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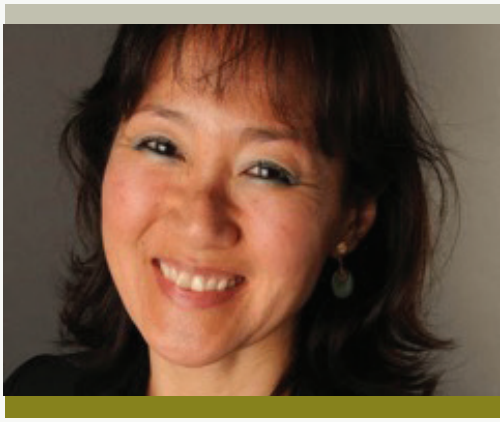
TABLE OF CONTENTS



1413
EVER Lecture - and is delivered by the Past President: The Pupil: A marker of visual and non-visual light sensitivity

*KAWASAKI, Aki**
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Summary
The well-recognized, rapid pupillary constriction in response to an abrupt increase in illuminatino is largely mediated by rods and cones and pupillary size trends with the rapid adaptation function of these photoreceptors. The melanopsin-mediated light response of intrinsically photosensitive retinal ganglion cells (ipRGCs) displays unique features whose influence on pupillary movement can be best differentiated in the post-illumination phase of the pupil light reflex. Even the longterm adaptation to cyclic environmental light is reflected in the pupil response. As such, our understanding of "deficit" in patients with ophthalmological disorders is no longer limited to visual perception and has broadened to consider non-visual light functions directly or indirectly mediated by melanopsin.

1711
Uveal melanoma: millimeters, personalized prognosis, and new therapies

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Summary
The management of uveal melanoma is going through tremendous transition into the realm of early detection, personalized prognostication and potentially new systemic and local therapies. In this Keynote Lecture, we will discuss four topics relevant to current melanoma management including (1) the importance of detection of small melanoma where thickness is approximately 3 mm or less, (2) optical coherence tomography angiography (OCTA) of melanoma before and after plaque radiotherapy, (3) DNA analysis of >1000 cases of uveal melanoma and the ability to personally prognosticate each patient based on cytogenetic profile, and (4) new systemic and local therapies.

2511
The genetics revolution as seen through the eye

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Summary
Up to the early 1980s, a molecular understanding of the disease process for retinal dystrophies such as retinitis pigmentosa (RP) was almost nil. Given the complex nature of the retina, it was clear that significant clinical variability would exist but no clues that could explain the disease. Fortunately at this time molecular biology techniques were maturing that started the new genetics revolution and the field of ophthalmology saw the greatest progress in understanding the molecular basis of inherited retinopathies. A "reverse genetics" approach laid the foundation for the eventual isolation of the first gene for RP, namely 'rhodopsin' in 1989. Family based studies became the driving force that began unraveling the immense genetic heterogeneity defining retinal dystrophies. RP affects 1 in 3000 people worldwide. Initially the rod photoreceptor cells are affected leading to night-blindness and constriction of the visual field. In later stages cone cells may also die often resulting in total blindness. RP can be inherited as an autosomal dominant or autosomal recessive or X-linked trait. So far over 60 retina-specific as well as ubiquitously expressed genes have been implicated, describing a wide variety of functions including enzymes, structural proteins, transcription factors and splicing factors. Taken together that include RP, cone-rod dystrophy, cone dystrophy and a variety of macular dystrophies, well over 250 genes have been identified so far (RetNet, http://www.sph.uth.tmc.edu/Retnet/), underpinning a real advance in our knowledge of retinal dystrophies. This knowledge is steadily leading the way to developing exciting new genetic therapies for these incurable diseases.

3211
Why do eyes become myopic?

*KLAVER, Caroline**
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Summary
Refractive errors are the most common eye disorders worldwide and the largest source of visual impairment. In particular, high myopia is associated with a significant risk of visual complications, such as myopic macular degeneration, glaucoma, and retinal detachment. The absolute risk of severe visual impairment increases significantly with each diopter of myopic refractive error, ranging from 3% to 5% in individuals with errors of -6.00 D to more than 40% in those with -15.00 D or more. Reports have shown that the prevalence of myopia is on the rise worldwide with the highest prevalence in Asia. This figure is dramatic and demand effective counteractions. The lecture will address the main question "Why do eyes become myopic?" from various perspectives including epidemiological data (genetics, environmental factors, etc.) and animal studies.

