bones, phosphate, water.
Methods Multidisciplinary studies, biophotonic and electronic tests performed at the International Institute of Biophysics Neuss, on biological samples ***Onchorynchus mykiss*** (rainbow trout), with photo-multiplier PMS1 and PMS2. The samples optical axis is oriented parallel, obliquely,90°C and 180°C angels to optical stimulus .
Results BL transmission is present all biological systems studied; energy values are the maximum when the optical axis BL of the sample is parallel to the direction of the external stimuli; appear an optical amplification from the eye to the brain -bones and muscles, and two optical paths cross over the nervous system.
Conclusions In your eyes, like in bifocal and confocal laser system, any color simultaneously reach from one pole to another. The sense of BL is from outside to inside daytime,and reverses direction nighttime.The presence of the laser active substance LAS (phosphate, water, liquid crystals) in cells, allows stimulation and the propagation of light, step by step, as thermodynamic cycles, but reduce the light speed. By overlapping the ocular optical axis over the object axis, begins conversion non-coherent light into coherent light In the cornea, when on the surface of the cornea appears a geometric place of coherent points, that dispersed light in color components, rotary polarization and separation dextro, levo-gyrate radiation.The BL amplification on the route of the nervous system is produced by interference (ventre) as digital optical pulses and by adding visible and caloric energy. BL energy is ultra-weak but has large effects due to energy transformation of each stimulus, as four secondary effects: biochemical; electrical; magnetic; optic (holographic, laser heat).

• F066

Modulation of the contrast response function of V1 neurons by the pulvinar

CASANOVA C, Lai J, Thomas S
Université de Montréal, Ecole d'Optométrie, Montreal, Canada

Purpose The pulvinar establishes reciprocal connections with nearly all the visual cortices and is thus in a strategic position to influence analyses taking place at the cortical level. Projections from the pulvinar to the primary visual cortex (V1) are considered to be modulatory, altering decoding properties of neurons without changing their basic receptive field properties. Results from our laboratory, based on optical imaging, have supported this assumption (Soc. Neurosci. Abst. 2011. Vanni et al.).
Methods Here, we investigate further by studying V1 single unit responses during reversible deactivation of the lateral posterior (LP) - pulvinar complex in the cat through microinjections of gamma-aminobutyric acid. Recording and injection electrodes were positioned to obtain overlapping thalamic and cortical receptive fields.

Results No change in the preferred orientation or direction selectivity of V1 neurons was observed during pulvinar deactivation. However, for 67% of the cells tested (n=39/58), the response amplitude to the optimal stimulus was reduced by a mean of 65%. The contrast response function of neurons was modeled with the Naka-Rushton function and analysis of the effects of pulvinar deactivation revealed at least three types of modulation based on the function parameter predominantly affected: 24% of cells had a decrease in Rmax, 13% had an increase in the exponential factor and 11% had a C50 increase.
Conclusions Our results suggest that the pulvinar modulates activity of neurons in the primary visual cortex in a contrast-dependent manner. Consequently, this extrageniculate nucleus is likely to contribute to cortical processing in shaping spatiotemporal activity patterns of V1 neurons.

• F067

Evaluation of a portable manual stretching device to simulate accommodation

DANTIN J C , Pinilla Cortés L , Montenegro G A , Barraquer R I , Michael R
Instituto Barraquer, Investigación, Barcelona, Spain

Purpose To evaluate the performance of a manual lens stretching device using clinical scanners to analyze variations in lens topography and cross sections.
Methods The stretching device consists of 6 pulling elements, attached to an external ring, which act like an aperture. The anterior segment of enucleated eyes from six months old pigs were glued to the device, then the cornea and the posterior segment of the eye were removed; finally, the whole setup was placed inside a container, which controls the stretching process. Different clinical scanners (Casia OCT, Orbscan and Pentacam) were used to analyze variations in lens shape. Calibrations were achieved using an artificial lens of known dimensions and refractive index.
Results The device allows for a radial increase of 1.8mm. Lens topography could be analyzed using the Orbscan and the Pentacam. While lens cross sections were obtained using the Casia OCT and the Pentacam. The posterior surface of the lens could not be correctly visualized. With our tests we observed changes in porcine lens diameter, shape, surface topography and dioptric power during stretching.
Conclusions This stretching device allows for the analysis of the anterior surface and cross sections of the lens. Its capabilities are comparable to larger static stretchers, but has the advantage of being portable, allowing it to be used with the clinical scanners the center already has destined to patients, making it a cheaper alternative. However, the forces can't be measured.

• F068

Objective assessment of cataract: Comparison between the Lens Opacities Classification System III and a Scheimpflug camera

BIRKELDH U (1), Domínguez-Vicent A (2), Laurell C G (1), Brautaset R (1), Nilsson M (1)
(1) Karolinska Institutet, Clinical Neuroscience, Stockholm, Sweden
(2) University of Valencia- Optometry Research Group, Department of Optics, Valencia, Spain

Purpose Develop an automatic system for cataract classification using the Sirius Scheimpflug for both nuclear and cortical cataract.
Methods Scheimpflug images were taken using the Sirius system in 50 patients with nuclear and/or cortical cataract (mean age 69±9.2 years). The nuclear opacity (NO) and cortical opacity was graded by an ophthalmologist according to the Lens Opacities Classification System (LOCSIII) by comparing the slit-lamp image with the LOCS's standard nuclear images. A custom-made MATLAB program was used to calculate the pixel intensity value within a region of interest (ROI) of the nucleus and to calculate the percentage of opaque pixels in the cortex.
Results Eighty-nine eyes with nuclear and 81 eyes with cortical cataract were analysed. Both average and maximum NO pixel intensity units obtained from the ROI had a significant correlation with LOCS III (r=0.731; P<0.01 and r=0.738; P<0.01). The mean average NO was 21.77±11.59 pixel intensity units and the mean maximum NO was 38.94±18.52. A significant and positive correlation with LOCS III (r = 0.812; P<0.01) was found when the whole cortex area was analysed.
Conclusions The results from this study indicate that the Sirius Scheimpflug has a good correlation with LOCS III for lens density measurements. The use of a Scheimpflug camera might be a valuable tool in clinical practice to grade nuclear and cortical cataracts automatically and objectively.

• F069

Cataract surgery in adult patients with uveitis

BACQUET J L , Fel A , Butel N , Remond A L , Le Hoang P , Bodaghi B
Hôpital de la Pitié Salpêtrière, Paris, Paris, France

Purpose To determine current challenges and visual results in patients with uveitis who underwent cataract surgery in 2013.
Methods We retrospectively collected data from every consecutive uveitis patient who underwent cataract surgery during the year 2013 and studied demographic data (age, gender) along with uveitis etiology and therapeutic management. Pre and post operative anterior chamber flare was evaluated by laser flare photometry. Postoperative rate of macular edema (ME), ocular hypertension, epiretinal membrane (ERM) was also evaluated. Every patient was operated by the same surgeon (BB) and received a subconjunctival injection of dexamethasone at the end of the procedure. Use of perioperative oral prednisone was noted.
Results Twenty eight eyes of 24 patients were operated. The mean age was 57.6, and 24 were female (85.6%). Preoperative mean best corrected visual acuity (BCVA) was 0.90 logMar. A week after surgery mean BCVA was improved to 0.26 logMar. A month later, mean BVCA was 0.26 logMar. BCVA was 0.38 logMar at 6 months and 0.27 logMar at one year. The mean preoperative flare value was 26.4 ph/ms. It increased to 42.8 ph/ms at one day and 35.0 ph/ms at one week. ME was noted postoperatively in 11 eyes (39%), of which 4 were preexistant. Four eyes (14.3%) had inflammatory glaucoma and ERM was noticed on OCT examination in 6 eyes (21.4%). Oral prednisone was used prior to surgery in 6 patients (25%) and after surgery in 10 patients (41.6%).
Conclusions Cataract surgery in adult patients with uveitis has a satisfactory outcome in most of the cases. It is important to achieve a strict preoperative control of ocular inflammation. The incidence of complications such as macular edema, epiretinal membrane or glaucoma has been dramatically reduced by an appropriate management of the disease.

• F070

Anterior segment changes after femtosecond cataract surgery measured with optical coherence tomography and scheimpflug imaging technology

PEREZ CARRASCO M J (1), Fernández-Cuenca S (1), Lorente-Hevia M P (1), Alvarez de Rementería L (2), Aldaham S (1), Puell M (1)
(1) Complutense University, Óptica II, Madrid, Spain
(2) Clínica Rementería, Surgery, Madrid, Spain

Purpose To determine changes in anterior chamber depth (ACD), iridocorneal angle size (IAS) and central corneal thickness (CCT) using optical coherence tomography (OCT) and Scheimpflug imaging technology (SIT) in subjects implanted with multifocal intraocular lens (IOL) after femtosecond cataract surgery.
Methods Prospective study of 36 healthy eyes (68.8±7.9 years) undergoing femtosecond laser assisted-cataract surgery and AcrySof REsTOR SN6AD1 IOL implantation. The anterior segment parameters were measured preoperatively and 1 month after surgery with the Visante-OCT (Zeiss) and the Oculyzer™ II (WaveLight® AG) systems. Analysis of agreement and interchangeability of the preoperative 2 systems measurements was performed by the Bland-Altman method.
Results After femtosecond cataract surgery, the ACD and IAS measured with Oculyzer™ II showed a significant mean increase of 1.54 ± 0.28 mm and 10.2º±4.23 respectively. Also, using the Visante-OCT there was a significant mean increase: 1.27±0.34 mm for ACD and 9.38º±6.52 (Temporal) and 8.29º±7.13 (nasal) for IAS. CCT showed no significant changes. The range of agreement indicated that the 2 techniques cannot be used interchangeably for preoperative measurement of ACD and IAS.
Conclusions After cataract surgery with femtosecond laser, ACD and IAS increased significantly when measured using OCT and SIT. Visante-OCT and Oculyzer™ II systems can be used interchangeably for CCT evaluation but not for ACD and IAS.

• F071

Anterior chamber and refractive parameters in diabetic patients according to metabolic status

COSTA L , Cardigos J , Vicente A , Borges B , Ferreira J , Cunha J P , Amado D
Centro Hospitalar de Lisboa Central, Ophthalmology, Lisbon, Portugal

Purpose Diabetes Mellitus is associated with changes in refractive parameters. Some aspects already studied were the corneal biomechanics and lens thickness. Although, the discussion about anterior chamber angle and depth is still open. The author objective was to analyze and correlate the anterior chamber depth, lens vault and lens thickness with disease duration and metabolic status.
Methods Prospective case-control study. The anterior chamber and refractive parameters were studied using the Visante OCT and the differences between diabetic patients with metabolic control and disease stability were determined (group 1), without (group 2) and group-control (3). The metabolic control is based on HbA1c levels. The cut-off considered was 7%.
Results A total of 64 patients were evaluated (group 1 – n = 21; group 2 – n = 20; group 3 – n = 23). The mean age was 64.32 ± 7.55 years and approximately 5 years of disease duration. In both groups of diabetic patients we found thicker lens, narrow anterior chamber and higher lens vault compared to control group. There was a difference between diabetic groups exists, but it was not statistically significant.
Conclusions The anterior chamber angle and lens vault are influenced by the serum glucose levels. Further studies will be necessary to clarify the physiopathology mechanism responsible for the anterior segment modifications.

• F072

New Parameter for Predicting the Postoperative IOL Position: Preoperative Lens Equator Depth measured By Three-Dimentional Anterior Segment Optical Coherence Tomography

HWANG K Y (1), Joo C K (2), Yoon G Y (3)
(1) konyang university hospital, ophthalmology, daejon, South-Korea
(2) Seoul St. Mary's Hospital- College of Medicine- The Catholic University of Korea, Department of Ophthalmology and Visual Science-, Seoul, South-Korea
(3) Flaum Eye Institute- University of Rochester, The Institute of Optics- Center for Visual Science-, Rochester- New York, United States

Purpose To test the hypothesis that the preoperative crystalline lens equator depth (pre-LED) measured by three-dimensional anterior segment optical coherence tomography (OCT) is an effective predictor of the postoperative anterior chamber depth (post-ACD).
Methods Thirty-nine eyes that underwent phacoemulsification and implantation of a one-piece, plate-haptic intraocular lens between December 2013 and June 2014 were examined to develop the new algorithm for predicting the post-ACD. The pre-LED was defined as the depth from the back surface of central cornea to the line connecting the intersecting points between the anterior and posterior capsule intraoperatively using 3-D OCT in Catalys (Abbott Medical Optics). The post-ACD was measured by Pentacam (Oculus) in each case at 2 months postoperatively and was analyzed by multiple linear regression for covariance with preoperatively defined variables including the pre-LED, lens thickness, lens vaulting measured by the OCT and the preoperative ACD (pre-ACD) measured by the OCT and Pentacam.
Results The mean pre-ACD, pre-LED, AL, lens thickness and lens vaulting was 2.74±0.50 mm (range, 1.75-3.36); 4.14±0.35 mm (range, 3.36-5.91); 23.97±1.37 mm (range, 21.89-27.63), 4.23±0.46 mm (range, 3.01-5.12) and 1.42±0.27 mm (range, 0.82-1.89). Single regression analysis showed significant correlations between the post-ACD and pre-LED, $R2 = 0.468$, $P<0.001$; pre-ACD, $R2 = 0.379$, $P<0.001$) Using a new regression formula with the two most significant variables (pre-LED and pre-ACD), the post-ACD can be predicted with an accuracy of 47.3%. In the prospective study, the postoperative ACD was predicted with a correlation coefficient of 0.696.
Conclusions The crystalline lens equator depth may be a promising preoperative parameter to predict the postoperative IOL position.

• F073

Impact of a pre-cut on clear cornea incision architecture in cataract surgery

DRASCHL P , Hirnschall N , Doeller B , Nguyen P M , Findl O
VIROS - Hanusch Hospital, Department of Ophthalmology, Vienna, Austria

Purpose To assess the influence of a 600 µm corneal pre-cut on incision architecture compared to a stab-incision in cataract surgery.
Methods This randomised bilateral study included patients scheduled for cataract surgery in both eyes without any other relevant ophthalmological co-morbidities. Pre-operatively, optical biometry and topography were performed (IOL Master 500 and the Atlas; both CZM AG). The first eye to be operated randomly received a corneal pre-cut, or a single-plane stab incision and the second eye received the other incision technique. In the pre-cut group, a vertical cut was performed using a 600 µm guided blade. Incision size was 2.4 mm in both groups. Incision architecture was assessed intra-operatively using a continuous intraoperative-OCT device (ReScan 700, Carl Zeiss Meditec AG, Germany) after the incision, after I/A and after IOL implantation. Additionally, OCT measurements were assessed (Spectralis, Heidelberg engineering, Germany) one hour, one week and one month post-operatively. Additionally, autorefraction and subjective refraction were performed at the one-month-follow-up.
Results In total, 40 eyes of 20 patients were included. The intra-operative measurements were possible in all cases and details of the morphology of the incision was visible in nearly all cases. Intra-operative findings of endothelial and epithelial gaping, as well as Descemet detachment correlated well with post-operative findings at the 1 hour follow-up. Correlations between wound architecture and residual astigmatism were found to be weak.
Conclusions Intra-operative OCT measurements using spectral-dmoain technology were found to be useful to observe and document the incision architecture during cataract surgery.

• F074

Small pupil and pupil dilatation methods. Comparative study in cataract surgery

CARAMELLO C M (1), Del Buey M (1), Cristobal J (1), Mateo Orobia A J (2), Martinez Velez M (1), Sanchez Marin J I (1), Idoate A (1), Pinilla I (1), Casas P (1)
(1) Hospital Clinico Universitario Lozano Blesa, Oftalmología, Zaragoza, Spain
(2) Hospital Universitario Miguel Servet, Oftalmología, Zaragoza, Spain

Purpose To compare dilatation pupil devices implemented on cataract surgery, their advantages and disadvantages.
Methods Prospective, interventional study to analyze the following pupil dilatation techniques: iris-retractor hooks and Morcher-5s, Perfect-pupil, Graether, Malyugin and Oasis dilator ring. The following properties were studied: handiness, dilatation obtained, stability, and facility to remove the dilator ring in relation with the form, material, size and length of the necessary incision to proceed with the insertion.
Results Iris-retractor hooks are the best option in cases of zonular instability and retropulsion syndrome. The principal advantage is their versatility. Dilator-rings obtained similar results in stability and dilatation. Malyugin and Oasis dilator rings had the best handiness results. Graether and Oasis were the easiest to remove and Morcher and Perfect-pupil the most complicated.
Conclusions Having a small pupil is one of the main causes of complications in cataract surgery. There are different surgical devices that allow minimizing intra-operative risks. Each surgeon needs to select the best option compatible with to his surgical technique. Our study revealed that the most used devices were the iris-retractor hooks due to the capsular stability that they provides and the Oasis dilator-ring because of its flexibility and how easy they are to remove.

• F075

Effects of optic's shape for contraction of anterior capsulorhexis

MAYUMI N , Hiroyuki M , Tadashi S
Dokkyo Medical University, Ophthalmology, Tochigi, Japan

Purpose Evaluation of capsulorhexis contraction in two different shapes of hydrophobic acrylic intraocular lenses (IOLs).
Methods The study was conducted on 69 eyes that had undergone cataract surgery. FY-60AD (HOYA) or ZCB00V (AMO) were randomly selected and implanted after phacoemulsification. The FY-60AD has usual shapes of optics; however, the ZCB00V has rim at peripheral of optics. Anterior retro illumination images were photographed using slit lamp and EAS1000 (NIDEK) at 1 weeks, 1 month, 3 months and 6 months postoperatively. Capsulorhexis opening area were analyzed and the reduction ratios of capsulorhexis area were compared. After that, fibrosis in anterior capsule were also measured using area analysis software (Area Q, S-Tech) after 3 months postoperatively.
Results Reduction rate of capsulorhexis opening area were 5.44±10.15% (FY-60AD) and 0.25±2.36 (ZCB00V) after 6 months postoperatively. There were statistically significance (P<0.01). The area of fibrosis in anterior capsule were 62.24±21.32% (FY-60AD) and 16.90±8.34% (ZCB00V). There were statistically significance, too (P<0.01).
Conclusions The ZCB00V prevent the contraction of capsulorhexis opening area. And the increase of fibrosis is also prevented at the same time. The shape of optics may be an important factor to prevent the contraction of capsulorhexis.

• F076

Effect of Preconditioning Intraocular Lenses in Moxifloxacin Solution

FILIPE H P (1), Bozukova D (2), Pimenta A (3), Mata J L G (3), Colaço R (4), Saramago B (3), Serro A P (3,5)
(1) IOGP, Ocular Surface- Ocular Imaging- Cataract Surgery, Lisboa, Portugal
(2) Physiol, Physiol, Liége, Belgium
(3) Instituto Superior Têcnico, Centro de Química Estrutural, Lisboa, Portugal
(4) Instituto Superior Têcnico, Departamento de Engenharia Mecânica, Lisboa, Portugal
(5) Centro de Investigação Interdisciplinar Egas Moniz, ISCSEM, Lisboa, Portugal

Purpose The goal of our research was to investigate the possibility of using drug loaded intra-ocular lenses (IOLs) as an alternative to topical antibiotic usually prescribed after cataract surgery.
Methods Although widely used in drug release studies due to its simplicity in comparing systems, static conditions are far from reproducing biological conditions. A microfluidic cell mimetizing chamber's aqueous humor hydrodynamic is a much closer approach. With a volume of 250 µL , the cell is fed with a continuous flow of saline solution at a physiological similar rate.
Results Results showed that 30 days preconditioned IOLs were able to maintain a MXF concentration above the minimum inhibitory concentrations for ***Staphylococcus aureus***, ***Staphylococcus epidermidis*** and ***Streptococcus pneumoniae*** for 20 days.
Conclusions Further investigation in using moxifloxacin loaded IOls as effective to prevent post cataract surgery endophthalmitis is encouraged.

• F077

Thermal cataract induced by near infrared radiation (IRR)

YU Z (1), Schulmeister K (2), Talebizadeh N (1), Kronschläger M (3), Söderberg P (1)
(1) Gullstrand LAB, Neuroscience/Ophthalmology, Uppsala, Sweden
(2) Seibersdorf Labor GmbH, Laser- LED & Lampen-Sicherheit, Seibersdorf, Austria
(3) Hanusch Hospital, Ophthalmology, Vienna, Austria

Purpose To estimate the threshold radiant exposure for 1090 nm IRR and the time evolution of lens damage;To determine the temperature time evolution in the eye during the previously found threshold exposure, and the associated heat diffusion;To investigate if 1090 nm IRR induces cataract photochemically considering irradiance exposure time reciprocity.
Methods The 6-weeks-old albino rats were anesthetized intraperitoneally, ten min before exposure. The pupils of both eyes were dilated with tropicamide. Five min after pupil dilation, the animals were unilaterally exposed to 1090 nm IRR within the pupil area. Temperature was recorded with thermocouples placed in the selected positions of the eye. At the planned post-exposure time, the animal was sacrificed and the lenses were extracted for measurements of forward light scattering and macroscopic imaging.
Results The in vivo exposure to 197 W/cm2 1090 nm IRR required a minimum 8 s for cataract induction with a delayed onset of approx 16 h. The same radiant exposure was found to cause a temperature increase of 10 °C at the limbus and 26 °C close to the retina. The in vivo exposure to 96 W/cm2 1090 nm IRR with exposure time up to 1 h resulted in an average temperature elevation of 7 °C at the limbus with the cornea humidified and no significant light scattering was induced one week after exposure.
Conclusions An in vivo exposure to 197 W/cm2 IRR at 1090 nm within the pupil for 8 s induces cataract with a time delay. This threshold exposure causes a temperature rise of 10 °C at the anterior segment of the rat eye. IRR at 1090 nm produces thermal cataract, probably by indirect heat conduction from absorption in tissues surrounding the lens. There is no cataract development given that the limbal temperature increase is below 8 °C.

• F078

Uveal melanoma and renal cell carcinoma both metastatic to the liver

TURUNEN J (1), Markkinen S (2), Wilska R (1), Kivelä T (1)
(1) Helsinki University Hospital, Ophthalmology, Helsinki, Finland
(2) Folkhälsan, Folkhälsan Institute of Genetics, Helsinki, Finland

Purpose Germline mutations in the BRCA1-associated protein-1 gene (*BAP1*) predispose carriers to several types of cancer, including uveal and cutaneous melanoma, mesothelioma, renal cell cancer, and possibly other diverse tumor types. Approximately 2% of consecutive Finnish uveal melanoma patients harbor a germline mutation in *BAP1*.
Methods Case report.
Results A 53-year-old man was diagnosed with renal cancer in 2006. No metastasis was detected during a 5-year follow-up after surgery. In 2011, he noted decreased vision in his left eye. Ophthalmological examination revealed a suspicious choroidal mass and the patient was referred to the ocular Oncology service, Helsinki University Eye Clinic. A choroidal melanoma with a largest basal dimension of 15.5 mm and thickness of 11.1 mm and no metastases was detected (T3aN0M0, stage IIB). He received brachytherapy with an iodine plaque. Three years later he had liver metastases, and biopsies indicated the presence of both uveal melanoma and renal carcinoma metastases. Further, a sister of his father also has had uveal melanoma. Given that the patient was a candidate to harbor a germline *BAP1* mutation we sequenced the gene. No mutation was found in the coding regions or adjacent intronic sequences. Further, we carried out whole exome sequencing, and no mutations or mosaicism were found in *BAP1, BRCA1, SF3B1, or EIF1AX*.
Conclusions Not all familial uveal melanoma patients even with history of renal cell cancer harbor an obvious *BAP1* germline mutation. Currently, we are analyzing histological samples to further investigate the possible role of *BAP1* in tumor tissue and genetic data to find or exclude indirect effect on BAP1 function.

• F079

Clinical Experience with the Ruthenium- plaque Brachytherapy in Case of Choroidal Melanoma

GRAJEWSKI L (1), Kneifel C (1), Ciernik I (2), Ebrahimi F (2), Krause L (1)
(1) Städtisches Klinikum Dessau, Dept. of Ophthalmology, Dessau, Germany
(2) Städtisches Klinikum Dessau, Dept. of Radiotherapy and Radiation Oncology, Dessau, Germany

Purpose The brachytherapy with β- emitting ruthenium- plaques is a well-established treatment for patients with choroidal melanoma. This treatment modality has been used in our department since January 2011.

Methods A retrospective study of 104 eyes with choroidal melanoma that were treated with ruthenium- brachytherapy between January 2011 and December 2014. Patients were followed for regression and associated side- effects. The study included patients that had a follow- up time of at least 3 months.
Results Of the 104 melanomas nine also showed an infiltration of the ciliary body, 32 manifested at a central location and 59 eyes showed an exudative retinal detachment prior to brachytherapy. The mean sclera contact dose was 519 Gy, the mean apical dose applied was 105 Gy. The mean apical depth of the melanoma prior to therapy was 4,3 mm and after 12 months 2,2 mm. In three cases a movement of the plaques was necessary since the plaque did not cover the tumour margins in total because of the diameter of the melanomas. In eight cases the tumour showed regrowth after an initial regression was noticed. All together four eyes had to be removed. In eight cases distant metastasis were detected and two eyes showed a radiation retinopathy.
Conclusions For the treatment of choroidal melanoma the β- emitting ruthenium-plaques represent a therapy with a local tumour control rate of 92,3% and eye salvaging rate of 96,2%.

• F080

The Liverpool Uveal Melanoma Prognosticator Online (LUMPO) for prognosing metastasis free survival in the absence of cytogenetic data after ruthenium brachytherapy for uveal melanoma

ROSPOND-KUBIAK I, Wroblewska-Zierhoffer M , Twardosz-Pawlik H , Kociecki J
Poznan University of Medical Sciences, Department of Ophthalmology, Poznan, Poland

Purpose Liverpool Uveal Melanoma Prognosticator Online (LUMPO) is a tool developed by Eleuteri *et al.* to establish the prognosis for uveal melanoma patients according to the initial tumour characteristics and cytogenetic data. It has been validated with two separate cohorts of patients in United Kingdom and more recently in US. The aim of this study was to test the prognosticator in a homogenous group of patients treated with with ruthenium brachytherapy where genetic analysis was not performed.
Methods Material and methods: The records of the patients treated with ruthenium brachytherapy for uveal melanoma at the Department of Ophthalmology, Poznan University of Medical Sciences between 1994 and 2012 were retrospectively reviewed. The probability of 3-year, 5-year and 10-year metastasis free survival were obtained for each patient using the LUMPO accessed online and then compared with the existing follow-up data.
Results Results: We identified 102 patients, 60 women, 42 men in a mean age of 59 years. Mean largest basal diameter of the treated tumours was 9.29 (range: 4.04 – 18.9)mm, mean tumour thickness: 4.8 (range: 2.6-7.01) mm. Follow-up ranged from 3 to 22 years, mean: 7,55 years. 33 patients died, 18 (17,65%) out of metastatic disease. The metastatic death was not related to patients' age (p=0,6866), LBD (p=0,3049) or tumour thickness (p=0,7063) alone. The probability of metastasis free survival according to LUMPO was significantly lower for the metastatic group comparing to the surviving group at 3 years (p=0,0017) and 5 years post treatment (p=0,0001).
Conclusions Conclusions: LUMPO is a useful tool for prognostication for uveal melanoma patients. However, the use of cytogenetic data makes this prognosis more precise.

• F081

3D Sphere cultures of uveal melanoma reveal a molecular signature with a potential target for cancer therapy

NESS C (1), Garred Ø (2), Eide N (1), Bærland T (1), Nicolaissen B (1), Moe M (1), Noer A (1)
(1) Oslo University Hospital, Center for Eye Research- Department of Ophtalmology, Oslo, Norway
(2) Oslo University Hospital, Department of Pathology, Oslo, Norway

Purpose Uveal melanoma (UM) is the most common intraocular malignancy and is fatal in approximately 50% of the cases. Cancer relapse can be seen years after treatment. Diverse mechanisms have been proposed to explain the late relapse of UM e.g cancer dormancy and the presence of cancers stem cells (CSCs). UM has the disadvantage of being difficult to culture, thus a limited number of cell lines are available. 3D sphere cultures of early passages offer a lower degree of clonal selection and perhaps a more accurate reflection of the primary tumours. The propagation of cells as spheres is believed to enrich for a CSC-like population.
Methods 2D cultures were expanded in RPMI 1640 with 10% FBS, while 3D sphere cultures were expanded in hESC + MEF for 7-10 days. We compared UM primary tumours fresh frozen vs. 2D culture and 3D sphere culture of the same donors by microarray, qRT-PCR, transmission electron microscopy (TEM), immunohistochemistry (IHC) and chromatin immunoprecipitation (ChIP).
Results 3D sphere cultures induce signalling pathways that enhance survival and increase oncogenic activity. They show ultrastructural resemblance to *in vivo* UMs. The metabolic shift seen in 3D cultures could reflect the survival patterns of pre-metastatic cancer cells.
Conclusions The molecular signature of the 3D cultures reveals the presence of attractive targets for future epigenetic modulation or cancer cell vaccines.

• F082

Intravitreal chemotherapy in advanced retinoblastoma:results and complications

HADJISTILIANOU T, Borri M, De Francesco S, Sparagna C
Dipartimento di scienze oftalmolgiche, Centro Regionale di Riferimento per il Retinoblastoma, Sienna, Italy

Purpose to describe the technique and evaluate the efficacy of intravitreal melphalan in advanced retinoblastoma with focal or diffuse vitreous seeding.
Methods this is a retrospective non-comparative study. Our analysis was conducted at our referral center of retinoblastoma, Siena, Italy. The study included 19 eyes of 19 patients with naïve ,persistent or recurrent vitreous seeding in advanced retinoblastoma. All eyes received intravitreal injection (20 μg) of melphalan under general anaesthesia .Outcome measures included vitreous seeding control and eyeball preservation, treatment complications and drug toxicity.
Results we used concomitant therapy, including systemic chemotherapy ,intra-arterial chemotherapy and peribulbar chemotherapy. All patients are alive without evidence of extraocular dissemination and global salvage was attained in 83% of cases. Complications included central vein thrombosis.
Conclusions this study suggests that intravitreal melphalan injection for naïve,persistent and recurrent vitreous seeding can provide seeding control and avoid enucleation with minimal toxicity and complications.

• F083

Clinical characteristics and surgical outcomes of mesectodermal leiomyoma of the ciliary body and choroid

PARK H J, Lee J H, Lee S C
Yonsei University College of Medicine, Department of Ophthalmology, Seoul, South-Korea

Purpose Mesectodermal leiomyoma is a rare tumor that can arise from smooth muscle tissue in the iris or ciliary body or from heterotopic smooth muscle in the choroid. The purpose of this study was to describe the clinical characteristics and surgical outcomes of mesectodermal leiomyoma of the ciliary body and choroid.
Methods Retrospective observation case series of 8 patients who were diagnosed with mesectodermal leiomyoma with histopathologic and immunohistochemical confirmation.
Results The median age at presentation was 37.5 years. The median follow-up period was 27 months. Ultrasonography showed dome-shaped smooth surface with low to medium internal reflectivity and regular internal structure in all tumors. The tumor had a median largest base diameter of 10.4 mm and a median thickness of 7.7mm. They revealed pinkish colored surface and vessels that more developed than other intraocular tumors. The tumors located on ciliary body only in 4 eyes, on choroid only in 2 eyes, and on ciliochoroid in 2 eyes. 6 patients who had tumors on ciliary body only or ciliochoroid underwent lamellar sclerouvectomy. 2 patients who had choroidal tumor received enucleation or partial excision for biopsy each. On immunohistochemistry, all the tumors were stained positively for smooth muscle actin and desmin. After lamellar sclerouvectomy, the tumor did not show recurrence in follow up period. But the patient that underwent partial removal of tumor on choroid showed irregularly changing surface with increasing size.
Conclusions Mesectodermal leiomyoma did not show the recurrence after lamellar sclerouvectomy and malignant change of tumor. However these tumors are difficult to differentiate from other intraocular tumor and to conclude definitely that they do not develop malignant change because they have heterogeneity from benign leiomyoma of other body organs.