Acta
Ophthalmologica

2211
Ocular imaging: What we see and what we would like to see

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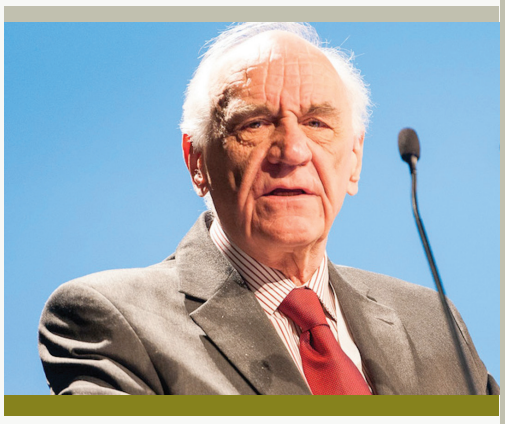
Summary

Imaging is a highly innovative field in ophthalmology. Optical coherence tomography (OCT) has gained widespread clinical importance for both, the anterior and the posterior segment of the eye and is routinely used in diagnosis, follow up and treatment monitoring. While OCT has continuously improved in performance the question is what comes next: higher resolution, faster data acquisition, functional imaging, molecular contrast? In the present talk a perspective is given in terms of clinical needs. Unsolved challenges in terms of screening, diagnosis, follow up and treatment monitoring will be discussed and potential ways to overcome these issues will be provided.



1611
Evolution of our understanding and management of monogenetic retinal disorders

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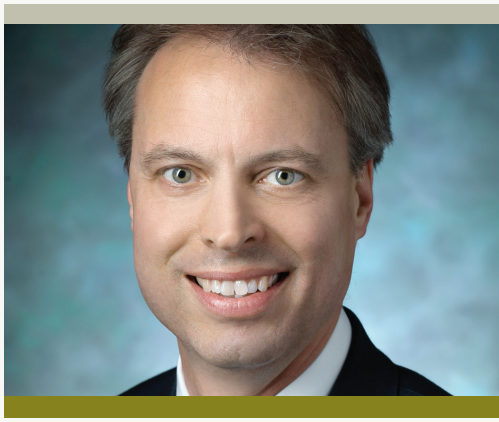
Summary
Night blindness as a hall mark of many monogenetic retinal disorders has been known for over a thousand years. Indirect evidence implies that this was due to vitamin A deficiency in some of these early descriptions. In the 18th. century it was recognised that it may be seen in families implying a genetic origin of disease. A secure diagnosis of retinitis pigmentosa became possible with the invention of the ophthalmoscope in the mid-19th century and by 1908 Nettleship synthesised reports of over 1,000 reported cases. He generated an accurate clinical description of the disorders and there was little revision of his conclusions until the 1970's apart from early electrophysiological studies. Thereafter, there has been highly productive research that has led to identifying the causes, and pathogenetic mechanisms involved in disease, followed by early attempts at intervention. It is likely that over the next 10 years successful treatment will become available in disorders that were ill understood 40 years ago.



Ophthalmic Research
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4211
Emerging therapies for retinal and macular dystrophies

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Summary
Inherited retinal degenerative diseases, a genetically and phenotypically heterogeneous group of disorders, affect the function of photoreceptor cells and are among the leading causes of blindness. Recent advances in molecular genetics and cell biology are elucidating the pathophysiological mechanisms underlying these disorders and are helping to identify new therapeutic approaches, such as gene therapy, stem cell therapy, and optogenetics. Several of these approaches have entered the clinical phase of development. Artificial replacement of dying photoreceptor cells using retinal prostheses has received regulatory approval. Precise retinal imaging and testing of visual function are facilitating more efficient clinical trial design. In individual patients, disease stage will determine whether the therapeutic strategy should comprise photoreceptor cell rescue to delay or arrest vision loss or retinal replacement for vision restoration.edu/Retnet/), underpinning a real advance in our knowledge of retinal dystrophies. This knowledge is steadily leading the way to developing exciting new genetic therapies for these incurable diseases.

EVER 2017
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• 1111

Ranibizumab in patients with neovascular age-related macular degeneration: results from the real-world LUMINOUS™ study

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Purpose
LUMINOUS(NCT01318941) was designed to evaluate the long-term safety, effectiveness, and treatment patterns with ranibizumab 0.5 mg in clinical practice across all licensed indications. We report, the effectiveness and safety of ranibizumab treatment in patients with neovascular age-related macular degeneration (nAMD) from the final analysis of LUMINOUS.
Methods
LUMINOUS is a recently-completed, 5-year, global, observational study. Consenting adult patients were treated as per the local ranibizumab label. Reported are the 1-year visual acuity (VA, primary treated eye), and injection pattern for the treatment-naïve nAMD patients. The incidence of adverse events (AEs) and serious AEs (SAEs) for the total treatment-naïve nAMD cohort is also presented.
Results
Baseline and 1-year VA data were available for 2701 treatment-naïve nAMD patients. At baseline, the mean (SD) age was 75.9 (9.7) years, 58.4% were female, and 78.4% were Caucasian. VA (letters) gains at 1-year in treatment-naïve patients receiving <3, 3–6, and >6 injections were 2.1 (n=372), 3.6 (n=1499), and 4.3 (n=830), from baseline of 45.0, 52.5, and 54.9, respectively. In all treatment-naïve nAMD patients, the mean (SD) gain in VA of 3.6 (16.2) at 1 year from 52.2 (20.8) at baseline was achieved with a mean (SD) of 5.3 (2.7) ranibizumab injections and 9.3 (3.3) monitoring visits. Across all treatment-naïve nAMD patients (n=6241), the incidence of ocular/non-ocular AEs and SAEs were 8.2%/12.8% and 0.9%/7.4%, respectively.
Conclusions
This analysis from LUMINOUS confirms the effectiveness of ranibizumab in treatment-naïve nAMD, and shows a relationship between VA improvement and the number of ranibizumab injections each patient received.
Conflict of interest
Any consultancy arrangements or agreements?:
Consultant for Allergan, Bayer, Novartis, Roche, and Thea.

• 1112

Aflibercept in neovascular age related macular degeneration previously refractory to standard intravitreal therapy: An Irish perspective to compare against international trends

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Purpose
To determine visual and anatomical outcomes of Age-Related Macular Degeneration (ARMD) patients, in a tertiary centre, following conversion to Aflibercept having been refractory to previous treatment with Bevacizumab and/or Ranibizumab and to make international comparisons.
Methods
A retrospective chart review of patients with a diagnosis of neovascular AMD (nvAMD) undergoing Aflibercept intravitreal therapy for at least six months who had previous treatment with three consecutive Bevacizumab +/- Ranibizumab injections prior to switch. Exclusion criteria included any other procedures affecting visual outcome performed within the treatment period. Outcomes measured included visual acuity (VA), central macular thickness (CMT) and injection frequency.
Results
Sixty eyes of 52 patients were included, 25 of which were male. Mean BCVA pre-switch was 55+/-15 letters and CMT was 285µm+/-77. Eyes received a mean of 14+/-8 prior Bevacizumab/Ranibizumab. The mean follow up post switch was 13.2 months (SD=5.5). Mean BCVA improved by two letters at six months (SD=6.6, p<0.05), by four letters at 12 months (SD=6, p <0.01). The mean VA at 18 and 24 months was unchanged from baseline VA. The mean CMT decreased by 44µm at six months (SD=73.5, p<0.0001), 48.4µm at 12 months (SD=88.1, p<0.01), 48µm at 18 months (SD=22.39, p<0.001). The mean number of injections in the six months pre-switch was 2.8 (SD=0.8), this increased to a mean of 4 injections (SD=0.94) in first six months post switch then decreased to 2 injections (SD=1) in each six month period thereafter (p=0.002).There were no significant systemic or ocular adverse events.
Conclusions
Switching to Aflibercept in patients with treatment resistant AMD produces statistically significant improvements in visual and anatomical outcomes with eventual maintenance of visual acuity levels at one year post switch.

• 1113

Internal limiting membrane peeling in retinal detachment complicated by grade B proliferative vitreoretinopathy