• F084

Case report of ring ciliary body and choroidal lymphoma.

BOGDALI A (1), Markiewicz A (1), Jakubowska B (2), Romanowska Dixon B (1)
(1) *Jagiellonian University- Medical College, Department of Ophthalmology, Krakow, Poland*
(2) *University Hospital, Department of Ofthalmology, Krakow, Poland*

Purpose The aim of the study was to analyze case of ring ciliary body and choroidal lymphoma.
Methods Retrospective analysis.
Results 54 years old man was sent in October 2014 to Department of Ophthalmology of the Jagiellonian University Medical College in Cracow with diagnosis of choroidal melanoma in left eye. Tumor was detected accidently. BCVA in both eyes was 1.0. Intraocular pressure in both eye was correct. In patients history stomach lymphoma treated in 1996 with radiotherapy and chemiotherapy. In fundus examination we found mass located temporally in choroid and cilary body. Ultrasound examination (USG and UBM) showed ciliary body and choroidal mass located between 2 and 7 clock hour (almost 180 degrees), thickness 8.2 mm, base 14.30 mm. The patient was qualified to biopsy of ciliary body and choroidal mass and I-125 brachytherapy. During 2 weeks tumor enlarged, was located in 270 -300 degrees and looks like ciliary body ring melanoma (thickness 9.0 mm, base 23.3mm) with iris elevation and conjunctival edema. Enucleation of left eyeball was performed. Histopathological examination reveled *neoplasma malignum probabiliter non epitheliale. Lypmoma malignum – marginal zone lymphoma*. Immunohistochemical profile of tumor showed experesion CD20+, CD5-, CD23-, CD3-, lack of expression lambda gains.
Conclusions Lypmoma malignum – marginal zone lymphoma may occur like ciliary body and choroidal ring which should be considered in the differential diagnosis of intraocular tumors.

• F085

Immunohistochemical characterization of a retinal hamartoma

VAN GINDERDEUREN R, Stalmans P
UZ St. Rafael, Ophthalmology, Leuven, Belgium

Purpose To describe the immunohistochemical features of a retinal hamartoma.
Methods A 38 y old man was referred for preretinal fibrosis on his right eye. There was loss of vision for more than 8 years with metamorphopsia. The left eye was normal. Oct imaging showed an epiretinal fibrosis with extensive macular oedema. A 27Gauge vitrectomy was performed. The lamina limitans interna (ilm) was peeled after staining with Membrane Blue Dual and sent for histopathology.
Results After removal the epiretinal membrane was immediately fixed with PreservCyt® in a ThinPrep® container. The specimen was routinely processed by the Cellient® embedding system. Microscopy showed a folded Pas positive membrane, recognized as ilm with on one side some glial remnants and on the other side a cuboidal non-pigmented epithelium. The glial remnants stained with glial fibrillar protein (gfap), the epithelium with prekeratin AE1/AE3. CD 34 stain was positive in preretinal capillaries.
Conclusions A strange retinal fibrosis consisted of glial tissue and a row of superficial cuboidal non-pigmented epithelium cells. This kind of hamartoma with immunohistological description was never investigated or published.

• F086

New device to applanate full thickness eyelid tumours for ex vivo confocal microscopy

GRIVET D (1), Cinotti E (2), Perrot J L (2), Labeille B (2), Cambazard F (2), Bernard A (1), Forest F (3), Gain P (1), Thuret G (1)
(1) University Hospital, Ophthalmology department, Saint-Etienne, France
(2) University Hospital, Dermatology department, Saint-Etienne, France
(3) University Hospital, Pathology department, Saint-Etienne, France

Purpose Immediate confirmation of the suspected diagnosis and verification of margin clearances are of crucial importance during surgery of eyelid tumours. In a multidisciplinary approach with Dermatologist, Ophthalmologist and Pathologist to increase treatment efficiency of these patients, we use a combination of handheld Dermatology in vivo confocal microscope to obtain pseudo histology and ex vivo confocal microscopy (EVCM, Lucid, NY) on fresh tissue to better study margins. Tissues are always fixed for standard pathology. In our first uses of the EVCM, tissue thickness and irregularity hinder from obtaining a full map of the tumour because some parts were not in contact with the glass slide. We designed a specific device to applanate the tissue.
Methods The prototype device was composed of a 3D printed plastic slide comprising 2,5 mm diameter tapped holes, and a slider destined to a standard glass slide. Thirty screws allowed precisely adjusting the distance between both plans. The tissue was placed on the glass slide, covered by a thin plastic sheet and by the slide with screws. By gently adjusting individual screws, the tissue could be evenly applanated in front of the EVCM. The pathologist assessed whether the device damaged the tissue
Results Without controlled applanation all tissues were only partially mapped. The applanator allowed obtaining a full map of the tissue in all cases with gentle local adjustments directly controlled by the image quality obtained in live. No significant damage was noted.
Conclusions This simple applanator is useful to improve image quality obtained with the EVCM on full thickness complex tissue like eyelids tumours

• F087

A case report of eyelid basal cell carcinoma with orbital invasion : an alternative to exenteration

JEANCOLAS A L , Maalouf J , Baudot A , Ameloot F , George J L , Angioi K
CHU Brabois, ophthalmology, VANDOEUVRE LES NANCY, France

Purpose Basal cell carcinoma (BCC) is the most common periocular skin cancer affecting eyelids. Lateral canthus location is very rare. The gold standard treatment consists in an extensive surgery which allows the lowest recurrence rate. We report the case of a man suffering of a lateral canthus eyelid BCC with intraorbital invasion and who declined exenteration.
Methods A 78-year old man consulted his ophthalmologist for a painless right ptosis associated with a tumefaction of the external orbital angle. He had neither oculomotor disorders nor decreased visual acuity. He was refered to our clinic 6 months later; we noticed a worsening of the ptosis up to visual axis and an abduction limitation. Visual acuity was steady. Pathological analysis revealed the diagnosis of BCC. Orbital tomography showed a location near the lacrimal gland with posterior invasion along the lateral rectus muscle. Multidisciplinary meeting suggested performing an exenteration. The patient refused this treatment. A conservative surgery was then suggested. The patient has been informed about risks of dissemination.
Results We performed a tumorectomy with large excision including the lateral part of upper and lower eyelids, the tumor itself, the lacrimal gland and the lateral orbital wall adjacent to the tumor. Pathological analysis revealed clear resection margins on all samples.The 4-month control revealed no complications.
Conclusions Exenteration is the gold standard treatment of orbital invasive BCC. In case of lateral canthus lesions, radiotherapy is not recommended because of major risks of orbital recurrences and side effects. Several authors showed that in case of bone-adjacent tumors, bone resection is necessary, because tomography is not specific enough to rule out bone invasion.Despite a complete tumor resection, a long term follow-up is mandatory patients with invasive BCC.

• F088

Reduced retinal nerve fibre layer thickness in multiple sclerosis patients with and without history of optic neuritis

BIRKELDH U (1), Wahlberg-Ramsay M (1), Hietala A (2), Brautaset R (1), Nilsson M (1)
(1) Karolinska Institutet, Clinical Neuroscience, Stockholm, Sweden
(2) Karolinska Institutet, Department of Clinical Neuroscience- Karolinska University Hospital, Solna, Sweden

Purpose Compare the retinal nerve fibre layer (RNFL) thickness in multiple sclerosis (MS) patients, with and without previous episodes of optic neuritis (ON), to disease-free controls, using optical coherence tomography (OCT).
Methods The RNFL was measured with a spectral domain OCT (Canon HS-100) in 433 MS patients and in 70 controls. The MS eyes were sorted into three groups: MS non ON eyes (MSON-), MS ON eyes (MSON+) and the fellow eye of MS ON (MSON_ fellow). One eye of each patient in the MSON-group and in the control group was selected randomly for analysis.
Results Seventy control eyes, 327 MSON- eyes, 106 MSON+ eyes and 106 MSON_ fellow eyes were analysed in a linear regression adjusting for age. The average RNFL thickness was found to be statistically thinner in the MSON- group (88.2±13.0 µm) compared to the controls (98.1±9.0 µm; p < 0.00).The average RNFL was thinner in the MSON+ group (77.3±15.2 µm) compared to MSON- eyes and the controls (p<0.00). A paired t-test showed a significant decrease in RNFL thickness in the MSON+ eyes compared to MSON_fellow.
Conclusions Multiple sclerosis causes RNFL loss. A mean reduction of ~10 µm was found in MS patients without history of ON and a mean reduction of 20 µm was found in MS patients with history of ON compared to healthy controls. This study showed that OCT is a useful tool that provides evidence of neural degeneration in MS patients, with or without the presence of ON.

• F089

Retinal thickness in children with anisohypermetropic amblyopia

TOMO N, Nahoko O
Nara Medical University, Ophthalmology, Kashihara, Japan

Purpose To determine the retinal thickness in eyes of children with anisohypermetropic amblyopia, their fellow eyes, and eyes of age-matched controls. To assess the effects of optical treatment on the foveal thickness in eyes with anisohypermetropic amblyopia.
Materials and Methods Twenty-five patients (6.0 ± 2.2 years, mean ± standard deviation) with anisohypermetropic amblyopia and 25 age-matched controls (5.6 ± 1.9 years) were studied. Spectral-domain optical coherence tomography (SD-OCT) was used. The foveal thickness and the thickness of the outer nuclear (ONL), photoreceptor inner segment (IS) layer, and outer segment (OS) layer were measured by the embedded OCT software.
Results The length of the OS was significantly longer in the fellow eyes (48.2 ± 5.9 µm) than in the amblyopic eyes (42.9 ± 4.6 µm, P = 0.03). One year after the optical treatment of the anisohypermetropia, the best-corrected visual acuity (BCVA) improved and the length of the OS was significantly increased (P=0.0001). After optical treatment there was no more significant difference in the OS length between in the amblyopic eyes and fellow eyes (P=0.94). The change of BCVA was significantly correlated with the change of the length of the OS one year after the treatment. (r=0.54; P=0.0004).
Conclusions We found anisohypermetropic amblyopic eyes had qualitative and quantitative differences in the microstructures of the retinal photoreceptor layers from control eyes. An increase in the OS length was detected in the amblyopic eyes after the optical treatment. There was a significant correlation between the increased OS length and better BCVA.

• F090

Seasonal variation of the pupil light reflex

KOURTI P (1), Münch M (2), Collomb S (1), Kawasaki A (1)
(1) Hôpital ophtalmique Jules Gonin, Neuroophthalmology, Lausanne, Switzerland
(2) Charité University- Medicine, Institute of Physiology, Berlin, Germany

Purpose Variation of retinal light sensitivity between winter and summer seasons may be a marker for seasonal affective disorder and the basis for response to phototherapy. As the pupil is a marker of retinal light sensitivity and shows a 24-hour variation that reflects circadian rhythm, we used the pupil as proxy to assess light sensitivity of rods, cones and melanopsin as a function of seasonal light in healthy adults.
Methods 37 adults were tested during the short (January-February) and long (July-August) annual photoperiods. All subjects completed standardized questionnaires of seasonality and sleep. Pupil responses to blue (470nm) and red (622nm) light were recorded under dark and light adapted conditions using an automated pupillometer. Main outcome parameters were maximal contraction amplitude and post-stimulus contraction amplitude.
Results All but two subjects reported good sleep quality. One subject was an extreme morning type. Twelve subjects reported a global seasonal variation in sleep, mood and appetite but without dysfunction or disability. Baseline pupil size of light adapted eyes was greater in summer compared to winter. Maximal contraction amplitudes to scotopic and photopic light stimuli were greater in summer. The post-stimulus pupil contraction was also greater in summer, but only after light adaptation.
Conclusions Baseline pupil size and pupil responses derived from rods, cones and melanopsin photoreception were greater in summer in healthy adults. This seemingly greater retinal sensitivity to light when the photoperiod (daylength) is long suggests a more central basis for seasonal regulation of the pupil light reflex.

• F091

Evaluation of the retinal nerve fiber layer thickness and its relation to visual evoked potentials in multiple sclerosis

STRUPAITE R (1), Mockeviciute E (2), Kizlaitiene R (3), Budrys V (3), Liveikiene A (1), Mamontovaite G (2), Cimbalas A (1), Asoklis R (1)
(1) Vilnius University, Center of Eye Diseases, Vilnius, Lithuania
(2) Vilnius University, Faculty of Medicine, Vilnius, Lithuania
(3) Vilnius University, Center of Neurology, Vilnius, Lithuania

Purpose To evaluate the retinal nerve fiber layer (RNFL) thickness by optical coherence tomography (OCT) in Lithuanian patients with multiple sclerosis (MS) and to assess the relationship between RNFL thickness and visual evoked potentials (VEP).
Methods From 2013 till 2014 a prospective study involving 71 patients with multiple sclerosis was conducted in Vilnius University Hospital Santariškių Clinic Center of Neuroscience and Eye Diseases. The epidemiological, clinical, laboratory and instrumental data was assessed: gender, age, oligoclonal bands, IgG index in cerebrospinal fluid (CRF), visual evoked potentials (VEP), OCT. RNFL and papilomacular bundel (PMB) thicknesses were performed with SD-OCT.
Results The distribution of gender for patients with MS was as follows: men n = 22 (31%), women n = 49 (69%); average age - 40.7 ± 10.7 years. OCT results were as follows: RNFL average thickness: right eye 85.5 ± 15.6 µm, left eye 86.3 ± 13.2 µm. According to the t-test: the upper nasal (NS) segment averages of right and left eyes differed statistically significant - 6.6 ± 14.7 µm (p <0.05). There was significant negative correlation between VEP P100 latency and RNFL thickness of the right eye TI segment (r=- 0.57; p=0.01) and the left eye PMB segment (r=-0.52; p=0.02). The most damaged segment was the temporal (T) one: right eye 84.5% (n = 60), left eye - 90.1% (n = 64). RNFL of both eyes revealed statistically significant mean differences with the IgG index.
Conclusions The most vulnerable segment of the retina is the temporal. If VEP gets prolonged thinning of RNFL is also observed. The CSF index is increased by immunologically more active multiple sclerosis. We think that more active form of MS may be associated with retinal segments violation. Hence we may conclude that RNFL thinning could be related with irreversible progression of the disease.

• F092

Visual dysfunction and its correlation with retinal changes in patients with Parkinson disease

SATUE M , RODRIGO M J, Mateo A , Otin S , Bambo M P , Fuertes I , Pablo L , Garcia-Martin E
Miguel Servet University Hospital, Ophthalmology, Zaragoza, Spain

Purpose: To evaluate visual dysfunction and its correlation with structural changes in the retina in patients with Parkinson disease (PD).
Methods Patients with PD (n=37) and controls (n=37) underwent visual acuity (VA), color vision (using the Farnsworth and L´Anthony desaturated D15 color tests), and contrast sensitivity vision (CSV; using the Pelli Robson chart and CSV 1000E test) evaluation to measure visual dysfunction. Structural measurements of the retinal nerve fiber layer (RNFL), and macular and ganglion cell layer (GCL) thicknesses were obtained using spectral domain optical coherence tomography (SD-OCT). Comparison of obtained data and correlation analysis between functional and structural results were performed.
Results VA (in all different contrast levels) and all CSV spatial frequencies were significantly worse in PD patients than in controls ($P < 0.05$). Color vision was significantly affected ($p<0.05$) based on the L´Anthony color test. Macular thinning was detected in the central, outer (inferior and temporal), and superior sectors ($p<0.05$), and the RNFL had significant thinning in the temporal quadrant ($p<0.05$). Significant GCL loss was observed in the superior and superonasal sectors and the GCL + minimum inner plexiform layer ($p<0.05$). CSV was the functional parameter most strongly correlated with structural measurements in PD. Color vision was associated with most GCL measurements. Macular thickness was strongly correlated with macular volume and functional parameters ($r >0.70$, $p<0.05$).
Conclusions Patients with PD had visual dysfunction that correlated with structural changes evaluated by SD-OCT. Macular and GCL measurements may be reliable indicators of visual impairment in PD patients.

• F093

Effects of smoking during pregnancy on retinopathy of prematurity

RODRIGO M J, Fernández S , De la Mata G , Ara M , Prieto E , González-Viejo I , Ferrer C , Pueyo V
Hospital Miguel Servet, Oftalmología, zaragoza, Spain

Purpose *Background:* Tobacco smoking during pregnancy is the first preventable cause of adverse birth outcomes such as vascular and neurodevelopment disturbation.
Aims: To asses how smoking during pregnancy would affect retinal vascularization causing retinopathy of prematurity.
Design: An observational cross-sectional study.
Methods *Methods*: Records of preterm newborns (n=293) and tobacco expossure were reviewed. Retinopathy of prematurity (ROP) grading was evaluated in accordance with the International Classification of Retinopathy of Prematurity. Factors were evaluated using a multivariate logistic regression analysis
Results *Results: Although most children did not develop ROP* (74.1%), *1*0.9% has mild, 9.6% severe and 5.5% aggressive posterior retinopathy. Twenty percent of mothers smoked during pregnancy and 10.2% smoked ≥5 cigarettes per day. Children of smoking mothers showed higher rate of Anterior Progressive ROP (6.9%) than those who were not expossed (5.1%), and as much severe as higher number of cigarettes (10.9% vs 5.1%). *However*, these results were not statsically significative ($p>0.05$).
Conclusions *Conclusions: A* tendency to higher severity grades of ROP in connection with heavy tobacco exposure during pregnancy was observed.

• F094

Visual functions in children with congenital myopia and with amblyopia with the same refraction.

BOYCHUK I, Mukhina A
Filatov Institute of Eye, Binocular Vision Disorders, Odessa, Ukraine

Purpose was to compare visual functions in children with amblyopia and with congenital myopia of the same refraction.
Principal causes of decrease in sight at children with congenital myopia is, besides high myopic refractions, this or that degree of undevelopement of the visual analyzer. The diagnosis at the given pathology is complicated, as often complicated congenital myopia and undevelopement of the visual analyzer identify as amblyopia.
Methods . 93 children (186 eyes) at the age from 5 до18 years were observed. Children with myopia of the same age with the same refraction have made group of 36 (72eyes). All ophthalmologic observations including visual acuity without and with correction, refractometry, skyaskopy, in conditions of cycloplegia, definition of reserves of accommodation, echobiometry of visual axies, ophthalmoskopy, biomicroscopy were carried out. Colour thresholds by Rabkin tables, an electrosensitivity threshold by phosphen , critical frequency of disappearance of flashings by phosphen, binocular vision by colour test, stereoacuity by stereograms (Lang's test II) and time of occurrence of stereoeffect were conducted.
Results The comparative analysis has shown, that at amblyopia with myopic refraction visual functions, such as visual acuity with correction, colour vision, stereoacuity are decreased more, than at congenital myopia with the same refraction. It is established, that at children with amblyopia colour vision on all colours is significantly decreased (espacially dark blue colour thresholds 7,5 ± 4,8 in comparison with 3,2 ± 3,3) in the absence of visible changes on an eye fundus
Conclusions Children of both groups had decreased stereovision in the presence of binocular vision. Thresholds of stereovision by Lang's test II (random-dot pictures) were specially high.

• F095

Stereovision in patients with intermittent exotropia before and after surgical treatment

BOYCHUK I, Tarak A
Filatov Institute of Eye, Binocular Vision, Odessa, Ukraine

Purpose To determine the effect of the initial stereovision on the outcome of intermittent exotropia surgical treatment
Methods 20 patients with intermittent exotropia aged 10-21 years with visual acuity with correction 0, 88 ± 0,29 who received surgical treatment were observed. Angle of deviation before surgery was 6-25 degrees, in average 15,7± 1,3 deg. for fare distance and near in average of 8,2 ± 2,18 deg, vertical component 0-3 degrees was observed in 65% of patients who underwent surgical treatment in accordance with generally accepted surgery tactic - recessions and resections of extraocular muscles (Avetisov E. S.,1977, Von Noorden, E. Campos, 2002). Before and after treatment conventional ophthalmic examination and stereoacuity were determined using the Test Lung 2 in all patients.
Results As a result of treatment the angle of exotropia decreased in all patients and was in average 3, 9 ± 1,9 deg for distance and 3,5 ± 1,4 deg for near, binocular vision was restored in 70% (14)of patients. Before treatment, only in 25% (5) of patients showed stereoacuity for near (200 - 600 arc sec) and 75% (11) did not show stereovision. After treatment, the stereoacuity for near increased and was detected in 65% of cases (13), compared to 5 that were before treatment ($\chi 2 = 6,4$, $p=0,01$). Alignment of eyes and best stereoacuity (200-400 arc sec) was found after treatment and appeared in individuals who showed stereoacuity for near 200 arc sec before surgery and the nearest point of convergence less than 6cm.
Conclusions Preliminary data suggest that in patients with intermittent form of exophoria good stereoacuity for near is a favorable factor for the prediction of treatment. In patients with orthotropic position of eyes stereoacuity after surgical treatment increased in 65% of cases.

• F096

Quantitative assessment of fixational saccades in school children. A new method.

LARSEN D A , Bek T
Aarhus University Hospital, Ophthalmology, Århus C, Denmark

Purpose To develop and validate a technique for automatic analysis of fixational saccades in clincal practise, and to study age-related changes in these parameters among normal children.
Methods Thirty-six normal children (19 boys and 17 girls, mean age = 9.8 years, range 5-16 years) were examined. Eye movements were recorded during two repeated 30-s fixation tasks from left eye with a video based eye-tracking system (iView XTM High-Speed, version 2.7.09 Senso Motoric Instruments, Berlin, Germany). Type). A special software programme was developed for the detection and quantification of fixational saccades including information about the length velocity and back shoot of the movements. The number of saccades within a 0.05-degree amplitude intervals were plotted as a function of the amplitude and the plots were fitted to a biexponential function. The amplitude and number defining the maximum of this saccade distribution curve as well as the area under the curve (AUC) were calculated.
Results The total number of saccades per examination was 115.5±71.3 (mean±SD), range 14-276, which amounted to a total of 8315 saccades during the duplicate recordings from all 36 children. There was no correlation between age and the number of saccades per second (r2=0.07, p=0.11), the number and amplitude of saccades at the maximum of the saccade distribution curve (r2=0.0002, p=0.93) and (r2=0.002, p=0.79), respectively, and the AUC (r2=0.09, p=0.08).
Conclusions The technique allows computerized quantification of small fixational eye movements and the extraction of measures of fixation in children that are independent of age. Studies of visual development using these parameters in children will not need a correction for age.

• F097

Comparison of effective group and refractory group to alternative patch treatment in overcorrected intermittent exotropia

LEE S J (1), Kim J Y (1), Park J M (2)
(1) Haeundae Paik Hospital - Inje University College of Medicine, Department of Ophthalmology, Busan, South-Korea
(2) Maryknoll Hospital, Department of Ophthalmology, Busan, South-Korea

Purpose To compare effective group with refractory group to alternative patching alone in patients with overcorrection after surgery for intermittent exotropia(IXT) .
Methods Medical records of 53 patients with overcorrection after surgery for IXT were reviewed. Alternative patching was prescribed from postoperative day 1 for patients who had esodeviation ≥ 18 PD, or esodeviation ≥ 10 PD after postoperative day 2 weeks. Refractory group was defined as remaining esodeviation ≥ 10 PD at least 3 months of treatment. Presumed risk factors were investigated.
Results Of total 53 patients, 30 patients (56.6%) were in effective group and 23 patients (43.4%) were in refractory group. Significant differences were found in gender (Female, Refractory 78.3% vs Effective 46.7%) and preoperative exodeviation at distance (Refractory 27.6±6.5PD vs Effective 25.8±4.5PD). Mean starting time of alternative patching in refractory group was later (22.4±25.4 days) than in effective group (10.2±9.6 days). The mean angle of postoperative maximal esodeviation at near was larger in refractory group (-20.0±6.9PD vs -14.7±8.5PD). The mean time of postoperative maximal esodeviation was later in refractory group than in effective group (at distance: 2.3±2.1 months vs 0.3±0.2 months, P<0.01, at near: 3.4±4.1 months vs 0.4±0.3 months.
Conclusions Female, large preoperative exodeviation at distance were predisposing factors for refractory to alternative patch treatment in overcorrected IXT. Prescription of alternative patching was late in refractory group. The mean angle of postoperative maximal esodeviation was larger and the mean time of postoperative maximal esodeviation was later in refractory group. Postoperative changes in angle of deviation was significantly larger in refractory group since 1 month.

• F098

Ptosis and diplopia after incidental botulinum powder exposure

CHO M
Kim's eye hospital, Ophthalmology, Seoul, South-Korea

Purpose To report the occurrence of an unilateral ptosis and diplopia not direct injection of botulinum but incidental botulinum power exposure.
Methods This is a case report of botulinum powder's local effect
Results Thirty years old woman visited our hospital due to ptosis and diplopia. She did botulinum powder purification at her laboratory and incidentally botulinum power was spattered to her right eye. Two days later, right lid ptosis was developed and the next day, diplopia was occurred. She also showed right eye pupil dilatation and hypotropia. She was taken brain MRI and we couldn't find pathologic lesion. One month later, the diplopia was disappeared and ptosis was much improved.
Conclusions In addition to direct periocular injection, only botulinum power exposure can also make local effect, such as ptosis, muscle paresis, pupil dilatation.

• F099

Consecutive esotropia in contralateral recess-resect for recurrent intermittent exotropia after unilateral recess-resect

CHO S Y (1), Lee S Y (2)
(1) Dongguk University, Ophthalmology, Gyeongju, South-Korea
(2) Keimyung University Dongsan Medical Center, Ophthalmology, Daegu, South-Korea

Purpose To report consecutive esotropia in contralateral recess-resect for recurrent intermittent exotropia after unilateral recess-resect. To evaluate the surgical outcome of 'modified contralateral recess-resect' for intermittent exotropia after unilateral recess-resect.
Methods 36 subjects were included in this retrospective study. All underwent, as a primary surgery for intermittent exotropia, unilateral recess-resect on the non-dominant eye. They were assigned to the subsequent contralateral recess-resect(CRR, n=19, surgical dosages based on Wright's surgical table) or modified contralateral recess-resect (MRR, n=17, surgical dosages 5Δ reduced on Wright's surgical table) for recurrent exotropia. Surgical success rate was evaluated. Re-operation rate or prism glasses prescription rate due to consecutive esotropia was evaluated.
Results The mean follow-up duration after the reoperation was 25.8 months in CRR group and 24.0 months in MRR group. Surgical success rate was 47.4% in CRR group and 76.5% in MRR group (p=0.078). Recurrence rate was 0% in CRR group and 17.6% in MRR group (p=0.059). Re-operation rate or prism glasses prescription rate due to consecutive esotropia was 52.6% in CRR group and 5.9% in MRR group (p= 0.003).
Conclusions Final outcomes were better in MRR group than in CRR group. Consecutive esotropia was significantly more frequent in CRR group than in MRR group. To reduce consecutive esotropia in surgery for recurrent exotropia, MRR is recommended.

• F100

Ophthalmic insert for pupillary mydriasis in neonates

BREMOND-GIGNAC D (1,2), Jacqz-Aigrain E (3), Abdoul H (3), Beresniak A (4), Baud O (3), Alberti C (3)
(1) APHP- Hôpital Universitaire Necker Enfants Malades, Pediatric Ophthalmology, Paris, France
(2) CNRS Unit FR3636, Binocular vision, Paris V University, France
(3) APHP- Hôpital Universitaire Robert Debre, 75019, Paris, France
(4) Data Mining International, Geneva, Geneva, Switzerland

Purpose To study efficacy and tolerance of ophthalmic insert Mydriasert® versus standard treatment phenylephrine and tropicamide eye drops for fundus examination in neonates.
Methods Prospective, randomised, single-blinded non-inferiority study of 80 premature and full-term babies and infants treated for fundus examination. Mydriasis was obtained with two groups randomly assigned. The eye drop group received three instillations of 2.5% phenylephrine and 0.5% tropicamide and the insert group received Mydriasert® containing phenylephrine and tropicamide. the mydriasis was evaluated 75 minutes after the introduction of the mydriatic agents.
Results The mydriasis was successfully achieved in both eyes in 97.5% of infants in the insert group and 90% in the eye drop group at 75 minutes after dispensation. The efficacy of the insert was non-inferior compared to the eye drops. To reach effective mydriasis, the insert group required fewer nursing interventions for one patient comparing to the eye drop group. Good general and local tolerance was observed in the two groups. However two patients reported an adverse event as bradycardia and gastro-oesophageal reflux that could be related to neonate pathology.
Conclusions Mydriasis obtained with the ophthalmic insert Mydriasert® was not inferior compared to standard eye drop treatment. Insert reduced the number of nursing interventions to obtain mydriasis for a fundus examination.

• F101

Comparison of long-term surgical outcomes of 2-muscle surgery in intermittent exotropia: Bilateral vs Unilateral

CHO S Y (1), Lee S Y (2), Bang S P (2), Lee Y C (3)
(1) Dongguk University, Ophthalmology, Gyeongju, South-Korea
(2) Keimyung University Dongsan Medical Center, Ophthalmology, Daegu, South-Korea
(3) Uijeongbu St. Mary's Hospital, Ophthalmology, Uijeongbu, South-Korea

Purpose To compare long-term surgical outcomes after bilateral lateral rectus recession (BLR) and unilateral lateral rectus recession-medial rectus resection (RR) for the treatment of intermittent exotropia.
Methods Consecutive patients who underwent BLR or RR for treatment of intermittent exotropia between 1999 and 2010 and had ≥5 years' follow-up were recruited. Surgical outcomes were grouped according to postoperative angle of deviation as overcorrection (esophoria/tropia>5Δ), success (esophoria/tropia≤5Δ to exophoria/tropia≤10Δ), or undercorrection/recurrence (exophoria/tropia>10Δ), and were compared between the BLR group and the RR group at postoperative 1 week, 1 month, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years, and at the final examination.
Results Of 99 patients, 37 underwent BLR and 62 underwent RR. The mean follow-up period was 99.6 months in the BLR group and 96.2 months in the RR group. At 1 week, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years and at the final examination the surgical outcomes in each group were not different (p>0.05). The surgical success rate was 44.6 % in the BLR group and 45.0% in the RR group (p=0.27). The re-operation rate was 29.7% in the BLR group and 40.3% in the RR group (p=0.67).
Conclusions Surgical outcomes by 5 years after surgery for intermittent exotropia were comparable between the BLR and RR groups. The surgical success rate and the re-operation rate were not different between the BLR and RR groups.

• F102

Diplopia as presenting sign of Turcot syndrome

NINCLAUS V (1), Walreadt S (1), Baert E (2), Laureys G (3), De Zaeytijd J (1)
(1) Ghent University Hospital, Department of Ophthalmology, Ghent, Belgium
(2) Ghent University Hospital, Department of Neurosurgery, Ghent, Belgium
(3) Ghent University Hospital, Department of Pediatric Hematology and Oncology, Ghent, Belgium

Purpose To describe a patient with diplopia who was diagnosed with Turcot syndrome
Methods A 10-year old boy presented with a history of left-sided sixth and seventh nerve palsy. He underwent imaging of the brain and colon, full ophthalmologic and genetic work-up.
Results A 10-year old boy was referred with combined left-sided sixth and seventh nerve palsy since one month without symptoms of raised intracranial pressure. BCVA was 6/6 in both eyes. Fundoscopy revealed bilateral, multiple, oval pigmented ocular fundus lesions (POFLs) in the 4 quadrants. These POFLs, together with the cranial nerve palsies raised the suspicion of Turcot syndrome, a familial neoplasia syndrome characterised by familial adenomatous polyposis and tumours of the central nervous system. Urgent MRI scan of the brain and stereotactic biopsy showed a primitive neuroectodermal tumour (PNET) at the pons. Coloscopy revealed multiple polyps. DNA analysis of the APC gene confirmed the clinical diagnosis of Turcot syndrome. The PNET was treated with combined radio- and chemotherapy. The patient underwent a prophylactic total colectomy as virtually all patients develop a carcinoma of the colorecal region if left untreated.
Conclusions Diplopia in childhood is rare and seldom innocuous. It requires a prompt and thorough diagnostic evaluation. The presence of POFLs should alert the clinician to the possiblility of Turcot syndrome. Recognition of this rare syndrome can lead to earlier diagnosis, which is vital to appropriate surveillance and early surgical intervention of the highly frequent neoplasias in Turcot Sydrome.

• F103

Double depressor palsy after bilateral paramedian thalamus infarction

KIM S J (1), Lee S (2)
(1) Maryknoll medical center, ophthalmology, BUSAN, South-Korea
(2) Kosin University College of Medicine, Ophthalmology, BUSAN, South-Korea

Purpose We report a rare case of double depressor palsy after bilateral paramedian thalamus infarction.
Methods Case : A 47-year-old male presented with complaints of diplopia upon awakening. He had atrial fibrillation, mitral valve regurgitation, aortic valve regurgitation and a history of spleen infarction 1 year prior. His right eye was hypertrophic and right eye downgaze was limited unilaterally of equal degree in adduction and abduction. Right eye horizontal and upward movements were intact. Left eye movement was intact in all directions. Pupillary light reflex response and convergence test were normal. Nystagmus was not observed.
Results The patient was diagnosed with double depressor palsy of the right eye. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the brain showed an old infarction of the left thalamus and diffusion MRI showed acute infarction of the right thalamus. The patient's daily warfarin dose was 2 mg and was increased to 5 mg with cilostazol 75 mg two times a day. Seven weeks later, the patient's ocular movement revealed near normal muscle action and, subjectively, the patient was diplopia-free.
Conclusions The patient presented with bilateral thalamic lesions and was diagnosed double depressor palsy. The paramedian territory is supplied by the paramedian (or thalamoperforating) arteries which arise from the P1 segment of the PCA. The paramedian arteries often supply the rostral midbrain. Thus, bilateral thalamic infarctions can be presented with or without rostral midbrain lesions. The bilateral lesions of rostal midbrain including riMLF can cause double depressor palsy. However, the lesions of bilateral riMLF infarction were too small to be seen in imaging study. So there was no obvious lesion over the rostral midbrain. Otherwise, there may be another unknown vertical movement mechanism.

• F104

Correlation between peripapillary retinal thickness and serum level of vascular endothelial growth factor in patients with POEMS syndrome

YOKOUCHI H, Baba T, Oshitari T, Yamamoto S
Graduate School of Medicine- Chiba University, Ophthalmology and Visual Science, Chiba, Japan

Purpose To determine whether there is a significant correlation between the peripapillary retinal thickness (pRT) and the serum level of vascular endothelial growth factor (VEGF) in patients with polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome.
Methods This was a cross sectional, observational case series. We studied 34 eyes of 17 treatment-naïve patients with POEMS syndrome whose intracranial pressure (ICP) was within the normal range. The spectral-domain optical coherence tomographic (SD-OCT) examinations consisted of circle scans around the optic disc (3.45 mm in diameter). The pRT was automatically measured in the SD-OCT images, and the average pRT was used for the statistical analysis. The serum level of VEGF was measured by Enzyme-linked immunosorbent assays (ELISAs), and the correlation between the pRT and the serum level of VEGF was determined.
Results The mean serum level of VEGF in all POEMS patients was 6085 ± 3332 pg/ml with a range of 1380 to 12000 pg/ml. The correlation between the pRT and the serum level of VEGF was significant (right eye, r=0.85, P<0.0001; left eye, r=0.65, P=0.004, Spearman's rank-correlation coefficient), and there was a strong positive correlation between the pRT of the right eyes and left eyes (r = 0.83, P <0.0001, Spearman's rank-correlation coefficient).
Conclusions The significant correlation between the pRT and the serum level of VEGF suggests that the higher serum level of VEGF might be associated with the development of the optic disc edema in patients with POEMS syndrome.

• F105

Late ocular changes after closantel (Flukiver) poisoning

ASOKLIS R, Augyte A , Cimbalas A
Vilnius University, Centre of Eye diseases, Vilnius, Lithuania

Purpose To describe late ocular changes in 5 women after harmful use of donated closantel (Flukiver).
Methods The study included 5 women from the report published by Hoen and Hodgkin in The Lancet journal in 1993 about 11 cases of donated veterinary drug closantel use in Lithuania. We analysed medical records from 1993 to 2015 and performed eye examination of 5 suffered patients 22 years after the event.The study was conducted at the Centre of Eye Diseases,Vilnius University Hospital Santariškių Klinikos,it adhered to the tenets of the Declaration of Helsinki.Eye examination included best corrected visual acuity (BCVA), perimetry, colour vision(CV), tonometry, slit lamp evaluation, fundus photography and optical coherent tomography.
Results In 2015 the mean age of the patients was 49.4 years In 1993 BCVA varied from 0.08 to 1.0.Right eye (RE)in average- 0.66,left eye(LE) – 0.68. In 2015 BCVA varied from 0.1 to 1.0.RE in average – 0.7 and LE – 0.6.22 years after the event average visual field defect in the right eye was 24.13 dB and in the left eye - 23.85 dB.CV Ishihara test showed decreased green color perception in 3 patients and 2 were not able to perform it, because of the visual field defects.The average central macular thickness 216.0 ± 36.1µm in RE and 196.0 ± 42.0µm in LE, retinal nerve fiber layer respectively 86.0 ± 11.0 µm and 93.2 ± 5.4 µm. Ophthalmoscopy showed atrophy of the optic nerve and changes of the retina reminding those in retinitis pigmentosa.
Conclusions Closantel is veterinary drug causing decades lasting damage of the optic nerve and retina in humans. Visual functions don't correlate with central macular and retinal fiber layer thickness.Fundus photography and perimetry reveal changes similar to retinitis pigmentosa. To our knowledge this is the first report about the late outcomes of closantel toxicity in humans.

• F106

Sarcoidosis of orbita and central nervous system presenting as a non-arteritic ischemic optic neuropathy.

DE BRUYN D (1), Ninclaus V (1), Leroy B P (1,2,3), De Schryver I (1), De Zaeytijd J (1)
(1) Ghent University Hospital & Ghent University, Ophthalmology, Ghent, Belgium
(2) The Children's Hospital of Philadelphia, Ophthalmology & Ctr for Cell. & Molec. Therapeutics, Philadelphia- PA, United States
(3) Ghent University Hospital & Ghent University, Ctr for Medical Genetics, Ghent, Belgium

Purpose To describe a patient who presented with non-arteritic ischemic optic neuropathy (NA-AION) as an initial manifestation of neurosarcoidosis.
Methods A case of a 70-year-old woman who presented with loss of vision in the left eye and normal neuroimaging, was initially diagnosed as a NA-AION. An extensive workup included MRI orbita and PET/CT scan.
Results At the initial presentation, the left eye showed loss of vision and papilloedema. Further ophthalmological examination was normal, as was a CT scan of the brain. A diagnosis of NA-AION was entertained. After 4 months, she had no light perception vision. Fundoscopy of the LE showed papilloedema with retinal infiltrates and severe ischaemia. MRI of the brain showed mass infiltration of the intraorbital and the intracranial optic nerve up to the optic chiasm. A complete systemic workup revealed a monoclonal gammopathy with cervical and hilar lymph nodes noted on PET/CT scan. Mediastinoscopy with biopsy of the hilar lymph nodes demonstrated a non-caseating granulomatous lesion and a diagnosis of sarcoidosis was confirmed.
Conclusions Sarcoidosis is a multisystemic disease characterized by granulomatous inflammation. Ocular involvement is seen in approximately 25% of patients with sarcoidosis. Uveitis is the most common ocular manifestation. Orbital and CNS manifestations of sarcoidosis are uncommon. Involvement of the optic nerve, chiasm and visual tract only represent 1-5% of neurosarcoidosis cases. In the latter, sarcoidosis can be initially misdiagnosed as NA-AION, before involvement of the orbit and the CNS. Systemic involvement should be ruled out in any case of AION with an atypical evolution.

• F107

Optic disc drusen with subretinal hemorrhage

HALFELD FURTADO DE MENDONCA R (1), De Oliveira Maia JR. O (2)
(1) Studio Oftalmologico Halfeld, Ophthalmology, Rome, Italy
(2) Monte Tabor Foundation. São Rafael Hospital, Ophthalmology, Salvador BA, Brazil

Purpose To report a rare and interesting case of optic disc drusen with subretinal hemorrhage
Setting: The hemorrhagic complications of the optic disk drusen are rare and interesting.
Methods A 25 year old white man complained of an acute blurred vision in his left eye over the past 6 days. Visual acuity in the right eye was 20/20 and in the left eye 20/200. He had photoreactive and anisocoric pupils (left>right). Fundus examination in both eyes showed an elevated optic nerve head with blurred and irregular disc margins. In the left eye was present a subretinal hemorrhage.
Results The neurological examination and brain computed tomography were normal. Fluorescein angiography (FA) of the left eye showed hypofluorescence (blocked) due to subretinal hemorrhage. No fundus autofluorescence was detected. Indocyanine green angiography was performed to exclude a neovascular choroidal membrane. Goldmann visual field exam showed in the right eye enlargement of the blind spot and paracentral scotoma and in the left eye a small constriction of the isopters and central scotoma. Ocular ultrasound demonstrates an echogenic focus within the optic nerve head. No treatment was performed. Spontaneous resolution of the subretinal hemorrhage was observed. At 3-months follow-up the visual acuity of the right eye was 20/20 and left eye 20/25.
Conclusions Optic disc drusen may be associated with subretinal hemorrhage as a result of direct mechanical compression and rupture of subretinal vessels at the optic disc. Optic disc drusen often mimic papilledema and must be distinguished from true papilledema. The subretinal hemorrhage can resolve spontaneously.

• F108

Clinical experience with Idebenone (Raxone®) in the treatment of patients with Leber's Hereditary Optic Neuropathy (LHON)

METZ G (2), Klopstock T (1), Gallenmüller C (1), Catarino C (1), Von Livonius B (3), Lob F (3), Meier T (2)
(1) Ludwig-Maximilians-University, Friedrich-Baur-Institute, Munich, Germany
(2) Santhera Pharmaceutcials Switzerland Ltd, Development, Liestal, Switzerland
(3) Ludwig-Maximilians-University, Department of Ophthalmology, Munich, Germany

Purpose LHON is an orphan mitochondrial disorder affecting the retinal ganglion cells leading to permanent blindness from which recovery is rare. An increasing body of evidence indicates that idebenone has therapeutic potential for the treatment of LHON. Data from a randomized placebo-controlled study (RHODOS), from a number of case reports and retrospective cohort studies demonstrate that patients with established vision loss may benefit from idebenone treatment and recover visual acuity (VA).
This study reports VA outcomes for patients with recent onset of vision loss who received idebenone treatment under an ongoing global Expanded Access Program (EAP) where currently 82 patients are enrolled and have been treated for an average of 15 months. The outcomes will be compared with findings of the RHODOS study and a Case Record Survey collecting VA data from untreated patients.
Methods Analyses are performed to assess recovery from the VA nadir. Clinically relevant recovery was defined as (i) improvement from nadir by at least 10 letters on the ETDRS chart or (ii) improvement from "off-chart" at nadir to being able to read at least 5 letters on-chart. Furthermore, the prevention of vision loss for patients with residual vision below 1.0 logMAR (20/200) at start of therapy was analysed.
Results A high proportion of patients (about 50% at submission of the abstract) treated with idebenone under this global EAP experienced a clinically meaningful recovery of vision. In addition, in patients with residual vision below 1.0 logMAR at start of therapy, loss of VA to above this level could be prevented in a large number of patients (about 60% at submission of the abstract).
Conclusions The therapeutic potential of idebenone in the treatment of LHON is further demonstrated by the clinical experience in a large cohort of patients under a global EAP.

Commercial interest

• F109

Nonarteritic anterior ischemic optic neuropathy (NAION): A misnomer. A non-ischemic papillopathy caused by vitreous separation

PARSA C (1), Hoyt W (2)
(1) Quinze-Vingts National Eye Hospital / UPMC-Sorbonne Universités, Ophthalmology, Paris, France
(2) UCSF School of Medicine, Ophthalmology, San Francisco, United States

Purpose Vascular abnormalities such as disc hemorrhages and swelling present at the time of visual loss in NAION, followed by peripapillary vascular narrowing and ensuing disc pallor is enticing, but not etiologically conclusive for ischemia. Optic disc as well as retinal findings of whiteness with disc swelling is indicative of axoplasmic stasis that may also occur simply from anatomic distortion of axons rather than occlusion of vessels. It may also occur from mechanical stretching with fracture of the axonal cytoskeleton.
Methods Review of the literature regarding 1) vitreous attachments and effects of separation from the optic disc, 2) dynamic shear force stretch injury to axons.
Results Within the normal population and in the age-goup in which NAION occurs, 10% have complete PVD, 70% partial PVD, and 20% no PVD. In those with acute NAION, however, either total vitreous separation from the disc, or complete parapapillary detachment, is always present. Any teleangectatic vessels on the disc surface correspond to areas of visual field sparing and encompass areas of unseparated vitreous still under tension.
Conclusions Where internal limiting membrane is absent over the disc and peripapillary retina, most notably in cupless discs where epipapillary membrane adhesions are strongest, vitreous separation may momentarily stretch and elongate axons, breaking the cytoskeleton in more aged and less distensible axons, leading to immediate axoplasmic accumulation and atrophy in the prelaminar sites of separation. Vitreous synchysis occurs more precociously in diabetics. Ischemic pathophysiology need not be invoked in so-called NAION, better termed papillary vitreous detachment, or *PVD-N*. In those at risk, the timely and controlled release of vitreous connections to the optic disc may prevent such optic disc injury.

• F110

Optic disc swelling : Prospective study of sixty-seven patients

SITBON C , Fel A , Bodaghi B , Le Hoang P , Touitou V
La Pitié Salpétrière, Ophthalmology- DHU Vision et Handicaps, Paris, France

Purpose To assess the clinical features and etiologic work-up of patients presenting with optic disc swelling (ODS) in the emergency room.
Methods Patients seen in the ophthalmology emergency department of a single tertiary center between november 2014 and october 2015 were prospectively included. Each patient underwent an etiologic work-up including a brain-MRI, blood work, fluorescein angiography, and visual evoked potential.
Results 67 patients (39 female and 28 male) were included in this study. Average age was 46 years (17-86 years). ODS was unilateral in 45% of cases and bilateral in 55% of cases. The average time between the onset of symptoms and diagnosis of papillary edema was 80 days (3 days to 8 months). The mean initial visual acuity was 0.2 logMAR, and the mean final VA was 0.1 logMAR. Final diagnosis was intracranial idiopathic hypertension (43%), anterior ischemic optic neuropathy (25%), inflammatory or infectious papillitis (22%), compressive optic neuropathy (2%) and unknown in 3 cases (8%). The etiologic work-up was contributive for the final diagnosis in 10% of cases for fluorescein angiography; 35% for MRI of the optical nerve; 32% for laboratory tests; 67% for visual evoked potentials; 90% for the visual field of Goldman. Findings of Goldman's visual field included central or caecocentral scotoma (32%), exclusion or enlarged blind spot (41%), inferior altitudinal scotoma (19%), and bitemporal quadrantanopia (5 %).
Conclusions Our results demonstrate that causes of ODS could be identified in 92% of patients presenting with ODS. According to the clinical features at presentation, the etiologic work-up can be further adjusted but a standard minimal etiologic work-up is usually efficient to state the diagnosis.

• F111

The Damato Multifixation Campimetry Online (DMCO) - A possible visual field test to detect neurological visual field defects

STEENSBERG A T (1), Olsen A S (2), Pinborg L H (3), Kolko M (1,4)
(1) Panum Institute, Department of Neuroscience and Pharmacology, Copenhagen N, Denmark
(2) Rigshospitalet - Glostrup Copenhagen University Hospital, Department of Ophthalmology, Copenhagen, Denmark
(3) Rigshospitalet, Neurobiology Research Unit, Copenhagen, Denmark
(4) Roskilde University Hospital, Department of Ophthalmology, Roskilde, Denmark

Purpose The aim of the present study is to determine the ability of DMCO to detect visual field (VF) loss after epilepsy surgery and to determine the risk of visual field defects related to the operation.
Methods Sixty patients will be tested by DMCO and Humphrey VF Analyzer (HFA). The patients will get a full eye examination to exclude eye diseases. A questionnaire will determine the subjective claims from the patients.
Results 16 DT Standard tests have been performed on ten eyes. HFA found that two patients had an almost complete quadrant anopsia, two had a smaller degree of quadrant anopsia, and one had no VF loss. DMCO detected the VF defect in the two patients with almost complete quadrant anopsia and not in the patients with the smaller VF loss. None of the patients perceived their VF loss before the test.
Conclusions The preliminary results indicate an eighty percent risk of VF loss after epilepsy surgery. Our study indicates that DMCO may be a useful tool to detect neurological unrecognized VF losses.

• F112

Homonymous hemimacular thinning in retrochiasmal lesions

CUNHA J P , Proença R , Dias-Santos A , Vicente A , Anjos R , Costa L , Cardigos J , Ferreira J , Amado D

Centro Hospitalar de Lisboa Central, Oftalmologia, Lisboa, Portugal

Purpose To evaluate the thickness of macular retina and determine which retinal layers are most affected by retrochiasmal visual pathways lesions.

Methods mean retinal thickness utilizing automated intraretinal layer segmentation of spectral domain optical coherence tomography scans was performed in 40 eyes of 40 patients with retrochiasmal visual pathways lesions and compared with 60 eyes of control subjects. Multiple linear regression analysis was used to determine the relationship between retinal thickness and follow-up, age and gender.

Results Ganglion cell and inner plexiform layer was thinner in the temporal hemiretina ipsilateral and in the nasal hemiretina contralateral than in healthy controls. The mean thickness was significantly reduced in lesions over 6 months of duration, with no differences in correlations with age or gender.

Conclusions This study demonstrate ganglion cell and inner plexiform thinning in the hemimacular area. These results support the concept that transneuronal retrograde degeneration of the retinal ganglion cells can be detected by OCT in humans with retrochiasmal visual pathways lesions.

This homonymous hemimacular thinning in OCT represents an imaging biomarker that can be of valu in diagnosis, prognosis and clinical trials of neuroprotectives therapies.

• S001

Posterior vitreous detachment: more a case of the fibronectin interface than the inner limiting membrane?

ETIENNE I, Jonckx B , Feyen J
ThromboGenics NV, R&D, LEUVEN, Belgium

Purpose Use the periodic acid shift and immunohistochemical staining to visualize the distribution of the inner limiting membrane components on eyes presenting **P**osterior **V**itreal **D**etachment (**PVD)** as detected by **O**ptical **C**oherence **T**omography (**OCT**)
Methods Porcine eyes with PVD confirmed by OCT were processed into paraffin tissue blocks. Transverse, serial 15 mm thick sections were cut. After deparaffinization and antigen retrieval stages, slides were incubated with selected primary antibodies. Amplification stages were performed before fluorescence visualization of the specified marker. Among the markers stained were collagen II and IV, laminin beta 2 and fibronectin. Periodic acid shift staining was also performed on adjacent cross sections to assess potential structural change (PVD). Images were acquired on a Zeiss microscope and image analysis performed using Metamorph software (Leica).
Results Different distribution patterns in the retina were observed for the selected markers. The inner retina blood vessels were labelled by laminin beta 2, collagen II and IV. Laminin beta 2 and collagen II was revealed on the Bruch membrane. Collagen II, IV, fibronectin and laminin beta 2 were detected at the inner limiting membrane. PVD area could be detected not only by periodic acid shift but also by fibronectin staining. Upon PVD, fibronectin staining completely migrated with the PVD front, cleanly detaching from the retinal cell layers.
Conclusions Fibronectin staining can be used to detect and therefore confirm PVD presence in histological sections, even if the PVD has evolved beyond the point where it can still be detected by OCT.

• S002

Improvement in retinal vessel oxygen saturation after vitrectomy

LIM S L (1), Tan L (2), Perera S (3)
(1) Singapore National Eye Centre, Vitreoretina, Singapore, Singapore
(2) Singapore National Eye Centre, Training and Education, Singapore, Singapore
(3) Singapore National Eye Centre, Glaucoma, Singapore, Singapore

Purpose To evaluate the effects of vitrectomy on retinal vascular oxygen saturation.
Methods This was a prospective observational study. 27 eyes of 27 patients who underwent vitrectomy for macular conditions were included. Retinal oximetry was performed using the Oxymap (Oxymap Inc., Reykjavik, Iceland) prior to vitrectomy and 3 months after surgery. The mean retinal arterial and venous oxygen saturation were measured and the arterial-venous difference (AVD) was calculated as the difference between the arterial and venous saturations.

Multivariate linear regression models were constructed to compare oxygen saturation before and after surgery, with adjustments for age, sex, hypertension, hyperlipidemia, diabetes mellitus and indication for surgery.
Results The mean age of the subjects was 68.4±8.9 years, 15 (55%) were male and the majority were of Chinese ethnicity (93%). The mean arterial saturation increased significantly after vitrectomy (101.93 ± 8.36% vs 96.16 ± 14.14%, p = 0.01). The mean venous saturation also increased significantly after surgery. (59.76 ± 8.52% vs 50.40 ± 11.72%, p = 0.02). The mean AVD significantly decreased from 45.76 ± 12.18% before surgery to 42.17 ± 10.94% after surgery (p= 0.02).
Conclusions Retinal arterial and venous oxygen saturation are significantly increased after vitrectomy, while the AVD is decreased after vitrectomy. Our results suggest that vitrectomy enhances retinal oxygenation. This may account for the apparent benefit of vitrectomy on conditions with retinal hypoxia such as diabetic retinopathy.

• S003

Imaging of intravitreal injected solution dispersion.

WILLEKENS K (1), Reyns G (2), Jonckx B (2), Feyen J (2), Yewei L (3), Coudyzer W (3), Yicheng N (3), Stalmans P (1)
(1) UZ Leuven, Ophthalmology, Leuven, Belgium
(2) Thrombogenics, Research and development, Leuven, Belgium
(3) UZ Leuven, Radiology, Leuven, Belgium

Purpose
The extent of activity of an intravitreal injected drug is linked to its dispersion within the vitreous body. Researchers have been trying to visualize dispersion of intravitreal injected solutions using Indian ink or fluorescein, either with subsequent dissection or with endoillumination, both invasive methods that could influence the dispersion pattern. Therefore, this pilot study aims at investigating and identifying the best minimal invasive imaging method for visualizing the dispersion of an intravitreal injected solution.
Methods To determine the optimal imaging concentration, a series of 5 enucleated porcine eyes were injected with 0.1cc of 100%, 50%, 25%, 20% and 10% standard iodium contrast medium, respectively. Injections were made using a standard 1cc syringe and 30 gauge needle at 3.5mm from the limbus aiming at the center of the globe. Subsequently, the dispersion of the contrast agent was monitored using high resolution imaging methods: mammography and ultra high resolution computed tomography (UHRCT). For the latter, 3D reconstructions were rendered.
Results A 1:10 dilution mixture combined optimal visualization contrast with low viscosity of the injection solution using radiographic ultrahigh resolution mammography. Both mammography and UHRCT images were taken from two eyes; one with a slow injection, the other with a fast injection.
Conclusions 3D reconstructed UHRCT images were favored over 2D mammography images for dynamic imaging of the intravitreal solution dispersion.

• S004

23-Gauge versus 25-Gauge vitrectomy for proliferative diabetic retinopathy: A comparison of surgical outcomes

MAGILL H (1), Guthrie G (2), Steel D (3)
(1) Watford General Hospital, Ophthalmology, London, United Kingdom
(2) Chelsea and Westminster Hospital, Ophthalmology, London, United Kingdom
(3) Sunderland Eye Infirmary, Ophthalmology, Sunderland, United Kingdom

Purpose This study compared clinical outcomes and complications between 23-gauge (23g) and 25-gauge (25g) transconjunctival sutureless vitrectomy in patients with proliferative diabetic retinopathy.
Methods It was a retrospective study using data prospectively defined and collected. 80 eyes underwent 23g transconjunctival sutureless vitrectomy, and 80 eyes underwent 25g surgery using the same vitrectomy system by one surgeon. Primary outcome measures were best-corrected visual acuity, intraocular pressure (IOP), and incidence of intraoperative and postoperative complications.
Results Vision was significantly improved after intervention in both groups ($p \geq 0.0001$). There was no significant difference in visual outcomes between the groups ($p = 0.43$) or in the type and frequency of retinal breaks occurring during surgery ($p = 0.63$). The 23g group had significantly more patients with a day 1 IOP of <6 mm Hg ($p = 0.034$) and significantly more patients requiring a sclerostomy suture postoperatively ($p = 0.014$).
Conclusions Both gauges are equally effective for the treatment of proliferative diabetic retinopathy.

• S005

Preoperative intravitreal bevacizumab effects on the course of Pars Plana vitrectomy in diabetic vitreous hemorrhage

ZAHAF A , Zghal I , Fekih O , Zayani M , Mahjoub A , Bouguila H , Nacef L
Institut d'ophtalmologie, Tunis, Tunis, Tunisia

Purpose To compare the rate of rehemorrhage in patients with diabetic vitreous hemorrhage (VH) undergoing pars plana vitrectomy (PPV) with versus without preoperative intravitreal bevacizumab (IVB) injection.
Methods Forty patients with proliferative diabetic retinopathy (40eyes) with an indication for primary vitrectomy were randomized to IVB group (20 eyes) or control group (20 eyes). Intravitreal bevacizumab group received intravitreal injection of 1.25 mg/0.05 mL bevacizumab, one week before vitrectomy.
Results The frequency of postoperative recurrent vitreous hemorrhage (5%, 1/20 vs. 40%, 8/20, P = 0.017) were significantly lower in IVB group than in control group .The number of intraoperative endodiathermy spots (0.63 ± 1.0 vs. 1.3 ± 1.4, P = 0.028) were also significantly lower in IVB group than in control group while mean bleeding frequency in IVB group was 0.7 ± 0.78 times/case with range between 0 and 2 bleeding attacks/case and mean bleeding frequency in control group was 3.12 ± 1.31times/case with range between 3 and 6 bleeding attacks/case and the difference was statistically significant as ($p < 0.001$). The frequency of reoperation due to recurrent vitreous hemorrhage within 4 weeks after surgery was significantly lower (P = 0.022) in IVB group (5%, 1patient) than in control group (35%, 7/20).
Conclusions Intravitreal injection of 1.25 mg/0.05 mL bevacizumab 1 week before vitrectomy blocked vascular endothelial growth factor production in vitreous and significantly reduced the incidence of reoperation due to early postoperative recurrent vitreous hemorrhage.

• S006

Management of acute submacular haemorrhage: Royal free hospital experience

SIM S Y , Elhousseini Z , Maragkos I , Asaria R
Royal Free London NHS Foundation Trust, Department of Ophthalmology, London, United Kingdom

Purpose To evaluate visual outcomes of patients presenting with acute submacular haemorrhage (SMH) secondary to neovascular Age Related Macular Degeneration (nAMD) treated with pars plana vitrectomy (PPV), subretinal recombinant tissue plasminogen activator (rTPA) and air.
Methods Retrospective, clinical case series. 7 patients with acute SMH secondary to nAMD, underwent PPV, instillation of 50mcg/0.1ml subretinal alteplase and air tamponade. Data was obtained from Electronic Medical Records (EDRM) of the Royal Free Hospital from October 2013 to March 2015. Patient demographics (age, gender, and laterality), duration between onset and treatment, visual acuity (VA) and any concurrent treatment were recorded.
Results 7 patients were included in our study with mean age - 69.1 years (Range: 60-87). 3 patients had cataract. No other ocular comorbidities. Mean period between onset of symptoms to treatment was 13.7 days (Range: 1-56). At presentation, six patients had hand movement (HM) VA and one patient had counting fingers (CF) VA. At one month post-operatively, 6 patients (85.7%) demonstrated VA improvement ≥ 1 line, of whom 3 (42.9%) improved by ≥2 lines. At 6 months post-operatively however, only 3 (42.9%) patients had sustained VA improvement. Post-operative OCT demonstrated complete displacement of SMH in 4 patients (57.1%), while 3 patients had residual submacular organised blood.
Conclusions Subretinal rTPA following vitrectomy with air tamponade may be used to dissolve submacular blood mass enabling physicians to resume NHS funded anti-VEGF therapy. Long-term visual outcome is often limited by underlying disease progression.

• S007

Management of unexplained haemorrhagic PVD at Southampton Eye Casualty Clinic

SHALABY A , Tossounis C , Andrew M
Southampton University Hospital, Eye Unit, Southampton, United Kingdom

Purpose To assess the management of unexplained haemorrhagic PVDs at the Eye Casualty Clinic and compare it with suggested management plans in the literature. Finally suggest possible changes which could improve outcomes.
Methods A retrospective review of patient electronic records at HICCS, e-Documents and MEDISOFT databases over a 5-month period (August 2014-December 2014). All patients attending eye casualty clinic with a diagnosis of a haemorrhagic PVD were included. Patients with pre-existing retinal neovascularisation or haemorrhagic ARMD and Macroaneurysms were excluded.
Results There were 43 patients recorded with unexplained haemorrhagic PVDs in 5 months. 28/43 (65.1%) patients were seen and Discharged at the Eye Casualty Clinic in Max 2 visits. The remaining 15/43 (34.9%) patients were referred to VR OPD for further review. Of these, 7/15 patients had a retinopexy performed prior to VR OPD visit. The patients were seen by different doctors every time and of varying clinical experience (SHO, SpR, Fellow, Associate Specialist, Locum Consultant).
Conclusions The retinal break was missed in 3/8 (37.5%) of the patients presenting at the Eye Casualty Clinic with an unexplained haemorrhagic PVD and a break despite the presence of a good fundus view.A significant number of patients (28/43, 65.1%) were managed solely at the Eye Casualty Clinic effectively.All the patients that had a laser retinopexy were referred to the VR OPD in 2 weeks for a review. Suggestions:
All patients with unexplained haemorrhagic PVDs and no fundal view should be referred to the VR service the same day for possible early vitrectomyAll patients with no obvious retinal break and reasonable view of their fundus (unless having a very clear view) must be referred to the VR OPD within 1 week for a more detailed fundoscopy.