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Purpose
To specify the benefits of internal limiting membrane (ILM) peeling as a surgical adjunct in primary repair of retinal detachments (RD) complicated by grade B proliferative vitreoretinopathy (PVR).
Methods
A retrospective comparative study included consecutive patients who underwent vitrectomy for primary RD complicated by grade B PVR between May 2010 and December 2015 at Nancy University Hospital (France). All patients were treated with SF6 or C2F6 gaz tamponade. The ILM was routinely peeled after staining from 2012. The best-corrected visual acuity and spectral-domain optical coherence tomography (SD-OCT) were collected at 1 and 3 months postoperatively, looking for epiretinal membrane formation, macular oedema or photoreceptor damage.
Results
Thirty seven eyes who underwent ILM peeling (group 1) and 38 eyes without ILM peeling (group 2) were included. At the end of follow-up, anatomic success after single surgery was higher in group 1 (89%) than in group 2 (66%, p=0.03). Mean final visual acuity was 0.41 ±0.40 logMAR in group 1 versus 0.43 ±0.22 logMAR in group 2 (p=0.82). After 3 months follow up, we found no epiretinal membrane (ERM) formation on OCT scans in group 1 whereas 5 ERM (20%) were detected in group 2 (p=0.012). The 2 groups did not differ in terms of cystoid macular oedema occurence, macular thickness or photoreceptor damage.
Conclusions
ILM peeling at the macula during vitrectomy for the treatment of retinal detachment complicated by grade B PVR may prevent a second surgery for redetachment or macular pucker.

• 1114

Photostimulation with subthreshold yellow micropulsed laser for chronic residual subfoveal rhegmatogenous retinal detachment after surgery

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Purpose
The aim of this pilot study, the first of this kind, was to evaluate the safety and efficacy of Subthreshold Yellow Micropulsed Laser (SML) to treat eleven patients with chronic residual subfoveal Retinal Detachment (RD) after surgery to repair Rhegmatogenous Retinal Detachment (RRD).
Methods
Eleven eyes with residual subfoveal RD after surgery, dating from eight to sixteen months before treatment have been evaluated. Evaluation included visual acuity, Amsler test, ophthalmoscopy, Autofluorescence (AF) and Spectral-Domain Optical Coherence Tomography (SD-OCT).
Results
After treatment we recorded improved visual acuity and Amsler test, disappearance of subfoveal detachment by ophthalmoscopy, reduced retinal pigment epithelial distress by AF and restored macular retinal profile without neuroretinal alterations by SD-OCT evaluation in nine eyes.
Conclusions
Photostimulation with SML, selective for the Retinal Pigment Epithelium (RPE), is proved to be painless, effective and safe. The possibility to reabsorb subretinal liquid by foveal and parafoveal RPE photostimulation, without neuroretinal damage, opens new prospects for the therapy of this pathology. If further studies confirm the results of the present pilot study, SML treatment can be considered the first and only non invasive option for chronic residual RD after retinal surgery to repair RRD.

• 1115

Evaluation of efficacy and safety of dexamethasone intravitreal implants between vitrectomized and non-vitrectomized eyes in a real-life study

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(4) Hôpital Neurologique, NeuroOphthalmology, Lyon, France

Purpose
To compare the efficacy and safety of dexamethasone intravitreal implant (Ozurdex) between vitrectomized and non-vitrectomized eyes in real-life conditions and to evaluate the change in intravitreal DEX-implant efficacy before and after pars-plana vitrectomy (PPV) in patients vitrectomized during follow-up
Methods
This was a bicentric, retrospective, observational study. Four hundred and one eyes in 361 patients were enrolled between October 2010 and February 2015. Sixty-seven eyes were vitrectomized at baseline, 301 had no vitrectomy at the last visit. Fifteen eyes were vitrectomized during follow-up and had at least one DEX-implant intravitreal injection before and after PPV. Eighteen eyes vitrectomized during the follow-up were excluded because these eyes did not have at least one intravitreal injection of DEX-Implant after pars-plana vitrectomy. Three hundred eighty-three eyes in 343 patients were studied. We evaluated the efficacy and safety of OzurdexÓ between vitrectomized and non-vitrectomized eyes and before and after PPV in patients vitrectomized during follow-up. Main outcome measures included changes in best-corrected visual acuity, central macular thickness and incidence of adverse effects.
Results
Variations of BCVA and CMT were not significantly different neither between non-vitrectomized eyes and baseline-vitrectomized eyes nor before and after PPV in patients vitrectomized during follow-up. The IOP profile was the same between non-vitrectomized eyes versus baseline-vitrectomized eyes and before versus after PPV in patients vitrectomized during the follow-up.
Conclusions
This large cohort shows that vitrectomy seems not to influence the efficacy and safety profile of DEXimplant regardless of the indication.