• S008

Resolution of postoperative macular hole with topical nepafenac: a case report

IDOATE A (1), Honrrubia A (1), Ascaso J (1), Cristobal J (2), Perez I (1), Almenara C (1), Esteban O (1), Martinez M (1), Sanchez J I (1)
(1) University Hospital Lozano Blesa, Retina, Zaragoza, Spain
(2) University Hospital Lozano Blesa, Cornea, Zaragoza, Spain

Purpose Macular hole (MH) is a rare complication of cataract extraction. Various etiologies are discussed but it seems that the combination of vitreous traction and pseudophakic macular edema are the causes most likely involved in its pathogenesis. Pars plana vitrectomy (PPV) and internal limiting membrane peeling is the gold standard treatment option for patients with postoperative MH. Medical treatment has not been very effective in resolving this pathology. We present a case of post-surgical MH treated with topical Nepafenac.
Methods Interventional case report showing the role of topical Nepafenac as a therapeutic tool in post-surgical MH.
Results An 81-year-old female with a history of uncomplicated cataract surgery in RE. Four weeks after surgery there was a progressive visual deterioration with a best corrected visual acuity (BCVA): 0.05. SD-OCT revealed a full-thickness MH. Nepafenac 0.1 mg/ml, 3 times a day, was administered for 8 weeks in RE. Four months later, an improvement of her visual acuity (BCVA: 0.4) and a recovery of the retinal structure were observed. No recidive has been observed in a follow-up of 1 year.
Conclusions We propose the therapeutic use of topical NSAIDs as a possible alternative to surgery for macular holes whose etiology is related to inflammatory processes.

• S009

The use of intraoperative spectral domain optic coherence tomography in vitreoretinal surgery: The evaluation of efficacy.

LYTVYNCHUK L (1), Glittenberg C (2), Binder S (2)

(1) Lviv Regional Clinical Hospital, Department of Ophthalmology, Lviv, Ukraine
(2) Rudolf Foundation Hospital- Karl Landsteiner Institute for Retinal Research and Imaging, Department of Ophthalmology, Vienna, Austria

Purpose To evaluate the feasibility of intraoperative spectral domain optic coherence tomography (iSD-OCT) in challenging cases during pars plana vitrectomy (PPV).
Methods Intraoperative imaging was performed using the first commercially available iSD-OCT system Rescan 700, fully integrated into the surgical microscope OPMI Lumera 700 (Zeiss, Oberkochen, Germany). The feasibility of iSD-OCT was assessed during three 23-gauge PPV cases: large macular hole (MH) with inverted internal limiting membrane (ILM) flap technique (Case #1), vitrectomy for asteroid hyalosis with age-related macular degeneration (Case #2), vitrectomy for morning glory syndrome with retinoschisis and exudative retinal detachment (Case #3).
Results Case #1. The use of iSD-OCT facilitated to safely initiate ILM flap, to form inverted flap, to invert the flap into the MH, to control position of the forceps concerning retinal layers, and to confirm the MH covering with the ILM remnants at the end of the surgery. Case #2. Standard OCT was not available before the surgery due to opaque vitreous. Intraoperative SD-OCT imaging assisted to reveal epiretinal membrane (ERM), retinal pigment epithelium detachment, intraretinal fluid and drusen. These findings required additional surgical steps: ERM removal and injection of anti-VEGF at the end of the surgery. Case #3. In the case of morning glory syndrome iSD-OCT facilitated to remove the strongly adherent posterior hyaloid, to control ILM flap initiation, to perform the peeling over the detached retina, to aspirate residual fluid after fluid/air exchange.
Conclusions The use of iSD-OCT facilitates real-time simultaneous to surgical workflow visualisation of tissue behaviour and surgical manoeuvres during pars plans vitrectomy. The obtained information can improve surgical technique and influence the decision making in difficult cases.

• S010

Epiretinal membrane peeling for eyes with asteroid hyalosis: a case-control study

MOUNA A , Conart J B , Kurun S , Ameloot F , Berrod J P
NANCY regional university hospital, ophthalmology, Vandœuvre-lès-Nancy, France

Purpose To evaluate anatomical and functional results of epiretinal membrane peeling for patients with asteroid hyalosis (AH) comparing with those of a control population without AH.
Methods Retrospective, case-control study, of a cohort of 1104 patients operated from an epiretinal membrane(EM) between January 2002 and February 2014. Forty four consecutive patient were included in the EM associated with AH group and were compared to 44 control patient without AH, matched for: age, sex, date of surgery, and axial length. The best corrected visual acuity (BCVA) and central macular thickness on OCT (CMT) were measured at baseline and postoperatively at 1, 6 and 12 months. intraoperative and/or postoperative complications were also analyzed.
Results 34 men and 10 women were included in the AH group. Respectively, the mean initial BCVA was 0.49+/-0.21 logMar for the AH group Vs 0.44+/-0.21 logMAR for the control group (p = 0.2), and the mean initial CMT was 415 +/- 71 µm Vs 422+/-73 µm (p = 0.6). No significant difference was found regarding the final BCVA, with respectively a mean of 0.37 Vs 0.24 logMAR(p=0.26) at 1month, 0.27 Vs. 0.23 logMAR(p=0.5) at 6 months, and 0.17Vs 0.2 logMAR(p=0.26) at 12 months. Also, no difference was found regarding the evolution of CMT, with respectively a mean of 368 Vs 353 µm(p=0.5) at 1 month, 347 Vs 358 µm(p=0.61) at 6 months, 345 Vs 349 µm (p =0.87) at 12 months. Only a single macular hole was recorded in the AH group in the follow up.
Conclusions The presence of asteroid hyalosis does not constitute a factor of poor prognosis for visual recovery after epiretinal membrane peeling

• S011

Project RESET. REtinal Surgery systEm for Training

COTIN S (1), Keppi J J (2), Allard J (3), Bessard R (3), Courtecuisse H (3), Gaucher D (3)
(1) INRIA, Ophtalmology, Strasbourg, France
(2) CHU Strasbourg, Ophtalmologuy, Strasbourg, France
(3) CHU Strasbourg, Ophtalmology, Strasbourg, France

Purpose Retina surgery is an increasingly performed procedure for the treatment of a wide spectrum of retinal pathologies.
Methods Yet, as most micro-surgical techniques, it requires long training periods before being mastered. To properly answer requests from clinicians for highly realistic training on one hand, and new requirements from accreditation or recertification from surgical societies on the other hand, we propose to develop a high- fidelity training system for retinal surgery.
Results This simulator will be built upon our strong scientific expertise in the field of real-time simulation, and a success story for technology transfer in the field of cataract surgery simulation.
Conclusions Members of the consortium have a long expertise in the development of prototypes, as well as collaboration with clinical partners. The simulation system that we propose to develop will be based on the Open Source simulation platform SOFA, and will rely on expertise from our partners to ensure clinical and industrial relevance.

• S012

Clinical outcome of YAG laser vitreolysis (Ultra Q Reflex®) for the treatment of floaters

KIM E , Kim H K , Yoo T Y
Pureun Eye Hospital, Department of Ophthalmology, JeonJu, South-Korea

Purpose Floaters are localized vitreous opacities that are products of vitreous degeneration or posterior vitreous detachment (PVD). Usually, observation was the only solution, however some patients are suffered from floaters. This study reports the clinical results of YAG laser vitreolysis for the treatment of floaters.
Methods The patients with floaters were involved who visited Pureun eye hospital between January and March 2015. The patients were involved who met the following criteria; the floaters caused by localized vitreous opacities or PVD; patients suffered from floaters and strong desire for cure. The patients with diabetic retinopathy, retinal detachment, severe media opacity and young age were excluded. Patients had pre and postoperative examinations including visual acuity, tonometry, wide fundus photography, slit lamp and fundus examination. Patients were examined 1, 4 and 8 weeks after treatment. The floater scores were measured with survey paper for the evaluation of subjective change. The wide fundus photography was used for the objective change.
Results The 47 eyes were involved (27 cases:male and 20 cases:female). The mean age was 69.5±14.3. Informed consent was obtained in all cases. The floater scores were significantly improved after treatment (preoperative: 73.6±10.5, postoperative: 8.2±4.6, P< 0.001). The visible floaters disappeared in 43/47 cases (91.5%) in wide fundus photography. There were no significant changes in VA and IOP. Other side effects such as retinal detachment or hemorrhage and cataract were not developed during follow up period.
Conclusions The clinical outcome of YAG laser vitreolysis using Ultra Q Reflex showed favorable results in subjective and objective measurement. There were no significant complications after procedure. We think YAG laser vitreolysis could be the excellent treatment option for the floaters.

• S013
Ampiginous choroiditis: heterogeneity in 2 cases

VANDEPUTTE J (1,2), Lambrecht P (1), Leroy B P (1,3), De Schryver I (1), De Zaeytijd J (1)
(1) Ghent University Hospital, Dpt of Ophthalmology, Ghent, Belgium
(2) KUL, Medical School, Leuven, Belgium
(3) Ghent University Hospital, Ctr for Medical Genetics, Ghent, Belgium

Purpose We report two heterogeneous cases with ampiginous choroiditis and describe fundus photography, blue light autofluorescence, fluorescein angiography, indocyanine green angiography and cross-sectional optical coherence tomography.
Methods Observational report about 2 heterogeneous cases of ampiginous choroiditis.
Results A 70-year old woman and a 21-year old man were referred to us with posterior uveitis. The female patient showed unilateral scattered chorioretinal lesions, whereas the male patient featured bilateral geographic chorioretinal lesions. In the first case, the lesions did not threaten the fovea. In the second case, the lesions involved the fovea of one eye and threatened the fovea of the second eye. Both patients presented with lesions showing blue light hyperautofluorescence. Fluorescein angiography showed early hypofluorescence with late staining of the borders whereas indocyanine green angiography showed hypofluorescent lesions through the early and late stages. Cross-sectional optical coherence tomography of the lesions showed outer retinal atrophy. The tuberculin skin test and interferon-gamma release assay were negative. The diagnosis of ampiginous choroiditis was withholded. A stepladder approach to obtain a corticosteroid-sparing immunomodulatory treatment was initiated with azathioprine and visual acuity remained stable.
Conclusions Ampiginous choroiditis is a primary inflammatory choriocapillaropathy with distinct features. However, the heterogeneous clinical findings can complicate the diagnosis.

• S014
Wide-Field Angiography in the management of retinal vasculitis

EL MATRI HASSAIRI A , Chebil A , Bouladi M , Kort F , El Matri L
Hedi Rais Institute of Ophthalmology, Department B of Ophthalmology, Tunis, Tunisia

Purpose To study the value of Wide-Field angiography in the management of patients with retinal vasculitis.
Methods A total of 48 eyes of 24 patients with systemic vasculitis underwent complete ophthalmic exam, followed by wide-field retinal angiography (WF- FA) with the Heidelberg Angiograph SLO using the Staurenghi contact lens. The primary outcome was diagnosing the extent of retinal vasculitis (RV) and monitoring disease activity. The secondary outcome was the percentage of patients whose management changed, based on the availability of WF –FA.
Results WF-FA assisted in revealing retinal vasculitis in 5 of 24 patients (20,8 %), in 2 cases retinal vasculitis was not clinically evident. The extent was quantified in the 5 patients and the disease activity monitored in 3 patients. Three of 24 patients (12,5 %) had management change: planning medical treatment or laser photocoagulation.
Conclusions WF-FA is a valuable technology in the management of patients with systemic vasculitis and can be used for the diagnosis, treatment and follow up of retinal vasculitis.

• S015
Toxoplasma chorioretinitis: value of polymerase chain reaction and intraocular antibody production in a patient with negative anti-Toxoplasma gondii serology

ROELS D (1), Nerinckx F (1), Leroy B P (2), Padalko E (3), De Schryver I (1)
(1) University Hospital Ghent, Dpt of Ophthalmology, Ghent, Belgium
(2) University Hospital Ghent, Dpt of Ophthalmology- Ctr for Medical Genetics, Ghent, Belgium
(3) University Hospital Ghent, Ctr for Molecular Diagnostics, Ghent, Belgium

Purpose To report a case of panuveitis with negative anti-Toxoplasma gondii serology, and serologic and PCR analysis of intraocular fluids positive for Toxoplasmosis.
Methods A 29-year-old male presented with left panuveitis and no view of the fundus, underwent a diagnostic vitreous biopsy. Work-up included serology, vitreous PCR and measurement of local antibody production in aqueous humour.
Results At presentation, BCVA in the LE was CF at 1m. The patient described a progressive decline of vision in the LE since 6 months. Examination showed panuveitis with dense vitritis obscuring the fundus. IOP was 29 mmHg. The RE showed a chorioretinal scar located superonasally to the optic disc. Toxoplasma chorioretinitis was suspected, but serology was negative. PCR on a diagnostic vitreous biopsy was positive for T. gondii DNA and negative for Herpes viruses. Treatment with clindamycin and trimethoprim/sulfamethoxazole was initiated. The anti-T.gondii serology remained negative. The Goldmann-Witmer coefficient was positive. Also, efficacy of treatment was supportive of a diagnosis of ocular toxoplasmosis.
Conclusions Although clinical presentation was suggestive of ocular toxoplasmosis, anti-T.gondii serology remained negative. In cases with high clinical suspicion of ocular toxoplasmosis, superior diagnostic efficacy is achieved by a combination of serology, PCR techniques and GWC.

• S016
Intravitreal Cysticercosis

HALFELD FURTADO DE MENDONCA R (1), De Oliveira Maia JR. O (2)
(1) Studio Oftalmologico Halfeld, Ophthalmology, Rome, Italy
(2) Monte Tabor Foundation. São Rafael Hospital, Ophthalmology, Salvador BA, Brazil

Purpose To describe a very interesting vitrectomy in a case of intravitreal cysticercosis. Setting: Cysticercosis is the most common ocular helminthic infection in man.
Methods A 14 year old Brazilian girl complained of blurred vision in her right eye over the past 6 months. During this period she had several episodes of hyperaemia. Visual acuity in the right eye was hand motion and in the left eye 20/20. The intraocular pressure was normal. Fundus examination of the left eye was normal. Fundus examination of the right eye showed a floating cyst in the vitreous cavity.
Results The patient underwent 23-gauge vitrectomy without any complications. Perfluorocarbon liquid was used to facilitate the removal of the cyst in the vitreous cavity. Laser photocoagulation was carried out around the retinal break, followed by silicone oil implantation. Light and electron microscopic studies suggested Cysticercus cellulosae as the infecting agent.
Conclusions The complete and active aspiration of the Cysticercus Cellulosae in the vitreous cavity was very interesting and efficient. We believe that the success of the surgery was due to the fact that the cyst was removed intact by pars plana vitrectomy.

• S017

Choroidal thickness in patients with central serous chorioretinopathy: Assessment of haller's and sattler's layers

KIM S W, Chung Y R, Kim J W, Lee K
Ajou University School of Medicine, Suwon, South-Korea

Purpose To investigate the change in choroidal thickness and subanalyze the Haller's and Sattler's layers among central serous chorioretinopathy (CSC) eyes, uninvolved fellow eyes, and control eyes of healthy subjects using enhanced depth imaging optical coherence tomography (EDI-OCT).
Methods Ocular findings and clinical features were analyzed retrospectively from medical records of the patients diagnosed with CSC from October 2014 to March 2015. The subfoveal choroidal thickness including the thickness of Haller's layer and Sattler's layer was measured using EDT-OCT in CSC eyes as well as in uninvolved fellow eyes, and compared to age, gender, and spherical equivalent-matched healthy control eyes.
Results Thirty-one eyes affected by CSC and 24 uninvolved fellow eyes were included in this study. Thirty eyes from healthy subjects were recruited for control. The mean subfoveal choroidal thickness and the mean thickness of Haller's layer were significantly greater in CSC eyes compared to fellow eyes or normal control eyes, while those of fellow eyes were also significantly thicker than those of normal control eyes. The thickness of Sattler's layer showed no significant difference among the three groups.
Conclusions The subfoveal choroidal thickness was increased mainly due to the increase in thickness of Haller's layer in CSC patients. It is believed that the Haller's layer was thickened by the enlarged large choroidal vessels and the action of non-vascular smooth muscle cells of choroid in response to increased sympathetic tone in CSC patients.

• S018

Our experience with anti-VEGF treatment on central serous retinopathy

PAPAVASILEIOU E, Younis S
Imperial College NHS Trust, Western Eye Hospital, LONDON, United Kingdom

Purpose To evaluate the short-term efficacy of intravitreal anti-VEGF for the treatment of subretinal fluid (SRF) and/or pigment epithelium detachment (PED) secondary to chronic central serous chorioretinopathy (CSR).
Methods Sixteen patients were treated with intravitreal injections of anti-VEGF at 6- to 8-week intervals until SRF and/or PED resolved. Main outcomes were Best-Corrected Visual Acuity (BCVA), central retinal thickness (CRT) measured with optical coherence tomography (OCT), performed at 6- to 8-week intervals and number of injections. Fluorescein angiography was performed at baseline visit and thereafter depending on clinical and OCT findings.
Results Patients received 3.16 (range: 1-15) intravitreal injections of anti-VEGF on average during a follow-up of 22+/-2 weeks. Mean BCVA increased by 11.2 letters and mean CRT decreased significantly over follow-up from 396.68µm at baseline to 250.36µm on last visit. 5 patients (31.25%) showed complete resolution of subretinal fluid and PED, 6 patients (37.5%) had persistent SRF and 5 patients (31.25%) had persistent PED.
Conclusions Anatomic and functional improvement following intravitreal anti-VEGF injections suggest that vascular endothelial growth factor (VEGF) may be involved in fluid leakage in patients with chronic CSR. The results suggest a possible role for anti-VEGF agents in the treatment of chronic CSR.

• S019

Mineralocortycoid receptor's antagonists in treatment of central serous chorioretinopathy

ROMANOWSKA DIXON B, Karska-Basta I, Pociej-Marciak W, Ozog-Baran J, Kubicka-Trzaska A
Jagiellonian University Medical College, Ophthalmology, Krakow, Poland

Purpose To evaluate the influence of eplerenon on the function and morphology of the macula in patients with central serous chorioretinopathy (CSC).
Methods The study included 17 eyes in 16 patients with central serous chorioretinopathy treated in the Department of Ophthalmology at the University Hospital in Krakow. There were 13 males, 3 women at the age of 32 to 66 years, mean age 41.71 years. The duration of symptoms was ranging from 4 to 24 months, an average of 8months. The patients were treated with eplerenone according to the scheme: 25mg/day for a week, then 50mg/day by 3months. The baseline examination and two controls (after 1-1,5 month and after 3-4 months) included best corrected visual acuity, central retinal thickness in optical coherence tomography and visual central disturbances in Amsler test.
Results The values for CRT decreased from 367 (+/-70) µm to 264 (+/-50) µm (the first control) and to 248 (+/- 50) (the second control), the difference was an average of 112.71 microns (p = 0.00001). The average BCVA improved from 0,61(+/-0,25) to 0,67 (+/-0,28) (the first control) and to 0,72 (+/-0,28) (the second control). 10 patients (58,8%) reported improvement of Amsler test while in the 7 patients (41,2%) deterioration in central vision stayed unchanged during the first control. During the second control 7 patients (50%) reported improvement of Amsler test while in the 7 patients (50%) deterioration in central vision stayed unchanged.
Conclusions The results of our observations indicate that eplerenone can provide an alternative treatment CSC especially in cases where there are contraindications for the use of other therapeutic methods such as laser photocoagulation of the retina. Further investigation is needed. .

• S020

Oral eplerenone as a first line treatment in chronic central serous chorioretinopathy : A case series evaluation

SENDON D, Graber M, Chiche A, Rambaud C, Berguiga M, Delbarre M, Froussart-Maille F
Percy Military Hospital, Opthalmology, Paris, France

Purpose To evaluate the effect of oral eplerenone on subretinal fluid (SRF), visual acuity, and choroidal thickness in patients with chronic central serous chorioretinopathy (CSCR).
Methods Retrospective review of all patients monitored for a minimum of 3 months with chronic CSCR lasting more than 3 months who were treated with oral eplerenone with four physicians retina practice. Visual acuity, dilated funduscopic examination, and spectral-domain ocular coherence tomography (SD-OCT) with enhanced depth imaging (EDI) were obtained at each visit. The primary outcome measure was the reduction in subretinal fluid (SRF) following initiation of therapy. Protocol was oral eplerenone 25 mg daily first week and 50 mg daily during 9 weeks.
Results 4 eyes of 4 patients were treated. At 3 months, all eyes had decreased SRF height on OCT and all eyes had improved their visual acuity. Mean SRF height decreased from 390 µm to 285 µm and mean visual acuity enhanced from logMAR 0.20 to 0.08 No significant side effect occurred. Only one eye showed reccurence after eplerenone was discontinued.
Conclusions Oral eplerenone appeared to be a safe and reliable treatment with significant anatomic and visual improvements in eyes with chronic CSCR.

• S021

Novel SRPK1 inhibitors specifically target alternative splicing in human primary retinal epithelial cells

ROWLINSON J (1), Batson J (1), Toop H (2), Allen C (1), Gibbons B (1), Babaei-Jadidi R (1), Zhang J (2), Wearmouth S (2), Knapp S (3), Morris J (2), Bates D (1)
(1) University of Nottingham, Division of Cancer and Stem Cells, Nottingham, United Kingdom
(2) University of New South Wales, Chemistry, Sydney, Australia
(3) University of Oxford, Structural Genomics Consortium, Oxford, United Kingdom

Purpose Specifically altering the splicing of VEGF-A from pro-angiogenic VEGF-A165a to anti-angiogenic VEGF-A165b could prove effective in the treatment of wet AMD. VEGF-A alternative splicing is controlled through RNA binding protein SRSF1 which when phosphorylated by the serine kinase SRPK1 induces pro-angiogenic VEGF-A165a expression. We aimed to use novel SRPK1 inhibitors that specifically alter splicing in retinal pigment epithelial (RPE) cells.
Methods RPE cells were treated with novel compounds, synthesized based on the structure of SRPK1, followed by extraction of RNA and protein. RT-PCR and digital PCR was used to examine splicing of genes expressed in the eye or known targets of SRPK1, and ELISA and immunoblotting were used to detect VEGF-A isoform expression.
Results Novel SRPK1 inhibitors dose-dependently increased the expression of the anti-angiogenic VEGF-A165b isoform. RT-PCR showed that SRPK1 inhibition altered alternative splicing of MKNK2, a known splicing target of SRSF1, resulting in a 2 fold change to isoform a in RPE cells. No change in splicing was observed for BCL2L1, ARR1, CAMK2D, RAC1, FN1 or hnRNPB1/A2. Other SRSF1 targets such as TEAD1, BIM and MST1R were not expressed in RPE cells.
Conclusions We have developed novel SRPK1 inhibitors that specifically target splicing within the retina and offer an alternative more specific therapeutics for patients with exudative AMD.

• S022

Association between drusen and blood test results in a colony of 1,174 monkeys

NISHIGUCHI K (1), Yokoyama Y (2), Fujii Y (2), Furukawa T (3), Ono F (4), Shimozawa N (5), Togo M (6), Suzuki M (6), Nakazawa T (2)
(1) Tohoku University Graduate School of Medicine, Department of Advanced Ophthalmic Medicine, Sendai, Japan
(2) Tohoku University Graduate School of Medicine, Department of Ophthalmology, Sendai, Japan
(3) Kurashiki University of Science and the Arts, Department of Comparative Animal Science, Kurashiki, Japan
(4) Chiba Institute of Science, Faculty of Risk and Crisis Management, Choshi, Japan
(5) Tsukuba Primate Research Center, National Institute of Biomedical Innovation-Health and Nutrition, Tsukuba, Japan
(6) The Corporation for Production and Research of Laboratory Primates, Tsukuba, Japan

Purpose To ascertain the association between fundus drusens and biological parameters in a colony of 1174 monkeys.
Methods Presence or absence of drusens was determined through the assessment of fundus photos taken during 2011 – 2013 from 1,174 *Macaca fascicularis* at Tsukuba Primate Research Center. Biological data from these monkeys including blood test result, age, sex, and body weight were tested for an association between the presence of drusens by applying *t*-test and logistic regression analysis.
Results We identified 387 and 787 monkeys with and without drusens, respectively. Among them, 317 and 628 monkeys with and without drusens that had a complete biological data set were further studied. After comparing each parameter in monkeys with and without drusens, 13 factors with a significance of $P < 0.1$ (t-test) were selected for logistic regression analysis. Regression analysis showed association of age (odds ratio: 1.092, 95% confidence interval: 1.061-1.125) and platelet count (odds ratio: 1.022, 95% confidence interval: 1.005-1.038) with drusens. In addition, an association was implicated between drusens and white blood cell count (odds ratio: 1.005, 95% confidence interval: 1.000-1.011).
Conclusions Age, platelet count, and white blood cell count may be associated with the development of drusens in *Macaca fascicularis*.

• S023

Age Macular Degeneration-Lipidomic Study: Relevance and interest of Lipidomic study in screening, follow-up and etiopathogeny of AMD

GONZALEZ C (1), Bertrand-Michel J (2)
(1) Cabinet du Dr Corinne Gonzalez, FUTUROPHTA, Toulouse, France
(2) I2MC INSERM U1048 ss Bat L3, plateau MetaToul-LIPIDOMIQUE, TOULOUSE, France

Purpose To evaluate the lipidomic study impact on AMD diagnosis, screening, etiopathogenie and interrelations,correlations between those 2 entities
Methods AMD:30 AMD patients.3 Groups:A:10 first stage AMD patients,B:10 Atrophy AMD patients, C:10 Neovascular AMD patients. Ophthalmologic exam:ETDRS visual acuity (VA), complete ophthalmic examination,Fundus examination, autofluorescence imaging (FAF),optical coherence tomography (Spectral Domain OCT) and fluorescein angiography (FA) and ICG when Neovascular complication.Lipidomic Study:Blood tests and analysis, all lipids qualitative, quantitative analysis, all the same for all patients,whatever group. Blood test is done during ophthalmologic exam. Plasma congelation "snap frost" in liquid nitrogen after total blood centrifugation, then liquid-liquid extraction for lipids analysis:neutral lipid by GC,as well as fatty acid but after BF3 methanol derivation,phospholipids by LC-MS directly,as sphingolipids but firstly hydrolysed. Polyinsatured fatty acids metabolites preparation: protein precipitation then pre-concentration by SPE(solid phase extraction) before m'analyses by LC-MS
Results Analysis will determine qualitative,quantitative lipids values in each patients group, each of them proportion, characterization, singularity; so, characterization, prevalence, specifics of and for each group. Lipidomic study'evaluation, identification, classification in AMD patients groups allow AMD screening,follow-up, particularly according to AMD type and stage. Lipidomic study have biomarker feature, let AMD prevention, etiopathogenic concept
Conclusions Lipidomics study and so better AMD characterization allow better diagnosis, follow-up, screening of AMD. Interrelations and correlations between AMD and Lipidomics lead to better etiopathogenie understanding and therapeutics prospects

• S024

AMD Drusenoid deposits "L", Lipid type, characterization, structural analysis with multimodal imaging and morphology-structural software

GONZALEZ C (1), Lay B (2)
(1) Cabinet du Dr Corinne Gonzalez, FUTUROPHTA, Toulouse, France
(2) ADCIS, 3 rue Martin Luther King, Saint-Contest, France

Purpose To study AMD drusenoid deposits "L" with multimodal imaging and morphology-structural software and see all the input of this technique and software
Methods 25 eyes of 25 patients, 8 men, 17 women, with AMD drusenoid deposits "L", Lipid Type (soft Drusen, Drusenoid PED "L"). Deposits were evaluated by Autofluorescence, IR imaging, OCT, notably OCT en FACE (Spectralis HRA-OCT, spectral domainOCT), and Morphology-Structural software (M-S software). ETDRS visual acuity (VA), complete ophthalmic examination with Fundus exam were added. Size, characteristics, number, topography of the "L" deposits, their environment above and below (particularly IS-OS, plexiform layer, choriocapillaris structure and thickness) were evaluated, each element was studied, compared cut to cut, layer to layer and time to time. M-S software let analyze drusenoid deposit volume and contours, let a 3D deposit reconstruction, display in 3D space, let volume, density(grey levels of deposits),structure (structural measures, texture parameters),composition (density calculation) evaluation and characterization of those "L" lipid type deposits
Results AMD Drusenoid Deposits "L" Lipid Type (soft Drusen, Drusenoid PED) are larger, roughly uniform, dome-shaped, dark grey, translucent, optical empty , equal and the same in all cross-section, as lipid pearl drops, fatty, mounds of deposit under the RPE, abnormal Pigment epithelium above, but layer quite preserved. M-S software allows lipid composition confirmation, selective lipid characterization, to better differentiate lipid and more components
Conclusions Multimodal Imaging, Morphology-Structural Software contribute to and improve AMD Drusenoid deposits "L" Lipid type, study and knowledge and so AMD etiopathogeny understanding

• S025

AMD Drusenoid deposits "P", Protein-Cellular Type : Characterization and Evolution. Multimodal imaging and OCT, OCT en Face, Evaluation and Interest.

GONZALEZ C
Cabinet du Dr Corinne Gonzalez, FUTUROPHTA, Toulouse, France

Purpose To study AMD drusenoid deposits "P",Protein-Cellular Type with multimodal imaging,to characterize their morphologic type,evolution,to consider etiopathogeny,biomarker features
Methods 148 eyes of 74 AMD patients. AMD drusenoid deposits "P",Protein-Cellular Type:Cuticular drusen,Drusenoid PED "P",Subretinal drusenoid deposits (SDD),Pseudovitellifom AMD were evaluated by Autofluorescence,IR imaging,ETDRS visual acuity (VA),ophthalmic examination with Ocular Fundus,Ocular Confocal Tomography exam(spectral domain OCT,OCT en Face software). Size,characteristics,number, topography of the lesions,growth way were evaluated,also their environment above,below and evolution.Each element was studied,compared cut to cut,layer to layer,time to time
Results VA stabilized in 90%.Pseudovitelliform AMD are little,irregular upper limit drusenoid PED.Cuticular drusen appear,uniform,round,white,under retinal pigment epithelium (RPE).SDD deposits are white,homogeneous,quite similar in all cross-section,FA and ICG too,nearby upper side RPE layer.Drusenoid PED "P" were dense,white, granular,different in all cross-sections,heterogeneous PED,below RPE,with abnormal RPE above,heavily unstructured.Multimodal imaging,especially OCT en Face,let individualize "P" drusenoid deposits.Evolution was-choriocapillaris change-pigment epithelium involution:more dense,irregular,inhomogeneous,crumbled-inflammation-neovascular signs even net.Specific metabolic defect outcome,etiopathogenic pathways appear: "P"drusenoid deposit is mostly enrolled in protein-cellular metabolic pathway dysfunction with rather evolution to neovascular complication.So it would build up its biomarker feature
Conclusions AMD Drusenoid deposits"P",Protein-Cellular type study,knowledge,evol ution,notably with multimodal imaging,OCT en Face contribute to and improve AMD understanding,prognosis,etiopathogic concept

• S026

Long term outcomes in a real life setting treatment by anti-vascular endothelial growth factor for wet age-related macular degeneration

HAOUAS M (1), Girmens J F (2), Thuret G (1,3), Gain P (1), Paques M (2), Sahel J A (2)
(1) University Hospital, Ophthalmology department, Saint-Etienne, France
(2) Quinze-Vingts National Hospital, DHU SightRestore- Inserm-DGOS CIC1423, Paris, France
(3) Institut Universitaire de France, Bd St Michel, Paris, France

Purpose To report long-term visual outcomes for patients receiving a real life setting treatment by anti-vascular endothelial growth factor (VEGF) for neovascular age-related macular degeneration (AMD)
Methods Retrospective chart review of 500 patients who received a first anti-VEGF injection for wet AMD from January 1, 2006 to January 1, 2010 at the Quinze-Vingts National Hospital (Paris). Patients clinical characteristics, ETDRS letter score at baseline, every years and at the last follow-up were recorded. The number of injections and the date of the first and last injection were also recorded. The main outcome measure was mean change in letter score at 5, 6 and 7 years from baseline.
Results 150 eyes of 120 patients with at least 5 years of follow-up were identified. The eyes non-selected had an insufficient follow-up or another macular disease treated by anti-VEGF. The mean follow-up was of 77 months. Mean change in letter score at 5, 6 and 7 years was respectively + 2 letters, -1 letters and - 4 letters. A vision of 20/40 or better was achieved in 20% of treated eyes. Seventy percent of eyes was untreated since 6 months or more at the last follow-up. Patients received an average of 4 injections per year.
Conclusions Real life setting treatment of neovascular AMD by anti-VEGF results in a stabilization of vision at 5 and 6 years of treatment. At the seventh years of follow-up, visual outcomes tend to be worse. Mean duration of treatment was 46 months, with 70% patient no longer requiring reinjection after a mean of 34 months after initiation. Evolution of treatment settings suggests that visual outcomes would be better for recently diagnosed and treated patients.

• S027

Efficacy of intravitreal Aflibercept in patients with neovascular AMD who were previously treated with Ranibizumab based on a Treat and Extend protocol

TURKSEVER C , Prünte C , Hatz K
Vista Klinik, Ophthalmology, Baselland, Switzerland

Purpose To analyze the efficacy of Aflibercept in patients with choroidal neovascularization (CNV) due to Age related macular degeneration (AMD) who were previously treated with Ranibizumab based on a Treat and Extend protocol (T&E).
Methods We have reviewed 30 eyes of 30 patients with CNV due to neovascular AMD. All patients were previously treated with Ranibizumab based on a T&E protocol. Therapy was converted to Aflibercept following the same T&E protocol. Lesion activity was determined based on fluorescein angiography and spectral domain optical coherence tomography(Spectralis HRA+OCT", Heidelberg engineering). Data were retrospectively evaluated for best corrected visual acuity(BCVA) variation from baseline, central retinal thickness (CRT), sub- and intraretinal fluid characteristics, structural changes of CNV, the total number of injections, as well as therapy interval with Aflibercept over 18 months. A t-test was applied
Results The mean age was 81.5(+/- 6.5) years. The eyes had received a mean of 25.6(+/- 9.7) Ranibizumab injections. After the initiation of Aflibercept, at months 18, mean CRT was significantly improved from 470.2µm (+/-164.70) to 328.6µm(+/- 91.23); mean maximum(MM) subretinal fluid height reduced from 88.72µm(+/- 90.48) to 18.27µm(+/- 39.13); MM vertical intraretinal cyst size reduced from 100.16µm (+/-143.45) to 49.33µm (+/- 99.37), respectively. Mean height of pigment epithelial detachment reduced from 289.16µm (+/- 219.17) to 240.16µm (+/- 228.97), MM recurrence-free interval increased from 6.27 (+/- 1.99) weeks to 8.05(+/- 2.43) weeks, as well as the mean BCVA (decimal) was improved from 0.37(+/-0.23) to 0.41(+/-0.22)
Conclusions Switching from Ranibizumab to Aflibercept indicated a longer therapy interval as well as significantly reduced activity of lesion. Aflibercept allowed maintenance of BCVA and reduction of mean CRT

• S028

Visual outcome following treatment with aflibercept in patients with neovascular age-related macular degeneration.

SANDER B , Rasmussen A , Lund-Andersen H
Rigshospitalet - Glostrup Hospital, Ophthalmology, Glostrup, Denmark

Purpose
Objective: To evaluate the visual outcome, number of injections and causes for discontinuation of treatment with aflibercept in patients with neovascular age-related macular degeneration (nAMD).
Methods Design: Retrospective chart review.
Participants: The study included 350 eyes in 350 patients who initiated first time intravitreal therapy for nAMD in 2013-14.
Descriptive statistical analysis of change in best-corrected visual acuity (BCVA) from presentation to 3 and 12 months after the first injection.
Results Results: The patients' mean age and visual acuity at baseline were stable at 80 years and 0.24 Snellen. Visual acuity increased significant with a mean of 6 injections; at 3 months to 0.38 Snellen, by 1 year to 0.41 Snellen for patients still in treatment; and to 0.35 Snellen for all patients with last observation carried forward. By 1 year 77% of eyes were still in treatment, 10 % had discontinued treatment with no apparent activity of disease and only a mean of 3.3 injections; 10 % had discontinued treatment due to low visual acuity, 3% were lost to follw-up
Conclusions Conclusion: Treatment with aflibecept in patients with nAMD showed excellent visual outcome for the majority of eyes treated.

• S029

The protective effect of anti-blue lens against photo-induced cell death

YU W Y, Shan S W, To C H, Chan H H L
The Hong Kong Polytechnic University, School of optometry, Hong Kong, Hong Kong-China

Purpose Anti-blue lenses that selectively block the harmful portion of the blue light spectrum become commercially available recently. This study aimed to evaluate the protective effect of anti-blue lens on cultured porcine primary retinal pigmented epithelial (RPE) cells against photo-irradiation.
Methods Primary RPE cells were isolated from porcine eyes and cultured to confluence. The cells were characterised by RPE65 using Western Blot. White and blue light emitting diode (LED) light sources as well as the transmittance of the anti-blue and anti-UV lenses were characterised by a spectroradiometer. The RPE cells were exposed to ~1.8x104 cd/m2 white (peak wavelength at 443 and 533nm) or blue (peak wavelength at 448 and 523nm) LED light for 16 hours, with anti-blue, anti-UV lens or without lens. Control cells were incubated in the dark. Cellular viability under the different lighting conditions with the anti-blue or anti-UV lenses were compared using trypan blue staining and MTT assay.
Results Trypan blue staining showed that the RPE cellular viability under no light, white light and blue light conditions without any lenses were 94.8±0.4%, 93.7±1.1% and 88.7±2.0% respectively. Blue light irradiation significantly induced more cell death when compared to no light (p=0.001) and white light (p=0.005) conditions. MTT assay also revealed significant difference under blue light when compared to no light (p=0.002) and white light (p=0.014) conditions. When comparing the effect of anti-blue and anti-UV lenses on cell survival, we found that anti-blue lens showed significantly elevated viability (93.4±1.4% vs 90.6±1.4%) using trypan blue (p=0.022) and MTT assay (p=0.029).
Conclusions Blue light exposure induced significant cytotoxicity on RPE cells. The anti-blue lens significantly reduced the harmful blue spectrum and showed protective effect on RPE cell survival.

• S030

Microbiology of conjunctiva sac in intravitreal injections.

GRZYBOWSKI A (1), Gaca-Wysocka M (2), Paluch M (2)
(1) University of Warmia and Mazury, Dept. of Ophthalmology, Olsztyn, Poland
(2) Poznan City Hospital, Dept. of Ophthalmology, Poznan, Poland

Purpose To evaluate the conjunctival sac flora before and after intravitreal injection (IVI) in eyes with no prophylactic antibiotic use.
Methods 37 eyes of 37 patients not using systemic or local antibiotics for at least 30 days were included. Microbiological culture from conjunctiva sac to nutrient media was taken twice: before IVI and before any topical medications were given and 30 minutes after anty-VEGF IVI. Topical antibiotics were not used neither before, nor after IVI. Shortly before IVI conjunctival sac was rinsed with 5% povidone-iodine (PVI). Control group constituted eyes not treated with IVI of the same patients.
Results Negative microbiological cultures before and after IVI were noted in the studied group in 15 patients (40.5%) and in 9 control eyes (24,3%). Coagulase-negative Staphylococci (CNS) were cultured in 13 eyes (35.1%) before IVI and in 8 eyes (21.6%) after IVI. In 3 eyes (8.1%) Staphylococcus aureus was shown before IVI, with subsequent negative cultures. In the control group CNS was shown in 14 eyes (37.8%) before IVI and in 7% (18.9%) after IVI. Microbiological flora was identical in studied and control groups in 14 cases (37.8%). There was no case of post-IVI endophthalmitis.
Conclusions About 50% of cultures were negative, in 35% - CNS, and in 15% - other bacteria were cultured, including Staphylococcus aureus in 8%. The number of negative cultures after IVI (the use of PVI) was higher than before IVI, and all Staphylococcus aureus were eliminated. The eye antisepsis based on PVI in IVI is an effective and efficient prophylaxis method.

• S031

Endophthalmitis associated with intravitreal Ranbizumab: Microbiology and visual outcomes.

PENWARDEN A, Weston K, Lockwood A
Queen Alexandra Hospital NHS Trust, Ophthalmology, Portsmouth, United Kingdom

Purpose The purpose of this study was to examine the spectrum of pathogenic organisms isolated from all cases of endophthalmitis identified during an 11 year period (2003-2014) at a single eye unit. The study was undertaken at the Queen Alexandra Hospital in Portsmouth, UK.
Methods Eye casualty and theatre data bases (HICCS, Medisoft) were used to capture cases of endophthalmitis. Case notes were reviewed to identify whether an intravitreal tap had been taken and to note visual acuities prior to ranibizumab treatment as well as the best visual acuity achieved post endophthalmitis treatment. Microbiological data was gathered for these cases by using the pathology database (ICE).
Results There were 8 cases of endophthalmitis in the 11 year period. All except 1 had an intravitreal tap taken for gram staining and microbiological culture. 4 cultures grew coagulase negative Staphylococcus, 1 grew a Streptococcus species, 1 grew the gram negative organism Haemophilus influenza and 1 culture was sterile. All cases were treated with the intravitreal antibiotics Vancomycin and Ceftazidine.

5 patients had a starting visual acuity 6/12 or better and 3 were 6/18 or worse. Post recovery from endophthalmitis 4 patients had VA of 6/24 or better and 2 had Hand Movements or worse. The patient with the gram negative culture had NPL (no perception of light) vision.
Conclusions The proportion of coagulase negative Staphylococci was slightly higher than other published reports. 2 patients had a poor visual outcome of Hand Movements or worse despite treatment with intravitreal antibiotics, one of which had a gram negative culture. However, half of the patients retained a reasonable vision of 6/24 or better.

• S032

Functional Expression of Toll-Like Receptors in Human Retinal and Choroidal Vascular Endothelial Cells

STEWART E, Wei R, Branch M, Sidney L, Amoaku W
University of Nottingham, Academic Ophthalmology, Nottingham, United Kingdom

Purpose Toll-like receptors (TLRs) are a family of proteins that initiate the innate immune response in reaction to invading microbes. Studies confirm the expression of TLRs in a variety of ocular tissues and cells, and it has also been suggested that selected TLRs may be associated with geographic atrophy and neovascularisation in age-related macular degeneration, diabetic retinopathy and other vascular and inflammatory diseases of the ocular posterior segment. However, TLR expression and localisation in the retinal and choroidal vasculature has not been defined.
Methods In this study the gene (mRNA) expression of TLRs 1-10 was investigated using RT-PCR and comparative qPCR and the protein expression and localisation of selected TLRs (3, 4, 6 and 9) were examined using western blotting, flow cytometry and immunofluorescent staining.
Results PCR showed gene expression of TLR1-6 and 9 in human choroidal endothelial cells (hCEC) and TLR2-6, 9 and 10 in human retinal endothelial cells (hREC). Western blotting detected TLR3, 4 and 9 proteins in both hCEC and hREC with higher levels in hCEC, whilst TLR6 protein was not detectable in either cell type. Flow cytometry detected all four TLRs (3, 4, 6 and 9) on the cell surface and intracellularly, TLR6 expression was detectable but low. The expression and localisation of TLR3, 4 and 9 were confirmed by immunofluorescent staining and TLR functionality tested by expression of IL-6 (ELISA) in response to TLR ligands.
Conclusions This study has, for the first time, identified the differential expression and localisation of TLRs in intraocular endothelial cells. This profiling will help inform our understanding of different retinal and choroidal vascular diseases, as well as the development of future treatments for intraocular vascular diseases.

Commercial interest

• S033

Spontaneous oscillations in the diameter of retinal arterioles from normal persons decrease with age.

RAGUNATHAN S (1), Taborsky J (2), Bek T (1)
(1) Aarhus University Hospital, Opthalmology, Aarhus, Denmark
(2) Aarhus University, Graduate School of Science and Technology, Aarhus, Denmark

Purpose The retinal vascular system is devoid of autonomic nervous supply, and consequently retinal blood flow is autoregulated. This includes pressure autoregulation, metabolic autoregulation and spontaneous oscillations in the diameter of retinal arterioles, so called vasomotion. It has been shown that vasomotion is impaired in diabetic patients, but it is unknown to what extent vasomotion results in retinal vascular disease should be corrected for age.
Methods Methods: Forty-eight normal persons consisting of at least 8 persons within each of the age groups (in years): 20-29, 30-39, 40-49, 50-59 and 60-69 were included. The patients had been examined by video recording of the retinal vessels using the Dynamic Vessel Analyzer, and diameter changes at five different locations on both arterioles and venules were analyzed by Fourier analysis. The power of the oscillations was calculated in five frequency bands defined as: 1) <0.04 Hz the very low frequency (VLF), 2) ≥0.04 and <0.15 Hz as the low frequency (LF), 3) ≥0.15 Hz and <0.4 Hz as high frequency (HF), 4) ≥0.4 and <2 Hz (VHF) normally containing the heart rate, and 5) 2-12.5 Hz as a ultra high frequency (UHF).
Results Results: In all arteriolar segments the power of spontaneous diameter oscillations with high frequencies showed a negative correlation with age, and the correlation was also found for low frequencies 1½ disk diameter from the optic disk (R2=0,0038±, p< 0,003 for all comparisons).
Conclusions Power analysis of spontaneous diameter changes in retinal arterioles should be corrected for age before results from different patient groups can be compared.

• S034

Real Time, In Vivo Analysis of the Onset of Retinogenesis: Assessment of the Retinal Vascular Plexus, Electrophysiological Response and Architecture in Neonatal Mice

DENIRO M , AlQahtani A , AlAhmar S , AlMohanna F
King Faisal Specialist Hospital, Cell Biology, Riyadh, Saudi Arabia

Purpose To evaluate the retinal vascular network in P0 and P1 neonates in vivo in real time.
Methods C57Bl/6J neonates were dark-adapted overnight. Animals were subjected to clinical investigation by using electroretinography (ERG) and spectral domain optical coherence tomography (SD-OCT) coupled to fluorescein angiography (FA).
Results FA in P0 neonates revealed that vascularization starts as ring-shaped vascular sprouts growing radially from the optic nerve head, becoming progressively interconnected by a capillary plexus between them. OCT data indicated that neonatal retina consisted of three layers; ganglion cell, inner plexiform and neuroblastic. The retinal thickness in P0 and P1 pups were 45 ± 7 µm, 50.2 ± 2 µm, respectively. ERG recordings were observed as early as day 0; however they exhibited a nearly abolished b-waves and relatively preserved a-waves. This suggests that synaptic functionality develops at the onset of postnatal retinogenesis.
Conclusions We report here for the first time the imaging of the developing retina in real time as early as P0, which was coupled to focal-ERG and OCT measurements. Our data indicated that despite the nearly abolished b-wave, the retina was responsive to light stimuli. Our data also suggest that the positive-going b-wave of the dark-adapted ERG response is generated by the precursor neuronal cells within the developing NBL and the response to light stimulation occurs long before the appearance of the rods and cones in the developing photoreceptor layer.

• S035

Effects of selective retina therapy on retinal oxygen saturation compared to conventional photocoagulation in rabbits

KIM J R , Roh Y J
Yeoeuido St. Mary's Hospital Catholic Univ. Medical College, Ophthalmology, Seoul, South-Korea

Purpose Subvisible selective retina therapy (SRT) was designed to target retinal pigment epithelium (RPE) without damaging adjacent photoreceptors. This study evaluated the changes in retinal oxygen saturation and retina histology after SRT compared to conventional photocoagulation(PC) in rabbits
Methods One eye in each of 10 chinchilla bastard rabbits was treated with 144 spots of SRT (527 nm) or conventional laser treatment (577 nm), respectively. After treatment, fundus photography, optical coherence tomography, and fluorescein angiography were performed to detect lesions. At 1 week post-treatment,
retinal oxygen saturation in untreated, SRT-treated, and PC-treated areas was evaluated in five eyes. Histologic evaluation was performed using light and electronic microscopy. At 4 weeks post-treatment, the same procedures were performed in the remaining five eyes.
Results At 1 week post-treatment, mean retinal oxygen saturation in the PC-treated area (23.3 ± 7.2 mm Hg) was relatively higher than in the untreated (16.6 ± 4.3) and SRT (15.34 ± 5.3) areas. Similar results were found at 4 weeks post-treatment (PC-treated, 25.3 ± 8.5; untreated, 14.4 ± 5.2, SRT-treated, 15.2 ± 4.6). OCT and histological examinations revealed selective RPE damage while sparing photoreceptors in the SRT lesion. In contrast, broad damage in multiple retinal layers including the photoreceptors was observed in conventional PC lesions.
Conclusions Increased retinal oxygen saturation after conventional PC might be due to widespread destruction of retinal layers including photoreceptors which is most oxygen consuming structure in retina. In contrast, relatively unchanged retinal oxygen saturation was observed in SRT lesions with intact retinal layers and photoreceptors. SRT can be used as an photoreceptor saving laser therapy in RPE dysfunction diseases such as DME or CSC.

• S036

The effects of nitroglycerine and COX-inhibition on retinal vessel diameters during hypoxia

KAYA M , Petersen L , Bek T
Aarhus University Hospital, Department of ophthalmology, Aarhus, Denmark

Purpose Retinal hypoxia plays a role in the pathophysiology of retinal vascular diseases such as diabetic retinopathy. Previous studies have shown that nitric oxide (NO) and cyclooxygenase (COX) products are involved in hypoxia-induced dilatation of the retinal vessels. Therefore, the purpose of this study was to examine the effect of an NO donor and inhibition of COX products on the diameter regulation of retinal vessels during hypoxia in healthy subjects.
Methods Twenty normal persons were examined with the Dynamic Vessel Analyzer (DVA). Retinal vessel diameters were measured at rest, and during isometric exercise and flicker stimulation. The measurements were performed during normoxia and hypoxia before and after sublingual administration of the NO donor nitroglycerine, and were repeated on a second study day after topical administration of the COX-inhibitor diclofenac.
Results Hypoxia alone and combined with nitroglycerine significantly reduced both arteriolar constriction during isometric exercise and dilatation during flicker stimulation (p<0.0001). Diclofenac further reduced the arteriolar constriction induced by isometric exercise during hypoxia (p=0.005). Nitroglycerine alone had no effect on the retinal vessel diameters.
Conclusions Diameter regulation of retinal vessels during hypoxia in normal persons is affected by inhibition of COX products but not by increased NO. The results contribute to understanding of retinal flow regulation and thereby to the identification of possible new strategies for intervention on diseases characterized by disturbances in retinal blood flow.

• S037

Lack of tone response in retinal arterioles secondary to electrical field stimulation

KRATHOLM N (1), Simonsen U (2), Jensen P S (1), Kringelholt S (1), Bek T (1)
(1) Aarhus University Hospital, Department of Ophthalmology, Aarhus, Denmark
(2) University of Aarhus, Department of Biomedicine, Aarhus, Denmark

Purpose The retinal vascular system is devoid of autonomic nervous supply and therefore retinal blood flow is autoregulated. However, it is unknown to what extent electrical activity in the retina during the visual process contributes to this flow regulation. The purpose of the present study was to study changes in vascular tone in retinal arterioles during electrical field stimulation (EFS) simulating neuronal activity around the vessels.
Methods Porcine ciliary arteries and retinal arterioles were mounted in a myograph system and the tone was measured during: A) Six series of bipolar field stimulations with a frequency of 1 Hz successively doubled to reach 32 Hz. In each series 30 mA pulses with a duration of 0.3 msec were applied during 20 sec, followed by a resting period of 5 min. B) The successive addition of the Na+ channel opener veratridine in the concentrations: 10-6, 3x10-6, 10-5 and 3x10-5 mM. The experiments were repeated after addition of the Na+ blocker tetrodotoxin (TTX) and after removal of the perivascular retinal tissue.
Results EFS had no significant effect on the tone of retinal arterioles ($p>0.66$), whereas veratridine showed a concentration dependent relaxation of these vessels ($p<0.01$). The effect was partially reduced by TTX which depended on the presence of perivascular retinal tissue.
Conclusions EFS has no effect on the tone of porcine retinal arterioles in vitro, whereas veratridine induces relaxation of these vessels. The findings are in accordance with a lack of autonomic nervous supply in retinal arterioles.

• S038

New generation analysis of thrombin generation in retinal vein thrombosis

FRUSCHELLI M (1), Capozzoli M (2), Scapellato C (3), Calzoni P (4), Puccetti L (1)
(1) University of Siena, Scienze Mediche Chirurgiche e Neuroscienze, Siena, Italy
(2) University of Siena, Scuola di Specializzazione in Oftalmologia, Siena, Italy
(3) University of Siena, U.O.C. LABORATORIO PATOLOGIA CLINICA AOUS, Siena, Italy
(4) University of Siena, U.O.C. EMATOLOGIA E COAGULAZIONE AOUS, Siena, Italy

Purpose To investigate potential mechanisms involved in retinal vein occlusion (RVO) we evaluated thrombin generation and soluble CD40 ligand (sCD40L) with respect to other known thrombophilic factors.
Methods 68 patients affected by RVO (28 central, 40 branch) and 60 healthy controls were evaluated for endogenous thrombin potential (ETP) by a chromogenic method and sCD40L by ELISA technique. Polymerase chain reaction (PCR) was employed for genetic polymorphisms and coagulative/chromogenic methods for othe coagulation factors.
Results Independently of genetic polymorphisms ETP was increased in patients with CRVO whereas sCD40L was higher in the whole cohort.
Conclusions Our data indicate an involvement of global coagulative activation in CRVO patients as suggested by ETP.

• S039

Comparison of the lamina cribrosa thickness of patients with unilateral branch retinal vein occlusion and normal subjects

SAGONG M, Lim S H, Kim M, Chang W
Yeungnam University College of Medicine, Department of Ophthalmology, Daegu, South-Korea

Purpose We compared the lamina cribrosa thickness (LCT) of normal subjects and patients with unilateral branch retinal vein occlusion (BRVO), and investigated the correlation between the LCT and the BRVO subtypes.
Methods A total of 46 eyes of 46 patients with naïve untreated BRVO and 31 eyes of 31 normal control subjects were included in this study. The occlusion site was divided into 2 BRVO types: arteriovenous crossing BRVO (AV-BRVO) and optic nerve BRVO (ON-BRVO). The optic nerve head (ONH) was scanned using enhanced-depth imaging (EDI) with the Spectralis OCT system. The mean LCT was defined at the centers of the mid-superior, central, and mid-inferior horizontal B-scans. The inter-eye differences and intra-eye differences in the LCT in BRVO were analyzed using the paired t-test.
Results The mean LCT of both eyes in the patients with BRVO was thinner than that of the normal subject eyes (both $P < .001$). Although the LCT of the BRVO-affected eyes were slightly thinner than that of the fellow eyes (237.0 μm vs. 241.4 μm), there was no statistically significant difference. Moreover, there were no significant LCT differences according to site of occlusion (AV-BRVO 237.6 μm vs. ON-BRVO 234.4 μm, $P > .05$).
Conclusions The lamina cribrosa was thinner in both eyes of the unilateral BRVO patients than in those of the normal subjects, but there was no difference in the LCT regardless of the anatomical site of the occlusion. These findings suggest that BRVO and glaucoma may have a common structural pathogenic mechanism.

• S040

Effect of intravitreal bevacizumab on choroidal thickness in eyes with retinal vein occlusion and diabetic macular oedema

KUOLIENE K, Malysko K, Cimbalas A, Asoklis R
Vilnius University, Centre of Eye Diseases, Vilnius, Lithuania

Purpose To evaluate choroidal thickness (CT) before and after intravitreal bevacizumab injections in eyes with macular oedema due to retinal vein occlusion and diabetic maculopathy.
Methods In this pilot study, 18 eyes of 16 patients were treated with intravitreal bevacizumab injections. The central macular thickness was measured at baseline and after treatment with intravitreal bevacizumab using spectral domain optical coherence tomography (SD-OCT). The choroid was evaluated using SD-OCT with EDI mode (Spectralis® HRA+OCT, Heidelberg Engineering) at the fovea before and after intravitreal bevacizumab.
Results 18 eyes were treated with 1.25 mg of intravitreal bevacizumab every 4 weeks, with at least three injections per eye and then continued if oedema persisted. The mean number of intravitreal bevacizumab injections per eye was three. The subfoveal choroidal thickness was significantly thinner after intravitreal anti-VEGF treatment (214.82 ± 62.67 µm) than at baseline (265.52 ± 87.67 µm, $P < 0.001$). The mean central macular thickness decreased significantly after treatment with intravitreal bevacizumab (265.53 ± 83.20 µm) compared to baseline (522.63 ± 305.62 µm, $P < 0.005$). Decrease in central macular thickness did not correlate with decrease in subfoveal choroidal thickness.
Conclusions In eyes with macular oedema due to retinal vein occlusion and diabetic maculopathy, treatment with intravitreal bevacizumab significantly reduced subfoveal CT and central macular thickness.

• S041

Evolution of hiperreflective points after intravitreal dexamethasone implant injection in patients with macular edema associated with retinal vein occlusion

ALMENARA MICHELENA C (1), Ascaso F J (2), Idoate A (2), Caramello C M (2), Sánchez J I (2), Berniolles J (2), Cristobal J (2)
(1) ALMENARA MICHELENA Cristina, Oftalmologia, Zaragoza, Spain
(2) Hospital Clínico Lozano Blesa, Oftalmología, Zaragoza, Spain

Purpose To analyse the evolution of macular hyperreflective points (HRP) detected by spectral-domain optical coherence tomography (SD-OCT) in eyes with macular edema secondary to retinal vein occlusion (RVO), following treatment with intravitreal dexamethasone implant (Ozurdex®).
Methods Retrospective observational study of 45 consecutive cases of RVO-associated macular edema: 13 central RVO and 32 branch RVO treated with Ozurdex®. The relationship between best corrected visual acuity (BCVA), central macular thickness (CMT) and the presence of HRD in SD-OCT before treatment and two months post-injection was determined.
Results CMT decreased significantly following treatment (527.7 µm vs 308.3 µm, p <0.001). Although there was a visual acuity improvement in 18 of the 45 eyes (40%), the mean BCVA difference was not statistically significant (p=0.373). Numerous HRP were detected in 24 patients (53.3%), disappearing in ten of them (41.7%) after corticosteroid intravitreal therapy.
Conclusions Disappearance of HRP after an intravitreal dexamethasone impant would support the hypothesis that HRP could represent some inflammatory cells.

• S042

Macular Infarction Following Intravitreal Triamcinolone Injection for Treatment of Central Retinal Vein Occlusion

KIM T K, Lee J H, Lee M Y
Uijeongbu St. Mary's Hospital College of Medicine- The Catholic University of Ko, Ophthalmology and Visual Science, Gyeonggi-do, South-Korea

Purpose To report a case of macular infarction following intravitreal triamcinolone injection for treatment of central retinal vein occlusion
Methods A 75-year-old man visited our clinic for visual disturbance in his left eye, who had diagnosed with macular infarction in his right eye. The patient's best-corrected visual acuity was 0.6 in his left eye. His medical history included type 2 diabetes, alcoholic liver cirrhosis, hepatocellular carcinoma. After fundus examination, the patient was diagnosed with central vein occlusion with macular edema, intravitreal triamcinolone was administered in an attempt to reduce edema.
Results Within 1 week of treatment with intravitreal injection, the patient noted a significant decrease in visual acuity. Flurorescein angiogram demonstrated an enlargement of the foveal avascular zone following intravitreal triamcinolone, although optical coherence tomography (OCT) showed a decresed maculr edema. Despite normalization of macular thickness on OCT and cessation of leakage on angiography, visual acuity remained at the same level until 2 month of follow-up.
Conclusions Not only intravitreal anti-VEGF injection, but also intravitreal triamcinolone injection can cause macular ischemia. This must be taken into consideration when the treatment regime is adopted for use in patients with ischemic risk factors.

• S043

Retinal vein occlusion in a patient with jugular vein compression by metastasis of carcinoma of the oral tongue

PEREZ NAVARRO I, Ascaso F J, Sánchez J I, Esteban O, Martinez M, Del Buey M A, Núñez E
Hospital clinico universitario "Lozano Blesa", Ophthalmology, Zaragoza, Spain

Purpose Retinal Vein Occlusion (RVO) is the second retinal vascular disease after the diabetic retinopathy. It has been associated with multiple factors both systemic (arterial hypertension, diabetes mellitus, hemoglobinopathy,...) and local (glaucoma, hyperopia,...). We report the very uncommon case of a central RVO that appeared after the patient suffered an internal jugular vein compression syndrome secondary to metastases of squamous cell carcinoma of the oral tongue (SCCOT).
Methods Spectral-domain optical coherence tomography (SD-OCT) and fluorescein angiography (FA) were used in the diagnosis and follow-up of the visual disorder and PET-CT and cervical ultrosonography were used in the diagnosis of jugular compression.
Results A 48-year-old male complained with decreased visual acuity on his right eye. Best-corrected visual acuity (BCVA) was 0.2 in the RE and 0.63 in the LE. Fundus examination revealed image of impending CRVO. FA showed severe bilateral venous stasis especially on the RE. He had been diagnosed with a SCCOT. PET- CT revealed a tongue neoplasia with right anterior jugular adenopathy. A cervical ultrosonography showed a compression on both uptown jugular veins and more constricted in high area on the right one. The tumor was considered unresectable. The patient underwent palliative chemotherapy and the ophthalmological symptoms and signs significantly improved. VA improved to 0,5 in the right eye and 0 8 in the left eye after chemotherapy.
Conclusions Ophthalmologists should be aware of internal jugular vein compression as a possible cause of CRVO in patients suffering from metastases of cervicofacial neoplasies.

• S044

Intraarterial thrombocytic material revelative of essential thrombocytaemia in a 59-year-old woman

ROSPOND-KUBIAK I (1), Oszkinis G (2), Kociecki J (1)
(1) Poznan University of Medical Sciences, Department of Ophthalmology, Poznan, Poland
(2) Poznan University of Medical Sciences, Department of Vascular Surgery, Poznan, Poland

Purpose Aim: to present a case of accidentally detected thrombocitic material in retinal arteries that was revelative of essential thrombocytaemia.
Methods Material/methods: 59-year-old woman presented in July 2013 with a suspicion of intraocular tumour. The patient was asymptomatic. There was a white nodular mass in her left eye infernasally, highly reflective on ultrasound. Initial diagnosis of choroidal granuloma was made. 4 weeks later, on the next follow-up visit, a massive thromobocytic material circulating freely in the retinal arteries and multiple yellowish lesions were detected in her both eyes. Visual acuity was not disturbed.
Results The patient was admitted to hospital with the suspicion of right heart failure. Apart from the high level of thromobocytes and D-dimers no pathology was revealed. The patient was sent for further counselling and bone marrow biopsy which revealed no pathology. Few months later she was readmitted with a severe cerebral ischaemia, thrombocytaemia and critical stenosis of right internal carotid artery (RICA) to 80%. Haematologic treatment was not effective and the patient died due to cerebral ischeamia in June 2014.
Conclusions Conclusions: Thromobocytic material associated with essential thrombocytaemia might be visible in retinal vessels. This is a rare phenomenon and might be associated with a poor prognosis for the patient.