• 1116

Popper associated maculopathy – Case report and literary synthesis

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Purpose
Prevalence of Alkyl Nitrate, or 'Poppers' abuse has remained high since its putative birth in the urban disco scene of the 1970's, with UK figures from 2014 suggesting a 9.1% adult lifetime use rate. However, an associated retinal toxicity is a new and emerging phenomenon due to the recent change of its main compound and continued popular recreational use. Here, we describe a case of Alkyl Nitrate associated maculopathy.
Methods
Case report with literary synthesis.
Results
A 44-year-old Caucasian male with no previous ophthalmic history presented to our eye casualty department with bilateral central vision blurring following repeated inhalation of Alkyl nitrates. Drug use was believed to have occurred twice daily by inhalation over an interrupted 6-week period. Best-corrected visual acuity at presentation was 6/6-1 in the right eye and 6/9+1 in the left. Fundal photography reveals subtle yellow foveal spots bilaterally with an otherwise normal peripheral retina and optic disc. Optical coherence topography demonstrates marked disruption of the photoreceptor inner segment / outer segment junction. Fundus Fluorescein Angiography exhibits a subtle foveal hyper-fluorescence bilaterally. Multifocal ERG displayed attenuated responses from the foveal and parafoveal segments of the left eye with blunting of the foveal peak. A synthesis of current literature and various hypotheses to date is subsequently discussed.
Conclusions
The rarity of this phenomenon, along with tendencies of reluctant disclosure of substance abuse behaviours, can lead to diagnostic difficulties. When faced with bilateral painless central blurring, in otherwise healthy, young individuals, physicians should obtain a detailed history of possible substance abuse.

• 1121

Automated gonioscopy photography for iridocorneal angle grading

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Purpose
This study aims to assess inter-device and inter-observer agreement of iridocorneal angle grading using automatic gonio-photography and dynamic gonioscopy.
Methods
Cross sectional single-center observational study. Consecutive patients from Glaucoma Clinic were recruited to perform two types of gonioscopy. Manual gonioscopy (MG) was performed using a dynamic gonio lens, while the automatic Gonio-Photography (AG) was done using a contact-gonioscope prototype (from NIDEK). AG images were graded by two masked observers (glaucoma specialist and resident). Criteria for classification was similar in both methods. An eye was classified with angle closure when the posterior trabecular meshwork couldn't be seen in two or more quadrants. Inter-device agreement (AG vs MG) was ascertained by κ statistic and comparison of area under receiver operating characteristic curves (AUC). Agreement among raters was ascertained by Fleiss' κ statistic and intraclass correlation coefficient (ICC).
Results
Forty-eight eyes were analyzed. Mean age was 63 ± 16 years. Angle closure was detected in 11 eyes (23.4%) with MG in comparison with 2 eyes (4.3%) using AG images grading. The agreement for angle closure diagnosis between MG and AG was poor (κ=0.09±0.10; p=0.18). The AUC for detecting eyes with gonioscopic angle closure showed poor accuracy between automated and manual methods (AUC=0.53±0.05, confidence interval (CI) 95%: 0.44-0.62). The ICC for iridocorneal angle grading between the two raters was 0.34 [CI 95%: 0.10-0.51] and Fleiss' kappa coefficient for opening status was 0.13 [CI 95%: 0.04-0.30].
Conclusions
Only slight agreement was found when comparing automated with manual dynamic gonioscopy and also when comparing two raters. Manual dynamic gonioscopy is the gold standard and further technological development is desired for promising automated gonioscopy.

• 1122

Subject specific angular waist of the optic nerve head nerve fiber layer allows follow up detection of local nerve fiber bundle loss

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Purpose
To clarify if frontal plane angular Pigment epithelium central limit- Inner limit of the retina Minimal Distance (PIMD) measured with OCT has enough specific angular structure for detection of change of specific angular segments of PIMD over time within glaucoma subjects.
Methods
A Topcon OCT-2000 was used for capture of the 3D representations of the ONH. from one eye of each of totally 13 subjects with early stage primary open angle glaucoma. Altogether, 3 volumes were captured at two occasions within 3 months. PIMD was semi-automatically segmented in each volume in 500 equally spaced angular segments distributed over 2Pi in the frontal plane.
Results
Plots of the angular distribution of PIMD for all subject revealed specific low angular frequency overlaid with higher intermediate angular frequencies specific for each subject. High angular frequencies appeared similar for all subjects. A fast Fourier transform of the angular PIMD revealed a high to low frequency content ratio, 0.12, consistent for all segmentations of PIMD-2Pi. The rotational displacment of angular PIMD in the frontal plane among segmentations, volumes and occasions was determined with cross-correlation. Then, all PIMD-2Pi were phase adjusted over segments, volumes and occasions. Finally, the rotation of PIMD-2Pi was adjusted to a standard rotation. This allows comparison of angular segments of PIMD-2Pi between visits. The magnitude of different sources of variation were estimated with analysis of variance.
Conclusions
Angular correction in the frontal plane of recordings of angular PIMD of the ONH allows comparison of angular segments of PIMD-2Pi. This substantially increases the resolution of of an angular segment of PIMD. The resulting precision suggest that detection of an angular segment of PIMD is associated with better resolution than Humphrey visual field MD.