• S045

Retinal Vessel Oxygen Saturation and its implications in myopia

HEITMAR R
ASTON UNIVERSITY, Vision Sciences, Birmingham, United Kingdom

Purpose To evaluate retinal vessel oxygen saturation and its relationship with ocular volume and axial length.
Methods We included sixty-five healthy individuals (age range: 19-51 yrs) of varying axial lengths (20.74-28.24mm). All subjects underwent full ocular examination including intra-ocular pressure measurements and systemic blood pressure measurements which was followed by auto-refraction, axial length, anterior chamber, corneal radii and retinal oxygen saturation assessments. In addition, all subjects underwent routine retinal photography which was used to determine their retinal arterial and venular calibres.
Results Retinal vessel calibres, both arteries and venules were significantly decreasing with increasing axial length (arteries: β=-0.37; p<0.001 and venules: β=-0.37; p<0.001). Arterial vessel oxygenation showed a statistical significant relationship with axial length but not posterior volume (axial length: β=-0.88; p=0.032 and posterior volume: β=0.73; p=0.075). Venous vessel saturation and oxygen consumption (A-V) were independent of ocular length and volume.
Conclusions Structural vascular changes such as vessel narrowing combined with changes in posterior volume and those brought about from vitreous detachment and degeneration could explain oxygenation related glaucomatous changes in highly myopic individuals.

• S046

Assessment of choroidal thickness in high myopic glaucomatous eyes using SD OCT

EL MATRI L, Chebil A, Hassairi A, Maamouri R, Kort F, Chaker N
Institut Hedi Rais Of Ophthalmology, Ophtalmology B, Tunis, Tunisia

Purpose To measure macular choroidal thickness (CT) using spectral domain optical coherence tomography (OCT) in high myopic eyes with primary angle-open glaucoma (POAG), and to investigate whether the choroid is thinner in these eyes compared to high myopic eyes without glaucoma.
Methods We conducted a cross-sectional study of 68 eyes with high myopic glaucoma matched with 68 highly myopic eyes without glaucoma by age, central corneal thickness and axial length (AL). OCT scans were performed with the spectral domain OCT (Topcon 2000). The subfoveal CT was measured between the Bruch membrane and the internal aspect of the sclera.
Results In the subgroup without glaucoma, matched with the subgroup with glaucoma by age (P=0.48), central corneal thickness (P=0.28) and AL (P=0.14), the mean subfoveal CT was 98.56µm±31.37µm. In the subgroup with glaucoma, the mean subfoveal CT was 51.32µm±18.44µm. The comparison between the two subgroups found a statistically significant difference in subfoveal CT (P<0.0001).
Conclusions Foveal choroidal thickness is reduced in highly myopic eyes with glaucoma. The choroidal thinning can be a useful parameter for the diagnosis and the follow-up of highly myopic patients with glaucoma.

• S047

Adjunctive photodynamic therapy for type 1 choroidal neovascularization associated with thickened choroid

KIM N, Lee W K
Seoul St.Mary's Hospital-College of Medicine-The Catholic University of Korea, Department of Ophthalmology, Seoul, South-Korea

Purpose To evaluate the treatment outcomes of adjunctive photodynamic therapy (PDT) in patients with type 1 choroidal neovascularization (CNV) associated with thickened choroid and refractory to anti-vascular endothelial growth factor (VEGF) monotherapy.
Methods Data on 28 eyes of 28 patients with type 1 CNV with a minimum subfoveal choroidal thickness of 300 µm were reviewed. All showed persistent subretinal and/or intraretinal fluid after at least 4 anti-VEGF injections in the 6 months before adjunctive PDT. No eyes had certain polypoidal lesions on indocyanine green angiography. The main outcomes measured included the rates of complete fluid absorption at 3 months and the change in best-corrected visual acuity (BCVA) at 12 months.
Results At 3 months, complete fluid absorption was observed in 24 eyes (85.7%). The mean central macular thickness significantly reduced from 342±63µm to 242±60µm, and the mean subfoveal choroidal thickness from 386±80µm to 350±91µm compared to baseline (P<.001, P<.001, respectively). Over the 1-year follow-up period, 17 eyes (60.7%) were free from recurrent fluid accumulation. Anti-VEGF injection was mainly used in the re-treatment of persistent or recurrent exudation (mean: 1.5). At 12 months, the mean BCVA significantly improved compared to baseline (20/53 to 20/44, P=.039), and the logarithm of the minimal angle of resolution BCVA improved by ≥0.3 or maintained in 27 eyes (96.4%).
Conclusions Adjunctive PDT in eyes with type 1 CNV with thickened choroid refractory to anti-VEGF monotherapy resulted in complete fluid absorption in most eyes, which translated to visual improvement up to 1 year.

• S048

Treatment of peripheral exudative hemorrhagic chorioretinopathy by intravitreal injections of Aflibercept: report of 4 cases

MALCLES A, Russo A, Agard E, El-Chehab H, Dot C
Desgenettes Hospital, Ophthalmology, Lyon, France

Purpose Peripheral exudative hemorrhagic chorioretinopathy (PEHCR) is a rare disorder characterized by subretinal or sub-pigment epithelial hemorrhage and exudation localized outside the macular region.Some authors consider PEHCR as the peripheral version of age-related macular degeneration while others believe PEHCR is a specific variant of polypoidal choroidal vasculopathy (PCV).
Methods We report 4 cases of PEHCR (3 women and 1 man) treated by intravitreal injections of Aflibercept. The mean age was 78 years (range 62-83 years). In all cases the presence of PCV was confirmed with indocyannine green angiography. Examination revealed peripheral subretinal or sub-pigment epithelial hemorrhage with exudation extented into the macula in all patients. After 2 or 3 intravitreal injections of Aflibercept, PEHCR lesions and submacular exudation significantly regressed.
Results Generally PEHCR has a favorable prognosis, hovewer vision can be threated because of subretinal hemorrhage and fluid extension into the macula. In cases in which the macula appears threatened, intravitreal antivascular endothelial growth factor therapy and /or laser-based therapies may be indicated. Peripheral lesion can be difficult to reach with photodynamic therapy. Intravitreal Aflibercept, with its mechanism of action, may be an effective treatment option to reduce subretinal fluid.
Conclusions PEHCR is not well-recognized by the ophthalmologist and is often misinterpreted as a choroidal melanoma. To our knowledge this is the first report of Aflibercept use and efficacy in this indication.

• S049

Spontaneous subretinal pigment epithelium hemorrhage

HALFELD FURTADO DE MENDONCA R (1), De Oliveira Maia JR. O (2)
(1) Studio Oftalmologico Halfeld, Ophthalmology, Rome, Italy
(2) Monte Tabor Foundation. São Rafael Hospital, Ophthalmology, Salvador BA, Brazil

Purpose To describe a case of spontaneous subretinal pigment epithelium hemorrhage in a high myopic patient.
Setting: Subretinal hemorrhage is an accumulation of blood between the neurosensory retina and the retinal pigment epithelium. Sub-RPE (retinal pigment epithelium) hemorrhage is located between the RPE and Bruch's membrane.
Methods A 22 year old high myopic Brazilian man complained of acute blurred vision in his left eye over the past 2 days. The patient had no trauma and systemic pathology. Visual acuity in the right eye was 20/20 and in the left eye counting fingers (3 meters). The intraocular pressure and biomicroscopy were normal. Fundus examination of the right eye was normal. Fundus examination of the left eye showed a macular hemorrhage with well-defined borders.
Results The patient underwent optical coherence tomography (OCT), fluorescein angiography (FA) and Indocyanine green (ICG) angiography. In the OCT was evident the sub-RPE hemorrhage. Choroidal neovascularisation was not detected in any exam including ICG. No surgery was performed, only observation. At 30-days follow-up, the visual acuity in the left eye was 20/40. Fundus examination showed an absorption of the sub-RPE hemorrhage.
Conclusions Subretinal hemorrhage may cause retinal damage through a number of mechanisms. Sub-RPE hemorrhages have well-defined borders attributed to the tight cell junctions among RPE cells. Good visual outcome is sometimes possible in selected patients with submacular hemorrhage managed without surgical intervention. The OCT is an important tool to localize the level of the hemorrhage. The recover of the visual acuity of the present case is probably due to the healthy retinal pigment epithelium and photoreceptors prior to the hemorrhage.

• S050

Myofibroblasts in proliferative diabetic retinopathy can originate from infiltrating fibrocytes and through endothelial-to-mesenchymal transition (EndoMT)

ABU EL ASRAR A (1), De Hertogh G (2), Van den Eynde K (2), Alam K (3), Van Raemdonck K (4), Opdenakker G (4), Van Damme J (4), Geboes K (2), Struyf S (4)
(1) King Abdulaziz University Hospital, Ophthalmology, Riyadh, Saudi Arabia
(2) University of Leuven, Laboratory of Histochemistry and Cytochemistry, Leuven, Belgium
(3) King Saud University, Ophthalmology, Riyadh, Saudi Arabia
(4) University of Leuven, Rega Institute for Medical Research- Dept. of Microbiology and Immunology, Leuven, Belgium

Purpose The fibrovascular epiretinal membranes from patients with proliferative diabetic retinopathy (PDR) are characterized by the accumulation of a large number of myofibroblasts. We explored the hypothesis that proliferating endothelial cells via endothelial-to-mesenchymal transition (EndoMT) and/or bone marrow-derived circulating fibrocytes contribute to the myofibroblast population present in PDR membranes.
Methods Epiretinal membranes from 14 patients with PDR were studied by immunohistochemistry. In addition, we investigated the phenotypic changes that take place in human retinal microvascular endothelial cells following exposure to transforming growth factor-β1 (TGF-β1), connective tissue growth factor (CTGF) and the proinflammatory cytokines interleukin-1β (IL-1β) and tumor necrosis factor-a (TNF-a).
Results All membranes contained neovessels expressing the endothelial cell marker CD31. CD31+ endothelial cells co-expressed the fibroblast/myofibroblast markers fibroblast-specific protein-1 (FSP-1) and a-SMA, indicative for the occurrence of endoMT. In the stroma, cells expressing FSP-1, a-SMA, the leukocyte common antigen CD45, and the myelomonocytic marker CD11b were detected. Double labeling showed co-localization of CD45 with FSP-1 and a-SMA and co-localization of CD11b with a-SMA and matrix metalloproteinase-9, demonstrating the presence of infiltrating fibrocytes. Retinal microvascular endothelial cells changed morphology upon cytokine exposure, lost the expression of endothelial cell markers (endothelial nitric oxide synthase and vascular endothelial-cadherin) and started to express mesenchymal markers (calponin, snail, transgelin and FSP-1).
Conclusions These results suggest that endothelial cells as well as circulating fibrocytes may differentiate into myofibroblasts in the diabetic eye and contribute to pathologic fibrosis in PDR.

• S051

Stimulation of TLR4 Increases Angiogenic and Anti-Angiogenic Gene Expression in Choroidal Endothelial Cells

STEWART E (1), Wei R (1), Uribe M (2), May S (2), Amoaku W (1)
(1) University of Nottingham, Academic Ophthalmology- Division of Clinical Neuroscience, Nottingham, United Kingdom
(2) University of Nottingham, Nottingham Arabidopsis Stock Centre- School of Biosciences, Nottingham, United Kingdom

Purpose The Toll-like receptor (TLR) family initiate the innate immune response in reaction to invading microbes. Studies confirm the expression of TLRs in a variety of ocular tissues and cells, and it has also been suggested that selected TLRs may be associated with geographic atrophy and neovascularisation in age-related macular degeneration, diabetic retinopathy and other vascular and inflammatory diseases of the ocular posterior segment. However, the exact mechanisms of TLR stimulation and the mechanism of endothelial inflammatory and angiogenic effects have not been defined.
Methods Microarray analysis was performed on primary human choroidal endothelial cells stimulated with LPS, a specific TLR ligand. Microarray results were validated using qPCR and the functional significance of increased factors were investigated using proliferation and migration assays.
Results Microarray indicated a large increase in expression of angiogenic (e.g. CCL2, IL-8) and anti-angiogenic (e.g. CXCL10, CXCL11) molecules. The fold change in expression of these molecules was validated using qPCR and the secretion using ELISA. Reported angiogenic molecules were confirmed to have a pro-angiogenic effect in vitro.
Conclusions This profiling of factors increased during TLR4 stimulation will help inform our understanding of inflammation in choroidal vascular diseases, as well as the development of future treatments for intraocular vascular diseases.

Commercial interest

• S052

Development of Diabetic Retinopathy in a 22-Week Old Homozygous Ins2Akita Mouse: A Case Study

DENIRO M , AlQahtani A , AlAhmar S , AlMohanna F
King Faisal Specialist Hospital, Cell Biology, Riyadh, Saudi Arabia

Purpose Mice homozygous for *Ins2Akita* develop type 1 diabetes mellitus. These animals die by 12 weeks old age due to rapid and severe hyperglycemia, which leaves the mice with a short window period to manifest diabetic retinopathy (DR). Here we report the rare development of DR in a 22 week-old male Akita mouse.
Methods Electroretinography (ERG) and spatial-domain optical coherence tomography (SD-OCT) imaging as a measure of visual function, which was coupled to fluorescein angiography (FA) and trypsin digestion (TD).
Results The homozygous mouse exhibited hyperglycemia and retinal complications including early signs of vascular damage consistent with DR. TD demonstrated the presence of pericyte ghosts, whereas FA exhibited the manifestation of retinal neovascularization, vascular leakage and microaneurysm formation. ERG recording and OCT imaging were sensitive in detecting the degree of retinal degeneration and RPE tear as compared to the wildtype control. The RPE tear created an area where photoreceptors have no RPE support. Scotopic ERG analysis exhibited significantly faster b-wave responses as compared to wildtype control. Further analysis using b/a-wave ratio revealed a strikingly disproportionate reduction in the b- and a-wave amplitudes. SD-OCT demonstrated a reduction in the overall retinal thickness (OS-NFL) of homozygous Ins2Akita mouse but not age-matched control.
Conclusions Our study reports and for the first time the rare development of full-blown clinical expression of diabetic retinopathy in a 22-week old homozygous Akita.

• S053

Correlation of Different Circulating Endothelial Progenitor Cells to Stages of Diabetic Retinopathy in patients with type 2 diabetes mellitus

WU Z, Ty M, Wang F
Wuxi NO.2 People's Hospital, Department of Ophthalmology, Wuxi, China

Purpose To investigate vasculogenic endothelial progenitor cells (EPCs) in patients with type 2 diabetes mellitus (T2DM) with or without diabetic retinopathy (DR).
Methods A case-control study comparing 20 normal controls (CO) and 60 patients with T2DM with and without DR was performed. Patients with DR were studied and staged according to ETDRS severity scale.60 patients were included: 20 without DR (NDR), 20 with nonproliferative DR (NPDR), and 20 with proliferative DR (PDR). EPCs (CD34/CD309) were enumerated by flow cytometry.
Results The content of EPCs in PDR group (0.0316±0.0294) % was significantly higher than that of the other three groups($\chi2$=43.780, P <0.05).The content of EPCs of CO group (0.0179±0.0047) % was higher than that of the NPDR group (0.0123±0.1137) % and the NDR group (0.0151±0.0086) % too,but the difference was not significant($\chi2$=5.244, P =0.73), There was no significant difference of content of EPCs between NPDR group and the NDR group ($\chi2$=6.016, P =0.12).
Conclusions In patients with T2DM with DR, EPCs undergo stage-related regulation. In nonproliferative retinopathy, a reduction of EPCs was observed, and in proliferative retinopathy,a dramatic increase of mature EPCs was observed.

• S054

Dexamethasone reverses the effects of high glucose on human retinal endothelial cells in vitro

STEWART E, Saker S, Amoaku W
University of Nottingham, Academic Ophthalmology, Nottingham, United Kingdom

Purpose Diabetic retinopathy is the leading cause of preventable blindness in the working population and its prevalence continues to increase as the worldwide prevalence of diabetes grows. The main cause of visual loss in diabetic eye disease is diabetic macular oedema caused by an increase in microvascular endothelial permeability. Endothelial cell permeability is influenced by multiple factors which have not been fully elucidated, particularly in human models. Inflammation has been reported in the pathogenesis of diabetic retinopathy and the potential use of anti-inflammatory agents such as the glucocorticoid dexamethasone is being extensively studied.
Methods The effect of high glucose (25 mM) and dexamethasone on retinal endothelial cell proliferation and permeability were assessed using Cell-8 proliferation reagent and passage of Evan's blue albumin, respectively. qPCR was used to quantify gene expression of selected tight junction molecules (Occludin, Claudin-5, JAM-A and JAM-C) and adheren junction (VE-Cadherin) molecules with high glucose and dexamethasone.
Results High glucose decreased endothelial cell proliferation and this effect was reversed by dexamethasone. High glucose conditions significantly increased endothelial cell permeability and this effect was decreased with dexamethasone treatment for 24 and 72 hours. In retinal endothelial cell exposed to high glucose claudin-5, occludin and JAM-A gene expression were reduced and that of JAM-C increased when evaluated with qPCR; dexamethasone was effective in partially reversing these changes.
Conclusions Dexamethasone reverses high glucose induced alterations in retinal endothelial cell behaviour.

Commercial interest

• S055

The effect of glucose and insulin on the susceptibility of cultured photoreceptor-like cells to hypoxia

LAYTON C, DE MORAES G
University of Queensland, Gallipoli Medical Research Institute, Greenslopes, Australia

Purpose Diabetes causes a retinal neuropathy, however whether glucose itself is beneficial to stressed retinal neurons is controversial. This investigation aimed to assess the effect of glucose on the resilience of cultured photoreceptor-like cells to hypoxia.
Methods 661W cells were cultured in serum free media and 5mM glucose. Cellular insult and damage after CoCl2 induced hypoxia was measured by caspase 3/7 activation, annexin V binding and propridium iodide marking on flow cytometry and confirmed by immunofluorescence. hif 1α, VEGF expression and akt phosphorylation were assessed with primary conjugated antibodies and flow cytometry.
Results In 5mM glucose, hypoxia increased hif 1α activation and led to cell death by both apoptosis and necrosis in a dose dependent manner. Higher glucose levels increased hypoxia induced apoptosis and cell death. Photoreceptor-like cells expressed the insulin receptor, and the increase in apoptosis associated with 25 mM glucose was blocked by insulin treatment, which increased intracellular levels of phosphorylated akt, decreased VEGF production and decreased caspase 3 activation and Annexin binding. However in increased necrosis resulted in no significant difference in hypoxic cell death compared with 5 mM glucose. These effects of insulin were partially blocked by the PI3K inhibitor wortmannin, but not by PKC inhibition with chelerythrine.
Conclusions 661W photoreceptor-like cells were less resilient to hypoxia in "diabetic" glucose conditions. Insulin decreased apoptosis to levels equivalent to "non-diabetic" hypoxic cells, but increased necrosis led to no change in the percentage of dead cells. An insulin induced shift to cell death by necrosis in hypoxic photoreceptors may be one mechanism of the initial exacerbation of diabetic retinopathy with intensive treatment.

• S056

Insulin-induced dilatation of porcine retinal vessels in vitro is most pronounced in precapillary arterioles

JENSEN P S, Bek T
Aarhus University Hospital, Department of Ophthalmology, Aarhus, Denmark

Purpose Impaired retinal blood flow is involved in the pathophysiology of diabetic retinopathy, and it has been shown that the smaller and larger retinal vessels may contribute differently to these flow changes. Diabetes mellitus is accompanied with changes in a number of metabolic parameters including a reduced effect of insulin. However, the vasoactive effects of insulin on retinal vessels with different calibers have not been studied in detail.
Methods Porcine hemiretinas were mounted in a newly established experimental model specifically developed for studying diameter changes of retinal vessels with different caliber. Changes in the diameter of larger arterioles (25 µm or larger), pre-capillary arterioles (10-25 µm) and capillaries (smaller than 10 µm) were studied after intravascular and extravascular addition of insulin in retinal vessels preconstricted with the prostaglandin analogue U46619 from altogether 6 hemiretinas from different animals.
Results Insulin dilated preconstricted arterioles and pre-capillary arterioles significantly after both intravascular and extravascular application ($p<0.01$ for all comparisons), but had no significant effect on the diameter of capillaries after intravascular ($p>0.07$) and extravascular ($p>0.31$) application. The dilating effect of insulin was significantly more pronounced for pre-capillary arterioles than for the two other vessel types after extravascular application ($p<0.01$).
Conclusions Insulin dilates preconstricted retinal vessels, but the effect is most pronounced in pre-capillary arterioles. This may have importance for understanding disturbances in retinal blood flow in diabetic retinopathy.

• S057

Prevalence of diabetic retinopathy in children and adolescents with type 1 diabetes in Helsinki, Finland, 7-15 years after diagnosis

GRASBECK S (1), Gräsbeck T (1), Miettinen P J (2), Summanen P A (1)
(1) HYKS, Silmäklinikka, HUS/Helsinki, Finland
(2) HYKS, Lastenklinikka, HUS/Helsinki, Finland

Purpose The study focuses on the prevalence of diabetic retinopathy (DR) in children and adolescents who were diagnosed from 1999 to 2004 in Helsinki with type 1 diabetes (T1D) under the age of 15 years and subsequently photographed in 2011-2014.
Methods Fundus images of the patients were taken as a part of clinical follow-up at the Department of Pediatrics if aged 10–18 years, and at Herttoniemi Hospital if older than 18 years. Of the 238 patients, 201 (84 %) were included in this retrospective study (another 23 patients had moved from Helsinki, one patient never attended the fundus photography sessions, two had not yet been photographed due to young age, 10 patients who were transferred to adult care did not attend screening as planned, and one patient had died). The presence and severity of DR was determined from 60° fundus images taken with a digital Canon CF-60UD camera with a green filter by one observer (SG) using ETDRS classification. The eye with more advanced DR level represented the patient.
Results Of the 201 patients, 106 (53%) were males. The median age at diagnosis of T1D was 8 (range, 0.8–14) years. At the time of fundus imaging the median age was 19 (range, 10–28) years, and the median T1D duration was 11 (range, 7–15) years. Altogether 123 (61%; 95%CI, 54-68) patients had DR of whom the majority (113; 92%; 95%CI, 86-96) had mild DR (level 20 or 35). One patient had neovascularization on the retina. The age of the youngest patient with DR was 10 years. Of the 10 patients who did not attend fundus imaging in adult care, nine had had no DR and one had level 20 DR when analyzed in the pediatric unit.
Conclusions Our results indicate that over half of the young T1D patients in Helsinki have DR after a median duration of 11 years.

• S058

Hospital prevalence of visual of visual impairment caused by diabetic retinopathy

ROCHA DE SOUSA A (1), Tavares-Ferreira J (2), Perestrelo S P (2), Lima-Ramos P (3), Batista A M (3), Santana R (4), Macedo A F (3)
(1) Department of Senses Organs- faculty of Medicine- University of Porto, Ophthalmology, Porto, Portugal
(2) Centro Hospitalar de São João, Ophthalmology, Porto, Portugal
(3) Centre/Department of Physics and Optometry- University of Minho- Braga- Portugal, Lab. of Vision Rehabilitation, Braga, Portugal
(4) Universidade Nova de Lisboa, Escola Nacional de Saúde Pública, Lisboa, Portugal

Purpose To investigate cases of visual impairment caused by diabetic retinopathy (DR) in a hospital population.
Methods As part of an observational study to estimate the prevalence and costs of visual impairment in Portugal (PCVIP study), clinical records of all patients attending the ophthalmology department of a tertiary hospital were analysed looking for patients meeting the inclusion criteria. Inclusion criteria were: i) presenting visual acuity in the better eye <5/10 (20/40) and/or ii) visual field less than 20deg. Diagnosis of cases with VI were classified according with ICD9. Results reported here were selected from the total number of patients with VI by filtering ICD9 codes staring by 362.
Results In 12 weeks, 1920 cases of VI were detected, 586 (31%) caused by any type of DR. From those: 54% were caused by non-proliferative-DR, 40% by proliferative-DR and 6% by diabetic macular oedema. The mean age of the patients with VI caused by DR was 69.4 (sd=9.5) years and 57% were female. The estimated hospital prevalence (for 52 weeks) of VI caused by DR is 39% (95%CI = 38-41).
Conclusions Our results show that DR remains the leading cause of VI in the population attending our hospital. Information about the number of patients reaching VI will be fundamental to assess the cost-benefits of treatments and public health campaigns to reduce the burden of diabetic retinopathy in Portugal.

Commercial interest

• S059

Prognostics factors of poor functionally response in ranibizumab treatment for diabetic macular edema

JUILLIEN M (1), Deken-Delannoy V (2), Labalette P (1)
(1) HÔPITAL HURIEZ, OPHTALMOLOGIE, Lille, France
(2) MAISON RÉGIONALE DE LA RECHERCHE CLINIQUE, STATISTIQUES, Lille, France

Purpose Purpose was to identify prognostics factors of poor functional response to anti- VEGF (ranibizumab) in diabetic macular edema (DME).
Methods This retrospective study enrolled 36 eyes with DME treated with intravitral ranibizumab injections. The main outcome measures where the change in best corrected visual acuity (BCVA) after 12 months of treatment and its correlations with clinical findings.
Results BCVA at baseline examination was 61+/- 16 letters. In the final control after 12 months following injection, the median value of BCVA increased to 67+/- 18 letters. Two groups were analyzed: the responder group (22 eyes or 61%) corresponding to patients with an increase in visual acuity at 12 months and non-responders (39%). Sex, age, number of IVT, the focal laser history, blood pressure and diabetes duration evolution were similar in both groups. The median HbA1c was not significantly different between the 2 groups (p = 0.80). Patients who have received prior treatment (over 3 months before the first injection of ranibizumab) *i. e.* intravitreal injections of bevacizumab or intravitreal or sub-Tenon triamcinolone acetonide injections were significantly more numerous in the non-responder group (71.43% versus 27.3%, p = 0.0093). Best visual acuity was significantly different between the 2 groups at 3 months and 6 months compared to baseline (10.4 versus 2 letters, p = 0.02 at 3 months and 5 letters versus -2, p = 0.0004 at 6 months). Nine of the 19 eyes with available pictures of the fundus (47%) had extra-foveal exudates. 89% of these patients were responders but the small number of patients did not allow statistical analysis.
Conclusions In our study, the presence of previous treatments and the lack of response at 3 and 6 months are associated with poor functional response that could justify a management change.

• S060

Correlation of hyperreflective foci, status of photoreceptor layer, and visual acuity in diabetic macular edema

CHEBIL A , Ben Abdallah M , Kort F , Hassairi A , Maamouri R , El Matri L
Hedi Rais institute of Ophthalmology-, Department B of Ophthalmology-, Tunis, Tunisia

Purpose To investigate the correlation of hyperreflective foci**,** photoreceptor integrity and visual acuity (VA) in patients with diabetic macular edema (DME).
Methods Seventy-eight patients (114 eyes) with DME were analyzed retrospectively with Spectral-domain optical coherence tomography (SD-OCT).
Results SD-OCT showed that 28 eyes (24,5%) had hyperreflective foci in the inner retinal layers, and 66 eyes (57.9%) had hyperreflective foci in the outer retinal layers. The logMAR VA was significantly (P<.0001) worse in eyes with hyperreflective foci in the outer retinal layers than in eyes without them (0.478±0.241 vs 0.133±0.233, respectively). Disruption of the ellipsoid zone and ELM line on OCT were significantly (respectively P<.0001 and P<.0001) associated with both hyperreflective foci in the outer retinal layers and poor logMAR VA.
Conclusions The presence of hyperreflective foci in the outer retina is closely associated with a disrupted ELM and ellipsoid zone on SD-OCT images and decreased VA in DME.

• S061

Automatic method to distinguish manifestation areas of early diabetic retinopathy from image artefacts by using L*u*v* colour space

SUZUKI N (1), Yamane K (2)
(1) National Institute of Technology- Numazu College, Department of Mechanical Engineering, Numazu, Japan
(2) Hiroshima University, Ophthalmology and Visual Science, Hiroshima, Japan

Purpose The RGB colour space was converted into seven different colour spaces: XYZ, CMY, HSL, HSV, HSI, L*a*b* and L*u*v*. The L*u*v* colour space presented optimal results, with the highest sensitivity and best reproducibility. We employed three-dimensional analysis of L*u*v* colour spaces to detect early diabetic retinopathy.
Methods Six patients with small haemorrhages, hard exudates and photocoagulation marks were evaluated using fundus photography, which revealed image artefacts in the fundi of some patients. We constructed an experimental device similar to the optical system of a fundus camera, and created artificial eyes of the fundus, which were painted with four different colours. The image artefacts were photographed under each artificial eye using the experimental device. We analysed all images using Scilab 5.4.0 and SIVP 0.5.3 software. The software interpreted the values of the L*u*v* colour space as a three-dimensional graph, which was modified using a Gaussian filter.
Results We calculated the difference between the manifestation and perimanifestation areas and image artefact and periartefact areas using the L*u*v* values. The L*u*v* values' ratios of the image artefact to manifestation areas in the human eye were as follows: haemorrhage (6.2, 11.4, 7.4); hard exudate (3.2, 7.7, 2.5) and photocoagulation mark (8.1, 3.9, 6.2).
Conclusions L*u*v* colour space is an effective mean of differentiating between small haemorrhages, hard exudates and photocoagulation marks from image artefacts.

• S062

Choroidal Thickness and Systemic Examination in Diabetic Patients without Diabetic Retinopathy

CARDIGOS J (1), Vicente A (1), Costa L (1), Crisóstomo S (1), Marques N (1), Cunha J P (1), Pinto L A (2), Ferreira J (1)
(1) Centro Hospitalar de Lisboa Central, Ophthalmology, Lisbon, Portugal
(2) Faculdade de Medicina da Universidade de Lisboa, Pharmacology and Ophthalmology, Lisbon, Portugal

Purpose The choroidal circulation receives nearly 95% of ocular blood flow and it is essential for a normal retinal structure and function. Recently, several clinical studies showed a variation in choroidal thickness (CT) even before the presence of diabetic retinopathy (DR), which the meaning remains uncertain and questionable. Our objective was to analyze and correlate the CT with the disease duration, systemic blood pressure (SBP) and analytic evaluation.
Methods Prospective, observational case-control study. A complete ophthalmological examination was performed, including dynamic contour tonometry and axial length. CT was assessed by a non-invasive procedure using an OCT (Spectralis Heidelberg Engineering) with an enhanced depth mode (EDI) at 13 different locations (subfoveal and 3 measurements 500 µm apart in all 4 directions - nasal, temporal, superior and inferior). The SBP was measured and an analytical evaluation was performed, including glycemia, glycosylated hemoglobin - HbA1c, lipid parameters, renal function, ionogram and microalbuminuria. Correlation between variables was explored using Spearman correlations.
Results The study included 65 diabetic patients without DR (36 females; mean age 67.23 ± 9.08 years), with an average disease duration of 90.42 ± 81.82 months. The CT didn´t showed a correlation with disease duration, SBP, glycemia, HbA1c, renal function, lipid parameters, homocysteinemia, natremia or microalbuminuria. However, the CT was positively correlated with potassium and chlorine serum levels in 5 points, with statistic significance (r between 0.26 and 0.31, $p < 0.05$).
Conclusions CT may be positively influenced by serum levels of potassium-chlorine in diabetic patients but not in healthy controls. These abnormal CT relationships can be detected even with no visible DR. Further studies are needed to explore these differences.

• S063

Evaluation of intraocular pressure, choroidal and retinal thickness measurements using optical coherence tomography in non-diabetic haemodialysis patients

STRUPAITE R (1), Skvarciany I (1), Noreikyte M (1), Mockeviciute E (1), Galgauskas S (1), Rimsevicius L (2), Cimbalas A (1), Asoklis R (1)
(1) Vilnius University, Center of Eye Diseases, Vilnius, Lithuania
(2) Vilnius University, Center of Nephrology, Vilnius, Lithuania

Purpose The purpose of this study was to evaluate the ocular findings in non-diabetic patients with chronic renal disease undergoing haemodialysis (HD).
Methods We performed a pilot study in Vilnius University Hospital Santariskiu Klinikos departments of Nephrology and Ophthalmology. In this study 7 patients (14 eyes) with chronic renal disease undergoing haemodialysis underwent an ophthalmic examination including visual acuity (VA), intraocular pressure (IOP), central foveal thickness (CFT) and subfoveal choroidal thickness (SFCT) measurements using high-definition optical coherence tomography (OCT, Spectralis; Heidelberg Engineering) line scans with the activated enhanced depth imaging mode, (central corneal thickness (CCT) and endothelial cell density (CD). Each patient underwent examination 30 minutes before and 30 minutes after a HD session.
Results 14 eyes of 7 patients with chronic renal failure (CRF) undergoing HD were included. 5 males (35,5 %) and 2 females (14,3 %) participtated. Patients mean age was 72,71 ± 7,67 years. The mean VA was 0,83 ± 0,16. The mean IOP increased from 12,28 ± 1,89 to 14,14 ± 4,75 mmHg (p = 0,1). The change was statistically insignificant. The mean central foveal thickness decreased statistically insignificant from 227,07 ± 15,71 to 225,57 ± 14,10 µm (p = 0,69). The mean subfoveal choroidal thickness before HD was 207,57 ± 50,71 µm, after HD - 194,85 ± 55,39 µm (p = 0,016). There was a statistically significant decrease in the choroidal thickness before and after haemodialysis (p = 0.016). The mean CCT was 529,77 ± 32,12 µm. The mean CD 2777,11 ± 380,15 cells/mm2.
Conclusions Haemodialysis with a high ultrafiltration volume did not alter the retinal thickness and IOP but caused a significant choroidal thinning in non-diabetic end-stage CRF patients.

• S064

Retinal Layers Changes in Diabetic Patients without Diabetic Retinopathy

FERREIRA J (1), Vicente A (1), Proença R (1), Costa L (1), Dias-Santos A (1), Santos B (2), Cunha J P (1), Abegão Pinto L (3)
(1) Centro Hospitalar Lisboa Central, Ophthalmology, Lisbon, Portugal
(2) Associação Médica Olhar bem, Statistic, Lisbon, Portugal
(3) Faculdade Medicina Universidade Lisboa, Pharmacology & Ophthalmology, Lisbon, Portugal

Purpose To evaluate retinal layers thickness in diabetic patients without diabetic retinopathy (DR) using spectral-domain optical coherence tomography (SD-OCT). To correlate retinal layers thickness in diabetic patients with disease duration, systemic blood pressure (BP), glycemia, glycosylate haemoglobin (HbA1c), intraocular pressure (IOP) and ocular pulse amplitude (OPA).
Methods Prospective, observational case-control study. A total of 175 eyes from 175 patients (125 diabetic patients without DR; 50 healthy controls) were recruited from the outpatient clinic in a tertiary center. A complete ophthalmological examination was performed (visual acuity, refraction, Goldmann applanation and dynamic contour tonometries, fundoscopy, axial length and SD-OCT-Spectralis®). After automated retinal segmentation the thickness of each layer was calculated in the 9 ETDRS areas.
Results A significant increase of retinal nerve fiber layer (RNFL) thickness in inner and outer rings was found in diabetic eyes vs. controls (p between <0.0001 and 0.02). Thickness was also increased in specific sites of ganglion cell layer (GCL), inner nuclear layer (INL) and retinal pigment epithelium (RPE) in diabetic eyes (p between 0.001 and 0.03). A significant decrease of outer plexiform layer (OPL) was detected in diabetic eyes at two sites of the inner ring (p=0.04 and p<0.0001). The different retinal layers weren't correlated with systemic BP, glycemia, HbA1c, IOP and OPA, but the photoreceptor layer was negatively correlated with disease duration at 3 sites (r between -0.18 and -0.21, p <0.05).
Conclusions In diabetic patients without DR thickness of the inner retina seems to be increased. This suggests that metabolic and morphological changes of the cells of these inner retinal layers occur early and before the apoptosis and neural degeneration.

• S065

Heterogeneous choroidal thickness pattern in diabetic patients without diabetic retinopathy

VICENTE A , Costa L , Cardigos J , Santos A , Amado D , Cunha J P , Abegao Pinto L , Ferreira J
Centro Hospitalar Lisboa Central, Ophthalmology, Lisbon, Portugal

Purpose The authors intend to present an analysis and comparison of the choroidal thickness in more distant superior regions. Choroidal thickness is increased in a heterogeneous pattern superiorly to the fovea in diabetic patients without diabetic retinopathy.
Methods Observational case-control study of 60 eyes of 60 patients with diabetes mellitus type 2 without diabetic retinopathy. A control group of 31 eyes of 31 patients without diabetes with similar demographic features was also created. All the patients were recruited from the same outpatient clinic. Enhanced depth imaging spectral-domain optical coherence tomography (EDI SD-OCT SPECTRALIS®) was performed and high-resolution macular scans were obtained. Choroidal thickness was evaluated 2000µm superiorly to the fovea by manual layer segmentation. Previous studies have validated the validity of using a manual layer segmentation procedure in OCT. Statistical analysis was done with SPSS Statistics. A p value <0.05 was considered statistically significant.
Results Diabetic patients were in average 67.0±9.6years old and 56.7% were male. Average choroidal thickness 2000µm superiorly to the fovea was 287.77±74.32µm in diabetic patients and 249.81±53.96µm in non-diabetic patients. There was a significant increase in choroidal thickness in diabetic patients when compared to non-diabetic patients (T-student, p=0.014).
Conclusions Choroidal thickness can be accurately measured using high-definition macular OCT scans. This study documented structural differences in the choroid associated with diabetes mellitus type 2 that are not only present in the central foveal area as reported in previous studies. Diabetes Mellitus is associated with multiple microvascular dysfunctions that are probably coupled with choroidal vascular modifications that induce changes in thickness.

• S066

Focal choroidal changes on diabetic macular edema

DUARTE L (1), Ruão M (1), Gallego R (2)
(1) *Centro Hospitalar Entre o Douro e Vouga, Ophthalmology, Santa Maria da Feira, Portugal*
(2) *Hospital Universitario y Politécnico La Fe, Unidad de Macula, Valencia, Spain*

Purpose With the increasing interest in choroidal changes in Diabetes, we performed a pilot and prospective study to evaluate the morphological choroidal findings in diabetic macular edema detected with SD-OCT, compared with normal or non-macular edema diabetic eyes.
Methods Two groups of patient were selected: Diabetic patients with no or any stage of diabetic retinopathy with no history of ocular treatment; and non-diabetic patients as normal controls. Patients with other ocular diseases or surgery where not included. Complete ophthalmological exam was performed. A retinography, blood pressure measurement and OCT with the EDI or choroidal acquisition protocol was performed to all patients. For the analysis choroidal thickness was measured using automated calculation after manual segmentation. OCT images were analyzed for morphological changes in the choroidal space and vasculature, and findings were recorded.
Results 47 eyes were included in this study: 11 with macular edema, 16 with non-proliferative diabetic retinopathy, 10 from diabetic patients with no retinopathy and 10 control. Age ranged from 41 to 80 and matched for the sub-groups. Choroidal thickness varied from 75µm to 383 µm and no correlation was found with age, blood pressure or diabetic stage, except for advanced stages of retinopathy and macular edema where it appears to have a change in the architecture of the choroidal vessels with a tendency of vanishing of the large vessels in favor to the choriocapillaris, well related to the subjacent area of retinal active disease and edema.
Conclusions As a pilot study, the results only can direct to larger sample studies in order to look for the meaning of choroidal changes that are being reported in diabetic patients and other ocular diseases. It suggests that thickness changes may be due to specific vascular changes.

• S067

Correlation of visual acuity and central macular thickness in diabetic macular edema

EL MATRI HASSAIRI A , Chebil A , Ben Abdallah M , Maamouri R , Chaker N , El Matri L
Hedi Rais Institute of Ophthalmology, Department B of Ophthalmology, Tunis, Tunisia

Purpose To investigate the correlation of retinal thickness measured with SD OCT and visual acuity in eyes with diabetic macular edema (DME) before and after intravitreal injection of anti-VEGF
Methods Seventy-four patients (96 eyes) with DME who underwent three monthly intravitreal injection of bevacizumab (IVB) as their first treatment. Type of DM, duration, treatment, laboratory examinations, history of cardiovascular disease, hypertension, hyperlipidemia, diabetic nephropathy, were documented. Logarithm of the minimum angle of resolution (logMAR) best corrected visual acuity (BCVA) was evaluated using the international vision test chart. Foveal thickness was measured by SD OCT.
Results The correlation coefficients for visual acuity (VA) versus OCT center point thickness were 0.57 at baseline and 0.47, 0.38, and 0.40 at 1, 3, and 6 months post-laser photocoagulation. A subset of eyes showed paradoxical improvements in VA with increased center point thickening (5-13% at the three time points) or paradoxical worsening of VA with a decrease in center point thickening (12%-24% at the three time points).
Conclusions There is modest correlation between OCT-measured center point thickness and VA, and modest correlation of changes in retinal thickening and visual acuity following focal laser treatment for DME. In addition, paradoxical changes in VA and retinal thickening may be observed. Indeed, retinal thickness only accounts for up to 27% of variability in concurrently measured VA suggesting that other factors are important determinants of VA in the presence of diabetic macular edema.

• S068

Fundus photography as a screening method of diabetic retinopathy in children and adolescents with type 1 diabetes Outcome of the first fundus photography at the age of 9 to 17 years

GRASBECK T (1), Gräsbeck S (1), Miettinen P J (2), Summanen P A (1)
(1) *HYKS, Silmäklinikka, HUS/Helsinki, Finland*
(2) *HYKS, Lastenklinikka, HUS/Helsinki, Finland*

Purpose To study the success of fundus photography in screening of diabetic retinopathy (DR) in children <18 years with type 1 diabetes (T1D) in producing gradable images.
Methods Photographic success of black-and-white macula and optic disc-centered fundus images of both eyes of each patient was graded by one observer (TG) using a slightly modified classification of ARIC. All images were taken with a digital 60° Canon CF-60UD camera. Photography as a whole was graded as 'complete success' if the images of both eyes were at minimum of fairly good quality (i.e. gradable), and 'partial success' if the images of only one eye reached this level.
Results Of the 213 patients photographed for the first time in 2009-2013 at the Department of Pediatrics, 121 (57%) were males. The median age of diagnosis was 8 (range, 1-16) years and at the first photography 11 (9-17) years. At the first photography, the median duration of T1D was 2.3 (range, 0.2-9.6) years and the median HbA1c was 8.5% (range, 6.3-13.8).

At least partial success was reached in 153 (72%; 95%CI, 65-78) patients and complete success in 97 (46%; 95%CI, 39-52) patients. Complete success was equally common among those aged 9-10, 11-12, and 13-17 years (45%, 46% and 47%). The macula-centered images of 177 (83%; 95%CI, 77-88) patients, and the optic-disc centered images of 103 (48%; 95%CI, 41-55) patients were gradable in both eyes. Age at the first photography was not associated with success (p=0.20).
Conclusions Less than half of the first fundus images achieved complete success, but over 70% achieved at least partial success when photography was performed at the age of 9-17 years. No significant associations were identified. Photography is a reliable method for screening of DR also in pediatric setting.

• S069

The effect of panretinal photocoagulation and additive Intravitreal bevacizumab injections on central retinal vessel diameters in diabetic retinopathy

PARK J M (1), Lee S J (2)
(1) Maryknoll Medical Center, Department of ophthalmology, Busan, South-Korea
(2) Haeundae Paik Hospital, Department of Opthalmology, Busan, South-Korea

Purpose To evaluate the effect of Panretinal photocoagulation and additive Intravitreal bevacizumab injections on Central retinal vessel diameters in Diabetic retinopathy.
Methods Changes on central retinal vessel diameters were restrospectively analyzed before and 6 month after panretinal photocoagulation with or without additive Intravitreal bevacizumab injections in patients first diagnosed with diabetic retinopathy. Vessel diameters were measured using IVAN soft ware and Big6 fornula.
Results 21 patients were enrolled, mean age 54.9 years. There were significant decreases in central retinal artery diameters in both groups, with and without additive Intravitreal bevacizumab injections, 6 months after completion of panretinal photocoagulation($p<0.05$), but no significant changes in central retinal vein diameters. Additive Intravitreal bevacizumab injections did not bring the significant changes in central retinal vessel diameters before and after 6 months, compared to vessel diameters treated with panretinal photocoagulation only($p<0.05$).
Conclusions Panretinal photocoagulation has effects on changes of central retinal artery diameters but not central retinal vein diameters, and additive Intravitreal bevacizumab injections did not cause significant additive changes on central retinal vessels in this study. meters before and after 6 months, compared to vessel diameters treated with panretinal photocoagulation only($p<0.05$).

• S070

Intravitreal anti-VEGF treatment for refractory diabetic macular edema

PAPAVASILEIOU E , Quijano C , Younis S
Imperial College NHS Trust, Western Eye Hospital, LONDON, United Kingdom

Purpose To compare anti-VEGF monotherapy with combination treatment of anti-VEGF injections plus macular laser (focal or modified grid) for refractory diabetic macular edema (DMO).
Methods We included patients with DMO who had more than 6 anti-VEGF injections and were examined in the Macula clinic. Our outcomes were change in BCVA, CRT and number of anti-VEGF injections.
Results We included 22 patients (13 males and 9 females) with a mean follow up of 24 months. Mean age was 63.18 years (range: 47-77 years). 4 patients had Type 1 and 18 had Type II diabetes. 86.36% had hypertension and 68.18% hyperlipidaemia on treatment. 22.72% were pseudophakic, 45.45% had bilateral DMO and 45.45% had PRP laser. 70% of patients had Lucentis injections and 30% had Avastin injections. 70% were on anti-VEGF monotherapy and 30% had combination therapy (macular laser plus anti-VEGF injections). Mean baseline BCVA (in letters) was 27.24 and improved to 30.27 on last visit (+6 letters gain). Mean baseline Central Retinal Thickness (CRT) was 518,33µm and decreased to 356.24µm (-162.08µm) on last visit. Mean number of injections was 8.88. Subgroup analysis showed that those who had anti-VEGF monotherapy improved their BCVA during the follow up period to +7.6 letters and those on combination therapy improved to +5.82 letters. CRT decreased from baseline to last visit on both groups.
Conclusions Both treatment groups improved their VA and CRT from baseline, however, anti-VEGF monotherapy had better visual outcomes compared to combination treatment.

• S071

Switching to ranibizumab for diabetic macular edema with persistent fluid on bevacizumab : Who is likely to benefit from the switch?

LEE J H, Lee W K
Seoul St. Mary's Hospital, Department of Ophthalmology, Seoul, South-Korea

Purpose To evaluate the efficacy of switching from bevacizumab to ranibizumab in patients with diabetic macular edema (DME).
Methods The medical records of 41 DME eyes which showed p ersistent fluid after at least three monthly bevacizumab injections, and switched to ranibizumab injection were reviewed. Each patient received a single ranibizumab injection and followed up at 1 month. Anatomic responders to ranibizumab were followed up monthly and given ranibizumab injections on an as-needed basis until 3 months.
Results At 1 month, the mean central foveal thickness (CFT) decreased from 431µm to 349µm (P<.001), and mean best-corrected visual acuity (BCVA) improved from 20/53 to 20/48 (P=.062). Twenty-six eyes (65.9%) were classified as anatomical responders, and the mean CFT improved and maintained until 3 months (439µm to 320µm, P<.001) after repeated injections (mean number: 2.8), while the mean BCVA stabilized (20/59 to 20/54, P=.075) in these eyes. Dry macula were achieved in 9 of 26 eyes at least once during the follow-up period. Favorable anatomic response to ranibizumab at month 1 was related with previous partial response to bevacizumab.
Conclusions Switching to ranibizumab may present an alternative option in the treatment of DME with persistent fluid after repeated bevacizumab injections, and the switch was more effective in eyes that showed partial response to previous bevacizumab.

• S072

Effect of intravitreal dexamethasone implant (Ozurdex®) in the glycemic control of patients with diabetic macular edema

AGARD E (1), El Chehab H (1), Malclès A (1), Russo A (1), Leberre J P (2), Mounier C (2), Dot C (1)
(1) HIA Desgenettes, Ophthalmology, LYON, France
(2) HIA Desgenettes, Endocrinology, LYON, France

Purpose To evaluate the effect of intravitreal dexamethasone implant (Ozurdex®) in the glycemic control of patients with diabetic macular edema (DME).
Methods Ten patients with DME received an intravitreal injection (IVI) of dexamethasone implant (DXE implant, Ozurdex®). The mean age of patients was 72 years +/-13,3 years (range, 54-78 years). Glycated haemoglobin (HbA1C) was analyzed before and three months after IVI. The real-time glycemic readings, throughout the day and night, during at least one week, are provided by a new medical device (Dexcom G4® Dexcom, Fr). The primary outcome analysis was the comparison of HbA1C test before and after IVI. Other data included blood glucose average, the percentage of time spent higher, lower and in glycemic target, and standard deviation over the period.
Results The mean HbA1C test is 7,2% before IVI and 7,5% after IVI (p=0,83). Recording of blood glucose was performed on an average of 10 days +/-3. There is no statistical difference for the mean blood glycemic levels before and after IVI. It was 155,4 +/- 23,1 mg/dl before IVI and 163,3 +/- 32,8 mg/dl after IVI (p=0,25). No significant difference was found between extreme values of blood glucose: the mean highest values was 321,1 mg/dl versus 349 mg/dl (p=0,35), the mean lowest values was 54 mg/dl versus 64,57 mg/dl (p=0,40).
Conclusions This new continuous glucose monitoring system is indicated for detecting trends and tracking patterns in patients with diabetes. To our knowledge, this is the first study that analyses the glycemic control in human after DXE implant IVI with a daily continuous glucose monitoring. In this study, the use of intravitreal steroids in diabetic patients doesn't alter glycemic control or increase blood glucose levels. These preliminary results must be confirmed by further studies with a larger cohort.

• S073

Efficacy and safety of ranibizumab in diabetic macular edema : real life study

HRARAT L (1), Fajnkuchen F (2), Sarda V (2), Grenet T (2), Buffet S (2), Chaine G (2), Giocanti-auregan A (2)
(1) Avicenne, Bobigny, Stains, France
(2) Avicenne, Bobigny, Paris, France

Purpose To evaluate the efficacy and safety of ranibizumabin patients with vision loss secondary to diabetic macular edema (DME).
Methods Retrospective analysis of a cohort of patients withvision loss (VA) due to DME and treated by ranibizumab. Patients were examined before treatment and during treatment every 4 to 6 weeks. Ophthalmologic examination included:measure of the best corrected visual acuity (BCVA) on the ETDRS scale, examination at the slit lamp, fundus, and SD-OCT (Cirrus 5000, Carl Zeiss Meditec). All patients receiveda loading dose of 3 monthly injections followedby re-treatments on an as-needed basis (PRN regimen) The primary endpoint was the change in visual acuity at 12 months. The other criteria assessed were central retinal thickness (CRT) after loading dose, and at12 months, and the number ofintravitreal injections (IVT) during the first year of follow-up.
Results 109 eyes of 79 consecutive patients treateded since November 2012 have been included. At baseline the mean BCVA was 48.77 letters, the CRT was 517 microns. At 12 months the average BCVA was of 60.80 letters ($p < 0.05$), with an average VA gain of +14.67 letters and 25% of patients had a BCVA> 70 letters. The mean CRT after 3 injections was 344.32 microns ($p < 0.05$) and 332 microns ($p < 0.05$) at 12 months, with 57.23% of patients with CRT ≤ 300 microns. At 12 months the average VA in patients with CRT ≤ 300 microns was 63.51 letters ($p < 0.05$) and the average AV inpatients with ERC> 300 .microns was 57.39 letters ($p < 0.05$). The average number of IVT performed during the first year of follow up was 5.59. No serious adverse event was noted.
Conclusions Pivotal studies have clearly shown the benefit of ranibizumab treatment of vision loss due to DME. This study in a "real life"setting confirms the results obtained in randomized trials.

• S074

Outcomes of using intravitreal ranibizumab to treat patients with ischaemic diabetic maculopathy.

BEGUM S, Lockwood A , Mourtzouko S
Queen Alexandra Hospital, Ophthalmology, Portsmouth, United Kingdom

Purpose To report the functional and anatomical outcomes of using intravitreal ranibizumab (IR) for patients with ischaemic diabetic maculopathy (IDM).
Methods Retrospective analysis of 11 consecutive patients treated with IR for IDM from Nov 2008 to May 2015. The number of injections, fluorescein fundus angiography (FFA) results, visual acuity (VA) and central retinal thickness (CRT) prior to commencing IR were recorded. VA was assessed with logMAR.
Results Three eyes were excluded as one had a history of vein occlusion, one was amblyopic and the other patient had multiple vitreous haemorrhages and vitrectomy. There were equal numbers of females and males, the average age was 67 (34-82 years) and patients had on average 5 (range 3-11) injections of IR. Average length of follow up was 13 months (5-18 months). On FFA 4 patients had enlargement of foveal avascular zone (FAZ), 1 patient had fragmentation of FAZ, 1 patient had deregulation of FAZ and 1 patient had an increase in FAZ. The average initial VA was +0.9 (+0.3 to +1.78) and the average final VA was +1.05 (+0.6 to +1.78). The average change between initial and final VA was +0.15. Initial average CRT was 558 (306-785) reducing to an average of 447 (197-892) at the final follow up. The average CRT reduction was 111 between initial and final CRT.
Conclusions Anatomical thickness appears to be reduced with IR injections, but without improvement in visual acuity. No adverse complications were noted with this regimen.

• S075

Role of SD-OCT in the follow-up of a patient with macular edema associated with mucopoysaccharidosis type II (Hunter syndrome) undergoing idursulfase enzyme replacement therapy

SANCHEZ J I (1), ASCASO F J (1), Perez I (1), Almenara C (1), Esteban O (1), Martinez M (1), Idoate A (1), Torralba M A (2)
(1) Hospital Clínico Universitario Lozano Blesa, Ophthalmology, Zaragoza, Spain
(2) Hospital Clínico Universitario Lozano Blesa, Internal Medicine, Zaragoza, Spain

Purpose Mucopolysaccharidosis (MPS) type II (Hunter syndrome) is a variable, progressive, multisystem disorder including severe airway obstruction, cardiomyopathy, skeletal deformities and neurological problems. It is an X-linked recessive disease caused by deficiency of the lysosomal enzyme iduronate-2-sulphatase, leading to accumulation of glycosaminoglycans. Several ophthalmological disorders, including corneal opacities, glaucoma and retinal degeneration, have been previously reported. This is the first case of bilateral macular edema associated with MPS II. The patient underwent idursulfase enzyme replacement therapy with good response. We point out the utility of spectral domain optical coherence tomography (SD-OCT) in the diagnosis and follow-up of this condition.
Methods SD-OCT, fundus autofluorescence and retinography were used in the diagnosis and follow-up of the visual disorder.
Results Macular edema was successfully managed with idursulfase enzyme replacement therapy stabilizing visual loss. Central macular thickness measured by SD-OCT decreased significantly.
Conclusions Idursulfase enzyme replacement therapy seems to be a good treatment option for macular edema associated with MPS II. Furthermore, SD-OCT played a key role in the diagnosis and follow-up of this condition.

• S076

Use of directional optical coherence tomography and selected landmarks to determine foveal topography and microstructure. A strategy to characterize differences between normal and expremature cases.

SJÖSTRAND J (1), Rosén R (2), Nilsson M (2), Popovic Z (1)
(1) University of Gothenburg, Department of Ophthalmology, Gothenburg, Sweden
(2) Karolinska institutet, Unit of Optometry/Department of Clinical Neuroscience, Stockholm, Sweden

Purpose To determine the topography of the different layers of the fovea by combining directional and conventional optical coherence tomography (OCT) images and measuring layer thickness at the foveal center (FC) and selected eccentricity positions. Furthermore, to use a normative model of foveal microstructure to characterize signs of immaturity in cases with a history of prematurity.
Methods Selected eyes from normals and young adults with a history of prematurity were imaged using a commercial spectral domain OCT (SD-OCT) system. Centered and displaced SD-OCT entrance beam positions were used to obtain straight and tilted scans, respectively. Horizontal scans through FC with a distinct light reflex were selected for analysis. Straight and tilted SD-OCT images were registered and averaged prior to flattening to the retinal pigment epithelial (RPE) layer. Retinal layer thickness was measured manually at FC and four lateral positions along the temporal and nasal hemi-meridians and corrected for axial length differences.
Results The distance between FC and foveal wall maximum (FWM) was reduced to 4/5 of that of normals in expremature cases with incomplete extrusion of inner retinal layers (IRL) and reduced foveal pit depth. The Henle fibre layer (HFL) and the combined outer segment and RPE layer (OS+) showed little or no change whereas the outer nuclear layer (ONL) was thickened centrally with a more steep decline of the ONL bulge outside FC in expremature.
Conclusions Our pilot study in young adults demonstrates that signs of immaturity may still be present in adult life with changes in foveal topography similar to those present at the age of 6.5 years after extremely preterm birth (Rosén et al., 2015). It may be useful to use the FWM as a major landmark in studies of abnormal fovea.

• S077

Optical Coherence Tomography and Fundus Autofluorescence evaluation in an animal model of Retinal Degeneration

SEGURA F (1,2), Fernandez-Sanchez L (3), Sánchez-Cano A (2,4), Tamarit J M (5), Fuentes-Broto L (2,6), Del Buey M (1,7), Cuenca N (3), Pinilla I (2,7)
(1) University of Zaragoza, Department of Surgery- Gynecology and Obstetrics, Zaragoza, Spain
(2) Aragon Institute for Health Research, ISS Aragon, Zaragoza, Spain
(3) University of Alicante, Department of Physiology Genetics and Microbiology, San Vicente del Raspeig- Alicante, Spain
(4) University of Zaragoza, Department of Applied Physics, Zaragoza, Spain
(5) Bloss Group, Heidelberg Engineering Gmbh, Heidelberg, Germany
(6) University of Zaragoza, Department of Physiology, Zaragoza, Spain
(7) Lozano Blesa University Hospital, Department of Ophthalmology, Zaragoza, Spain

Purpose To evaluate fundus autofluorescence (FAF) and OCT changes comparing with immunohistochemical (ICC) analysis in long term degeneration of P23H rat and to investigate retinal and choroidal vascularization using fluorescein and indocianin green angiography.
Methods Twenty-albino homozygous P23H line 1 rats aging from 18 postnatal days (P18) to 27 months and wild-type albino Sprague-Dawley (SD rats) (2 and 15 months old) were used for this study. Normal pigmented Long Evans (LE) 2 months old rats were used to compare FAF findings. ICC was performed to correlate with the findings of OCT and AF changes.
Results FAF pattern varied from not findings at P18 to a mosaic of hyperfluorescent dots in the rats of 6 months or older. Retinal thicknesses diminished during the time: 205.2 to 183.18 µm in SD rats and 189.88 to 58.15 µm in P23H rats. In long term degeneration, OCT showed severe changes at the retinal layers; ICC helped to identify the cell loss and remodeling changes.
Conclusions Autofluorescent ophthalmoscopy is a non-invasive method that can detect changes in metabolic activity at the RPE in animal models of retinal degeneration in vivo. Retinal vascular plexus changed with aging. OCT showed a diminution of retinal thickness and retinal layer changes with the degeneration. ICC shows a good correlation.

• S078

Three optic disc pit maculopathy case studies by optical coherence tomography images supporting the role of cerebrospinal fluid in this pathology

MARTINEZ M (1), Ascaso J (1), Arias L (2), Filloy A (2), Almenara C (1), Esteban O (1), Del Buey M (1), Cristobal J (1)
(1) Lozano Blesa" University Clinic Hospital, Ophthalmology, Zaragoza, Spain
(2) Hospital Universitari de Bellvitge, Ophthalmology, Barcelona, Spain

Purpose Optic disc pit (ODP) is a rare congenital optic disc abnormality characterized by a localized grayish-white depression usually in the center or inferotemporal part of the optic nerve head. It is generally unilateral (85-90%) and its prevalence is estimated to be 1 in 11,000. Unless the ODP develops maculopathy, patients remain asymptomatic. Serous macular detachment may occur in up to 50% of cases, leading to significant decrease in visual acuity. Although the pathogenesis of ODP maculopathy is unclear, various theories about its onset have implicated fluid entry either from the vitreous cavity or from leakage of cerebrospinal fluid through the peripapillary subarachnoid space. The aim of this study was to evaluate the source of subretinal fluid under the macula in three patients with ODP.
Methods Three different optical coherence tomography equipments (*EDI-OCT Spectralis, Heidelberg; Swept-source OCT, Topcon and Spectral-domain 3D OCT-2000, Topcon*) were used.
Results These OCT images revealed a direct communication between a prominent serous macular detachment and the subarachnoid space through the ODP.
Conclusions These three cases support the theory that in some cases the source of serous macular detachment could be cerebrospinal fluid passing into the retina through the ODP due to an incomplete closure of the embryonic fissure.

• S079

Indocyanine green angiography findings in Stargardt disease

EL MATRI L , Chebil A , Charfi H , Largueche L , Hassairi A
Institut Hedi Rais Of Ophthalmology, Research Laboratory of Oculogenetic LR14SP01-Department B of Ophtalmology., Tunis, Tunisia

Purpose To evaluate indocyanine green angiography (ICGA) findings in Stargardt disease (STGD).
Methods We reported a retrospective and descriptive study of 20 patients (40 eyes) with Stargardt's disease with different stages. All patients underwent a complete ophthalmic examination, fluorescein angiography, indocyanine green angiography (ICGA). Spectral-domain optical coherence tomography (SD-OCT) and fundus autofluorescence were also executed.
Results In 27.5% of eyes affected by STGD, ICGA showed hypocyanescence from the areas of atrophy, more evident in the late phases. SD-OCT revealed morphologically intact choroid in STGD patients with ICGA-imaged dark atrophy. All the remaining eyes showed isocyanescence or mild hypercyanescence from the areas of atrophy in the late phase of ICGA.
Conclusions The ICGA-imaged dark atrophy may be the presence of material that obscures ICGA cyanescence. However, this hypothesis seems unlikely, since SD-OCT images failed to show any deposit between the choroid and the retina. This finding suggests a possible selective damage of the choriocapillaris in STGD.

• S080

Repeatability of wide-field autofluorescence lifetime imaging at the human retina in healthy volunteers

KLEMM M (1), Dietzel A (1), Nagel E (1), Schweitzer D (2)
(1) Technische Universität Ilmenau, Biomedical Engineering Group, Ilmenau, Germany
(2) University of Jena, Experimental Ophthalmology, Jena, Germany

Purpose The detection of metabolic changes in the retina is the goal of fluorescence lifetime ophthalmoscopy (FLIO). We performed an observational clinical study in young healthy volunteers to examine the usability of 55° wide-field fluorescence lifetime images.
Methods The time-resolved retina autofluorescence was measured (scanning laser ophthalmoscope: 55° of fundus, 62µm resolution; excitation: diode laser with pico-second pulses, 473nm, 80MHz repetition rate; detection: spectral channels 500-560nm (ch1) and 560-720nm (ch2), time-correlated single photon counting method) in the right eye of 11 healthy volunteers (28.7±3.6 years). Three repetitive measurements (m1-m3) on different days within one week at a similar time have been performed. All subjects had a crystalline lens and an undilated pupil. A modified 3-exponential approach was applied to determine the fluorescence lifetimes τ. τ were computed on the ETDRS grid and in a 15x15 pixel region 25° superior to the fovea.
Results 49% of the measurements had shadowing effects in the inferior image region caused by eye lashes. τ (mean ± std) over all volunteers are:

	outer ring ETDRS grid		superior region	
	ch1	ch2	ch1	ch2
m1:	350±25ps	255±11ps	348±20ps	260±7ps
m2:	357±27ps	257±12ps	357±20ps	261±7ps
m3:	350±26ps	257±12ps	327±17ps	254±5ps

Results for the inner ring of the ETDRS grid are similar to the outer ring. The coefficient of variation in the superior region is 5.5% in ch1 and 2.5% in ch2. τ of repetitive measurements as well as of ETDRS grid's outer ring and the superior region are within the standard deviation.
Conclusions FLIO measurements in young healthy volunteers using a 55° lens are repeatable. Spectral channel 2 is preferable because of its lower variability.

• S081

Characteristics of Artifacts Associated with Ultra-Wide Field Fundus Image

OH J R, Lee B, Ahn J, Kim Y H, Kim S W
Korea University College of Medicine, Ophthalmology, Seoul, South-Korea

Purpose To evaluate characteristic of artifacts associated with ultra-wide field fundus image.
Methods The retrospective study included 139 eyes of 139 patients who had artifacts in color images using Optomap 200Tx (Optos, DunFermline, UK). The artifact means hyperreflective or hyporeflective shadow due to anterior segment of the eye or vitreous except retina. Types and characteristic of red laser separation, green laser separation and autofluorescence image artifacts within each image were evaluated.
Results All image artifacts were categorized into two groups according to the location of artifacts. There were corneal opacity, cataract and posterior capsular opacity in the anterior artifacts group. And there were asteroid hyalosis, posterior vitreous detachment, vitreous opacity and vitreous hemorrhage in the posterior artifacts group. Anterior artifacts were more often hyporeflective in red and green laser separation images ($p<0.001$). Posterior artifacts were more often hyperreflective in green laser separation images and hyporeflective in red laser separation images ($p<0.001$).
Conclusions Ultra-wide field scanning laser ophthalmoscope images can frequently have various shadows from anterior or posterior lesion of eye. These shadows show a difference in reflectivity depending on their origins. To understand the difference helps interpretation of the fundus images.

• S082

Agreement between ophthalmoloscopy and ultrawide field image analysis in an outpatient clinic setting

BORDET J (1), Caliot J (1), Vardi K (1), Barbe C (1), Ducasse A (1), Angioi K (2), Arndt C (1)
(1) CHU ROBERT DEBRE, REIMS, France
(2) CHU NANCY, Nancy, France

Purpose Ultrawide field imaging of the retina is a rapidly developing technology. The purpose of this study was to evaluate the concordance between fundoscopy and ultrawide field image reading both performed by an ophthalmologist.
Methods A prospective two center study was performed at two university hospitals (Nancy, Reims) from January 2011 to November 2014. The first eligible patient presenting at the outpatient every working day was included. A wide field imaging optomap ® (optos) was performed by a nurse or an orthoptist before the medical examination. Indirect slit lamp fundoscopy was performed, with or without dilated pupils according to the clinical situation. Then the image lecture was performed by the ophthalmologist. In both cases, the characteristics of the optic disc, the vessel and the retina were noted. The agreement between both examination methods was considered excellent when kappa coefficient (k) was >0.8.
Results 901 patients were included in the study. A highly substantial agreement between both examination methods was found with the overall results of k=0.88 [0.85-0.90]. When comparing the agreement with retinal findings, (k= 0.83 [0.80-0.86]), optic disc findings (k=0.89 [0.86-0.92]) and vessel analysis (k=0.84 [0.79-0.89]), it was highly substantial. An abnormal finding was detected on ultrawide field image analysis only and was missed with fundoscopy in 42 eyes. In 12 eyes, an abnormal finding was seen with fundoscopy and was not detected on ultrawide field imaging.
Conclusions There appears to be an excellent agreement between ultrawide field image analysis and fundoscopy. However the false negative rate appears to be lower with fundoscopy and ultrawide field image analysis associated.

• S083

Wide field imaging in patients treated with vigabatrin

VARDI K (1), Brugniart C (1), Motte J (2), Ducasse A (1), Arndt C (1)
(1) CHU Robert Debré, Ophtalmology, REIMS, France
(2) CHU Robert Debré, Pediatry, REIMS, France

Purpose The purpose of this study was to evaluate the occurrence of retinal changes on wide field imaging and to compare the results with ERG recordings in patients treated with vigabatrin.
Methods Seven consecutive patients treated with vigabatrin were followed up with ERG and wide field imaging using scanning laser ophthalmoscopy (Optomap)
Results Three patients had abnormal ERG recordings and presented with peripheral pigmentary changes. Three patients had normal ERG recordings with no peripheral changes on wide field imaging. One patient had abnormal ERG with no peripheral pigmentary changes.
Conclusions The follow-up with ERG in children treated with vigabatrin is complicated because the recordings are regularly repeated. A follow-up protocol combining electrophysiological recordings and wide field imaging could simplify screening for retinal toxicity but it remains to be demonstrated with a prospective study.

• S084

An algorithm combining two lesion-detection methods of retinal microaneurysms for the reduction of human workload

OMETTO G (1), Bek T (1), Al-Diri B (2), Hunter A (2)
(1) Aarhus University Hospital, Ophthalmology, Aarhus, Denmark
(2) University of Lincoln, School of Computer Science, Lincoln, United Kingdom

Purpose Reduction of workload in the detection of microaneurysms (MA) from retinal photographs is crucial for the diagnosis and screening of diabetic retinopathy. Automatic algorithms for the detection of retinal lesions can help reduce human intervention especially when the lesions are present in large numbers.
Methods Two methods for lesion detection were combined in a single algorithm, one based on the analyses of the contrast between dark peak-points and surrounding circular regions, and a second one based on the correlation between the intensity values in the photographs and a MA-template. The two individual methods and the two methods combined were tested separately to compare their performance on retinal images from 26 high-risk patients.
Results Both individual lesion-detection methods missed clustered MAs. With the exclusion of grouped lesions, the two methods combined showed higher sensitivity and precision than the contrast and template methods alone, identifying 22% and 13% more lesions respectively.
Conclusions The combination of the two methods can provide repeatable detection of unclustered MAs in photographs from high-risk patients. Manual intervention is only required to select grouped MAs and to adjust the automatic results, considerably reducing human workload.

• S085

Comparisons of retinal sensitivity obtained by microperimetry with two different fixation targets in normal individuals

NIZAWA T, Kitahashi M , Yamamoto S
Chiba University Graduate School of Medicine, Department of Ophthalmology and Visual Science, chiba, Japan

Purpose To determine the retinal sensitivities obtained by microperimetry with an one degree single cross (Cr) or an one degree circular (Ci) fixation target in normal individuals.
Methods The retinal sensitivity within the central 2 degrees was measured in 32 eyes of 16 healthy volunteers (mean age 28.9±1.4, range 24-44) with Microperimeter 3 (MP-3, Nidek, Italy) using two fixation targets. The retinal sensitivity of the central 0 degree and mean central 2 degrees consisting of 8 points were measured with the two fixation targets. The Goldmann III stimuli were presented for 200 msec on a white background with a luminance of 31.5 asb.
Results The mean central retinal sensitivity (0 degrees) was 24.4±0.8 dB with the Cr and 29.8±0.6dB with the Ci targets. The central retinal sensitivity with the Ci target was significantly higher than that with the Cr. (P=1.2×E-5). The mean retinal sensitivity of the central 2 degrees was 32.0±0.3 dB with the Cr target and 31.4±0.3dB with the Ci target. The mean central 2 degrees retinal sensitivity with the Cr was significantly higher than that with the Cr target. (P=0.006)
Conclusions The differences in the retinal sensitivity is probably because the fixation targets overlap the stimuli. These results indicate that the size and shape of the fixation target must be considered when evaluating the central retinal sensitivity.

• S086

Postoperative Endophthalmitis: Incidence, Causes and Comparison Between Medical and Surgical Treatment in a United Kingdom Region in the Last 10 Years

SHALABY A , Di Simplicio Cherubini S , Lockwood A , Newsom R
Southampton University Hospital, Eye Unit, Southampton, United Kingdom

Purpose To investigate the incidence, procedures performed, isolated causative microorganisms if found and final visual outcome of Endophthalmitis in a UK tertiary referral centre.
Methods A retrospective audit of all cases treated as postoperative endopthalmitis in the last 10 years has been performed. Details of each case (preceding ophthalmic procedure, isolated microorganisms, management plan and visual acuity before and after treatment) were recorded.
Results Sixty patients have been diagnosed with post-operative Endophthalmitis over the audit period. Full data were available for 44 patients. Twenty-four patients (54.54%) had intravitreal injections procedures (IVI) of Anti-VEGF 4 weeks or less before day of presentation, eighteen patients (40.91%) had endophthalmitis following cataract surgery and 2 patients after trabeculectomy (4.55%). Incidence rates were calculated for cataract surgery and IVI in the last 5 years and were 0.024% and 0.048% respectively. All cases received intravitreal injections of antibiotics. Microorganisms were detected in 8 patients. There were 7 culture positive cases with coagulase negative staphylococcus aureus (6 cases after cataract operation, 1 after IVI) and one case with Staphylococcus Legdunens (after IVI). Eighteen patients presented with visual acuity of CF or worse. Eleven of them have been treated with vitrectomy (1st group) while the other seven have not (2nd group). Ten patients from the first group could achieve better visual acuity that that at the time of presentation, while only three patients of the second group showed improvement (p value= 0.04, Fisher Exact test)
Conclusions The incidence of endophthalmitis in this audit is comparable to larger studies. Vitrectomy may be recommended for postoperative endophthalmitis patients with visual acuity of CF or worse.

• S087

Endogenous panophthalmitis caused by sphingomonas paucimobilis ; A postpartum devastating rare condition

OZCAN A A , Esen E
CUKUROVA UNIVERSITY, OPHTHALMOLOGY DEPT, Adana, Turkey

Purpose Endogenous panophthalmitis is known as an infrequent condition with poor prognosis that mainly occurs in patients having underlying medical conditions. We present a very rare case of endogenous panophthalmitis in a postpartum patient.
Methods A 31-year-old woman was admitted with vision loss and pain in the right eye for two days that began the day after the delivery.
Results Her ophthalmologic examination revealed panophthalmitis. Despite intensive medication corneal melting and spontaneous perforation occurred, so evisceration had to be performed. ***Sphingomonas paucimobilis***, an opportunistic infection agent, was isolated in the conjunctival swab and evisceration specimen cultures of the patient.
Conclusions It is known that immune system is influenced and inflammatory responses are altered in pregnants and puerperants, so any symptom of eye infection should not be ignored in peripartum and puerperium periods.

• S088

Intraocular Pharmacokinetics of Povidone-iodine and the Effect of Repeat Injection with low concentration on the Experimental S. epidermidis Endophthalmitis

BYON I (1,2), Kim K (1), Yu J (3), Yoon I (4), Lee J (2)
(1) Pusan National University Yangsan Hospital, Ophthalmology, Yangsan, South-Korea
(2) Pusan National University, Ophthalmology, Busan, South-Korea
(3) Pusan National University, College of Pharmacy, Busan, South-Korea
(4) Mokpo National University, College of Pharmacy, Mokpo, South-Korea

Purpose To investigate the safety and a half-life of intravitreal povidone-iodine (PVI) and the efficacy of single and repeat PVI injection in experimental S. epidermidis endophthalmitis
Methods In Phase I study, the pharmacokinetics and the safety of PVI were investigated. Forty New Zealand White rabbits receiving intravitreal 0.1 % and 0.3% PVI were divided into Group I and II. The pharmacokinetics of PVI was analyzed using high performance liquid chromatography (HPLC). To confirm the safety of intravitreal PVI, electroretinography (ERG) and histologic examination were conducted at baseline, 6 and 12 hours.
In Phase II study, the efficacy of PVI for the treatment of ***S. epidermidis*** endophthalmitis was evaluated in 4 groups (n=10 in each group). After the induction of ***S. epidermidis*** endophthalmitis, 0.1% and 0.3% PVI were injected once in Group A and B, and three times every second day in Group C and D respectively. The fellow eyes receiving sham injection were the control. ERG, histologic examination and vitreous culture for ***S. epidermidis*** were conducted at day 14.
Results In Phase I, 0.1% and 0.3% PVI groups did not show notable retinal damage in ERG and histologic findings and half-life ***in vitro*** was 3.27 and 3.58 hours, respectively. In Phase II, all Groups showed a significant improvement of endophthalmitis, compared to the controls. However, four eyes in Group A and 3 eyes in Group B demonstrated a bacterial growth in vitreous at day 14, but none in Group C and D. In the histologic findings, retinal damage was detected as lymphocyte infiltration in the inner retinal layers of eyes with bacterial growth.
Conclusions 0.1% and 0.3% PVI can be tolerated in rabbit eyes. Half-life of the PVI was about 3 hours in vitreous. Repeat PVI injection with low concentration is likely to be effective and safe for the treatment of ***S. epidermidis*** endophthalmitis.

• S089

Tolerance of Dexamethasone intravitreal implant in GAO patients according to their initial treatment and repeated intravitreal injections.

VIE A L (1), Kodjikian L (1), Malcles A (2), Agard E (2), El Chehab H (2), Russo A (2), Dot C (2)
(1) Croix-Rousse Hospital, Ophtalmology, Lyon, France
(2) Desgenettes Military Hospital, Ophtalmology, Lyon, France

Purpose To evaluate the tolerance of dexamethasone intravitreal implant (DEX implant) in patients with history of open-angle glaucoma (OAG) or ocular hypertension (OHT) according to their initial treatment and the repetition of intravitreal injections (IVI).
Methods We performed a retrospective two-center clinical study which included 100 patients treated by DEX implants, divided into one group with OAG or OHT patients (n=50 patients), and one control group (n=50 patients) including patients with no history of OHT or GAO, matched by age and pathology. IOP was measured and hypotensive treatments were gathered in all patients respectively at baseline, one week, and each month during six months.
Results Mean age was 71,77(SD+/-10,5) years old in GAO/OHT group and 70,4(SD+/-10,7) years old in control group and mean number IVI was respectively 2.2 (1 to 7) and 2,8 (1 to 11). After the first injection, 50% of OAG/OHT patients and 42% of the control group increased their IOP more than 6 mmHg (p=0,42). There was no difference between the IOP responses of patients initially treated with monotherapy and the control group but there was significantly more high responders (+ >15mmHg) in patients initially treated with bi and triple therapy. The proportion of responders increased when patient had more than one injection (64 and 56% respectively in OAG and control group, p=0,22) and the number of high responders doubled (16% at the first IVI, 32% of multi-IVI). An increased of hypotensive therapy was required in 54% of OAG/OHT patients versus 38% in control group (p=0,1).
Conclusions DEX implant is well tolerated for the patients under monotherapy. In contrast Patient under bi or triple therapy were at risk of ocular hypertension and filtering surgery. Repeated IVI increased the risk of ocular hypertension.

• S090

Intra-ocular pressure spike after Aflibercept and Ranibizumab intravitreal injections

EL CHEHAB H , Agard E , Russo A , Malcles A , Dot C
HIA Desgenettes, Ophthalmology, Lyon, France

Purpose Since anti-VEGFs approval, intra vitreous injections (IVI) represent abooming therapeutic delivery mode. Immediate ocular hypertension (OHT) inducedis known after these IVIs. The purpose of this study is to compare the OHTafter Aflibercept and Ranibizumab IVI.
Methods In this prospective study, we compared30 patients who received an Aflibercept IVI (0.05mL) to 30 patients whoreceived Ranibizumab for wet AMD. IVI were performed with a 30G needle pushedto the hilt with an anti-reflux system. We measured intraocular pressure (IOP)using a portable aplanation tonometer PERKINS MK2 (Haag-Streit, Koeniz,Switzerland) before injection (T0), immediately after IVI (T1), 5 minutes (T5),15 minutes (T15) and 45 minutes (T45) after the IVI. IOP were compared by a t-test.
Results In Aflibercept group, at T0, IOP was13.4mmHg+1.5. All patients had a significant increase in IOP at T1(42.7mmHg+3, p<0.001). At T5, IOP decreased but was stillstatistically higher than baseline IOP (23.6mmHg+3.1, p<0.001). AtT15, IOP returned to normal values but was higher than T0 (16.2mmHG+2.1,p=0.009). At T45, IOP was 13mmHg+1.2, with no significant differencefrom baseline (p=0.65).
In Ranibizumab group, baseline IOPwas 13.8mmHg+1.1. IOP increased at T1 (45.6mmHg+2.2, p<0.001).At T5 and T15, IOP were still higher than baseline (24.6mmHg+2.2, p<0.001and 17.9+1.5, p<0.001). At T45, IOP was 12.7mmHg+1.5, with nosignificant difference from baseline (p=0.12).
At each time measure, there is nostatistically difference between two groups.
Conclusions Aflibercept and Ranibizumab IVI inducean IOP spike for a short time. It seems to be equal between the two drugs andessentially related to the injected volume.

• S091

Background ophthalmological changes following subretinal injection in the brown norway rat

VEZINA M (1), Li C (1), Bussieres M (2)
(1) Charles River Laboratories, Ocular and Neuroscience, Senneville, Canada
(2) V&O Services, Ophthalmology, St. Lazare, Canada

Purpose The purpose of the study was to evaluate the background changes associated with transscleral subretinal injection in Brown Norway (BN) rats.
Methods Fifteen BN rats received a bilateral transscleral subretinal injection of saline at a volume of 6 µL while under isoflurane anesthesia. The eyes were examined by slit lamp and indirect ophthalmoscope the day following injection and 1, 2, 3, 4, 8 and 12 weeks post injection.
Results Procedure-related changes included the following observations: Transient corneal opacities occurred in 16/30 eyes that were considered related to the anesthesia. Cataracts developed in 5/30 eyes associated with lens trauma at the time of dosing. Slight vitreous hemorrhages occurred post dose in 28/30 eyes, resolving in all but 2 eyes by 4 weeks. An area of focal depigmentation of the retina/choroid or white focal retinal opacity was seen at the needle insertion site at the retina in 22/30 eyes, resolving by 4 weeks for 13 eyes and persisting up to 12 weeks for the remaining 7. In the bleb itself, there were focal areas of irregular pigmentation in 13/30 eyes resolving in all but 2 eyes by week 4. The remaining 2 persisted up to week 12. This was considered secondary to the physical neuro-retinal separation caused by the bleb formation. Slight retinal/choroidal hemorrhages were also seen at the injection site in most eyes up to week 4.
Conclusions In conclusion, transscleral subretinal injection in BN rats generally resulted in slight ocular trauma that resolved in most eyes by 4 weeks post injection. It is important to take these changes into account when designing the study and evaluating therapeutics administered by this dose route.

Commercial interest

• S092

Clinical guidelines for acute exposure to laser pointer radiation

LÖFGREN S, Hengstler J , Jans E
Karolinska Institutet, St. Erik Eye Hospital, STOCKHOLM, Sweden

Purpose To describe clinical decision guidelines for eye health care professionals meeting patients exposed to laser pointers.
Methods The Eye Emergency Department at St. Erik Eye Hospital in Stockholm primarily serves the Stockholm Metro region with its 2.2 million people. Every week, on average one patient seeks help at the Eye Emergency after exposure to laser pointer light. The bulk of the patients are subway and bus drivers and police and security officers. Since no objective retinal damage so far has been documented and there is no proven treatment against laser pointer retinal damage we have instigated an information campaign in order to reduce the number of patients seeking emergency care. The information is spread to all public transportation services in Stockholm, police and security officers, aviation authorities, and to the general population.
Results The information to all non-medical staff is general, while the clinical guidelines details which procedures might be relevant and which may be inessential. The guidelines emphasize the importance of documenting a dynamic evolution of retinal damage before causality can be concluded. Within two months after the information campaign, there seems to be a decrease of patients seeking emergency eye care after laser pointer light exposure.
Conclusions The clinical guidelines streamline the care of this patient group, and the information to the public should alleviate some of the worries that are associated to laser pointer light exposure.

• S093

Cystoid macular edema associated with retinitis pigmentosa resolved by a dexamethasone intravitreal implant

ALMENARA C, Ascaso F J, Martínez M, Pérez I, Esteban O, Bartolomé I, Cristobal J
Hospital Clínico Lozano Blesa, Oftalmología, Zaragoza, Spain

Purpose Cystoid macular edema (CME) is a serious complication that threatens the relatively preserved central vision in patients with retinitis pigmentosa (RP). It occurs in 10%-40% of RP patients and, although the exact origin is unknown, a chronic low grade inflammation has been implicated. Currently, there is no gold-standard therapeutic option and treatment should be individualized.
Methods Interventional case report evaluating the efficacy of intravitreal dexamethasone implant (Ozurdex®) in the management of CME secondary to RP.
Results A 39-year-old man diagnosed with RP and a 5-month history of deteriorating vision was referred for evaluation. Best-corrected visual acuity (BCVA) was 0.1 and 0.4 in RE and LE, respectively. Slit-lamp examination and intraocular pressure (IOP) were normal in both eyes. On funduscopy, the findings were mottled retinal pigment epithelium (RPE) caused by bone spicule formation and attenuation of blood vessels. Spectral domain optical coherence tomography (SD-OCT) revealed CME in RE which was treated with topical dorzolamide twice a day. As no visual improvement was achieved, two months later the patient underwent 0.7 mg Ozurdex® implant in his RE. One month following the injection CME resolved (from 546 µm to 310 µm) and BCVA improved to 0.3. An IOP spike (34 mmHg) was controlled with topical antiglaucoma medications and no recurrence was observed during 1-year follow-up.
Conclusions Intravitreal dexamethasone implant (Ozurdex®) seems to be an effective treatment option for patients with macular edema associated with RP.

• S094

Impact of Storage Temperature on Gene Expression of Cultured ARPE-19 Cells

PASOVIC L (1), Eidet J R (1), Olstad O K (1), Chen D F (2), Lyberg T (1), Utheim T P (1)
(1) Oslo University Hospital, Department of Medical Biochemistry, Oslo, Norway
(2) Schepens Eye Research Institute, Department of Ophthalmology- Harvard Medical School, Boston, United States

Purpose The development of a suitable storage method for retinal pigment epithelium (RPE) is necessary in the establishment of future RPE replacement therapy, and storage temperature has proven to be pivotal for cell survival. We analyzed the gene expression profile of cultured human RPE cells after storage at 4°C, 16°C, and 37°C.
Methods ARPE-19 cells were cultured until confluence and stored in Minimum Essential Medium at 4°C, 16°C, and 37°C for seven days. DNA microarrays validated by qRT-PCR were used to determine the gene expression profile.
Results The gene expression profile of cultures stored at 4°C cluster closest to the control cultures that were not stored and display the least change in gene expression after storage (157 differentially expressed genes compared to controls), while cultures stored at 16°C and 37°C display much larger changes compared to controls (1787 and 1357 differentially expressed genes, respectively). Expression levels of key genes involved in phagocytosis, pigment synthesis, the visual cycle, cell junctions, and cellular transport were maintained close to control levels in cultures stored at both 4°C and 16°C in contrast to 37 °C.
Conclusions RPE cell cultures stored at 16°C appear to modulate their gene expression profile in a manner that supports cell survival during storage, while maintaining the expression levels of genes important for key RPE functions.

• S095

Transcription factors involved in cell death and regeneration in AGEs exposed retinal neurons

OSHITARI T, Bikbova G, Yamamoto S
Chiba University Graduate School of Medicine, Ophthalmology and Visual Science, Chiba, Japan

Purpose To examine the role of transcription factors in neuronal cell death and regeneration in advanced glycation end-products (AGEs) exposed rat retinas.
Methods The retinas of six SD rats were cultured in three dimensional collagen gels and incubated in serum-free control media, AGEs-BSA media, AGEs-BSA + several neurotrophic factors (neurotrophin-4, hepatocyte growth factor, glial cell line-derived neurotrophic factor, tauroursodeoxycholic acid) supplemented media. After 7 days, the numbers of TUNEL positive cells and regenerating neurites were counted. The explants were immunostained for nuclear factor-kB (NF-kB) and specific protein 1 (SP1) and counted the number of immunopositive cells in the explants.
Results In retinas incubated with AGEs, the numbers of TUNLE positive cells were more and the numbers of neurites were fewer than in control. All of the neurotrophic factors decreased TUNEL positive cells and increased the number of neurites, and the survival and regenerative effect was more significant in the neurotrophin-4 group. The numbers of NF-kB and SP1 immunopositive cells were higher in AGEs exposed retinas than in control. All of the neurotrophic factors decreased the number of NF-kB immunopositive cells but did not significantly affect SP1 expression.
Conclusions These results give the clue to understand the role of transcriptional factors involved in cell death and regeneration in AGEs exposed retinal neurons.

• S096

Expression of histamine receptors in the gerbil retinal neurons

MIYACHI E (1), Imada H (2), Ohkuma M (1), Sakai K (3)
(1) Fujita Health University School of Medicine, Department of Physiology, Toyoake, Japan
(2) Aichi Business College, Medical Secretary, Nagoya, Japan
(3) Fujita Health University School of Health Science, Department of Anatomy- Faculty of Clinical Engineering, Toyoake, Japan

Purpose The presence of histamine receptors (HRs) in mammalian retinae has been reported by several laboratories. In order to confirm the presence of histaminergic pathway in the retina, we made experiments using physiological and immunohistochemical analyses.
Methods All experiments were performed using the gerbil (***Meriones unguiculatus***). The activity of the HR was measured by fura-2 based calcium-imaging technique and by whole-cell patch-clamp technique from slice preparation of the retina. Localizations of the subtypes of HRs, H1 receptor (H1R), H2 receptor (H2R) and H3 receptor (H3R), were examined by avidin-biotin-peroxidase complex immunocytochemical staining or immunofluorescence in retinae from 1 to 350 postnatal days. All animal experiments are approved by the ethics committee of Fujita Health University.
Results *Physiology*: A bath application of 100 µM histamine increased the intracellular calcium concentration in some retinal ganglion cells (RGCs). Under voltage-clamp condition, histamine increased the amplitude of the outward or inward current in some RGCs.
Immunohistochemistry: We found that H1R, H2R and H3R expressed on RGCs. H1R expresses through the retinal maturation. On the other hand, the expressions of H2R and H3R became maximum from 14 to 21 postnatal days. Since the gerbil opens the eyes at 3 weeks old, it is considered that the H2R and H3R play some specific roles at the formation of the early visual system. Histidine decarboxylase, which produces histamine from histidine, also expressed in RGCs, and moreover, each of HRs and histidine decarboxylase were co-localized at the same RGCs.
Conclusions Our findings suggest that RGCs interact with each other via histamine, and that histamine is one of the important neurotransmitters and/or neuromodulators in the visual information processings of the mammalian retina.

• S097

Research on ophthalmic examination apparatus to diagnose multiple diseases which result in loss of eyesight

SUZUKI N (1), Yamane K (2)
(1) National Institute of Technology- Numazu College, Department of Mechanical Engineering, Numazu, Japan
(2) Hiroshima University, Department of Ophthalmology and Visual Science, Hiroshima, Japan

Purpose In Japan, the four major diseases which cause the loss of eyesight are glaucoma, diabetic retinopathy, pigmentary retinal degeneration, and age-related macular degeneration. We developed an ophthalmic examination apparatus having the functions of fundus camera, microperimetry, electroretinography, and visual acuity testing, designed to diagnose multiple diseases which result in loss of eyesight.
Methods We constructed the experimental device with the same optical system as a fundus camera. The device has previously been used for research involving the diagnosis of early diabetic retionopathy. The microperimetry optical system was calculated using the optical engineering software OpTalix-LT and was added to the experimental device. In addition, we added an Edmund infrared camera EO-0413, a lens with a focal length of 25 mm, a 45-degree cold mirror, a 12V/50W halogen lamp, and an 8-inch monitor. The artificial eye consists of a plane-convex lens, a black spacer, and a hemispherical cup. A small section paper was stuck on the bottom of the hemispherical cup. The artificial eye was photographed for 10 times using the experimental device. The software was generated to show the examination target on the monitor and save examination data using C++Builder XE6.
Results The device was able to show the retinal fundus on the monitor, at a length and width of 1 mm with a resolution of 63.25 ± 3.51 and 64.13 ± 6.10 pixels, respectively.
Conclusions We succeeded in adding the function of microperimetry to the experimental ophthalmic device.

• S098

Subthreshold Micropulse Yellow Laser (577nm) Photocoagulation for Subfoveal Serous Pigment Epithelium Detachment

PARK H
Nune Eye hospital, Retina center, Daegu, South-Korea

Purpose To evaluate the efficacy of subthreshold micropulse yellow laser photocoagulation(SMYLP) for subfoveal serous pigment epithelial detachment(SPED).
Methods We evaluated retrospectively 6 eyes of 5 patients with symptomatic subfoveal SPED treated with SMYLP. SMYLP was performed on the entire area of SPED with Supra 577Y Laser System(Quantel Medical). The SMYLP settings were 100 μm spot diameter, 20 ms duration, 15 % duty cycle, 3×3 pattern. If SPED was not definitely restored, we applied laser again with more increased power at 1 or 2 months interval.
Results All patients were received 3 or 5 times bevacizumab or ranibizumab injections before SMYLP. The total follow-up period was 26.5(18–36)months, mean follow-up period after laser application was 19.8(15–32) months. Mean height of PED before treatment was 349.2±53.22 μm. About 3(2-4) sessions SMYLPs were performed. All eyes showed nearly complete resolutions of the PED for 5.6(5–7) months, which were sustained during the follow-up. Mean BCVA before treatment was 0.11(0–0.22) logMAR and mean BCVA at final follow-up was 0.07(0–0.22) logMAR. After PED resolution, all patients had increased vision and metamorphopsia improvement. After PED resolution, usually there were seen in mild RPE atrophies in fundus and OCT image, and these atrophies were not aggravated.
Conclusions SMYLP for subfoveal SPED induced the resolution of SPED and symptom improvement. But after SPED resolution, mild RPE atrophy was detected. We think this finding was related to subsequent epithelial atrophy after resolution of SPED or laser damage. Prospectively, the study about long-term efficacy and safety of this treatment will be needed.

All authors index

ALL AUTHOR INDEX

All authors of abstracts are listed alphabetically.

One letter and three digit numbers refer to posters.
Four digit numbers refer to oral presentations.
The digit numbers marked in bold indicate a first author abstract.

ALL AUTHOR INDEX


EVER
European Association for Vision and Eye Research