• 1123

Advanced vascular exams improve the accuracy of conventional parameters in distinguishing normal tension from primary open angle glaucoma

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Purpose
The role vascular factors play in glaucoma is still not fully understood. We aim to understand if advanced vascular exams can improve our ability to distinguish primary open angle glaucoma (POAG) from normal tension glaucoma (NTG) patients.
Methods
We applied multivariate logistic regression on the Leuven Eye Study data (182 NTG and 202 POAG patients), and created three prediction models. One with conventional parameters, one with parameters from advanced vascular exams [colour Doppler imaging (CDI), retinal oximetry, ocular pulse amplitude and choroidal thickness] and one where both kinds of parameters were allowed in (mixed). The area under the curve (AUC) was calculated and compared between them. Intra-ocular pressure (IOP) and IOP-related variables were excluded.
Results
The conventional model included Raynaud phenomenon, mean arterial pressure (MAP), central corneal thickness, migraine, visual field mean deviation (VF MD), cup-disc (C/D) ratio, visual acuity and mean retinal nerve fiber layer (mRNFL) thickness (in decreasing order of importance). The advanced vascular model included parameters from CDI and retinal oximetry. The mixed model included Raynaud phenomenon, MAP, arterio-venous retinal oxygen saturation difference, acceleration (acc) of central retinal artery (CRA), end-diastolic velocity of CRA, resistive index of ophthalmic artery, VF MD, C/D ratio, mRNFL thickness, acc of temporal posterior ciliary artery and migraine (in decreasing order of importance). The AUCs were 0.687, 0.677 and 0,743, respectively. The mixed model was able to significantly increase the prediction ability of the conventional model (p=0.049).
Conclusions
Adding advanced vascular exams increased the accuracy of the conventional model to distinguish between groups. These results show how important vascular factors can be in the pathogenesis of glaucoma.

• 1124

Changes of anterior chamber morphometry with age in children using hand-held spectral domain optical coherence tomography

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Purpose
To identify the change of anterior chamber measurements with age in children using Hand-Held Spectral Domain Optical Coherence Tomography (HH-SDOCT).
Methods
A cross-sectional study involved 93 normal children (mean age= 5.19 ± 4.1 years, range: 2 days to 15 years). HH-SDOCT (Leica Microsystems Ltd) was used to image anterior chamber angle. B-scan showing both clear nasal and temporal angles were analysed using ImageJ. The iridocorneal angle landmarks: scleral spur (SS), Schwalbe`s line (SL) and angle recess (AR) were identified and used to calculate trabecular meshwork length (TML), scleral spur angle opening distance (SSAOD), Schwalbe`s line angle opening distance (SLAOD), trabecular iris surface area (TISA), TISA500, SS limbal distance (SSLD) and SL limbal distance (SLLD), nasal SS to temporal SS distance (SS-SSD), nasal SL to temporal SL distance (SL-SLD) and pupil diameter (PD). Linear mixed models were used to determine the correlation between ocular parameters and demographic data with log age.
Results
All measured parameters were significantly influenced by age (all P values <0.05). The changes of parameters per age were measured in 591 angle images. In the first year, TML increased by 159.6µm (30.5%), SSAOD 120.4µm (112.4%), SLAOD 347.4µm (95.7%), TISA 0.19 mm^2 (133.4%), TISA500 0.13mm^2 (96.4%), SSLD 33.7µm (4.2%), SLLD - 30.3 µm (3.9%), SS-SSD 2.4 mm (23.3%), SL-SLD 2.0 mm (21.4%) and PD 2.4 mm (114.3%). No significant changes were detected with gender or between both eyes (P values > 0.05).
Conclusions
HH-SDOCT can be an effective technique in understanding the morphometric changes of anterior chamber in children from birth. Our findings highlight the need for normative age adjusted data to detect abnormalities in angle measures clinically.

• 1126

Screening for glaucoma progression by using non-parametric tests

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Purpose
Automated perimetry still represents the gold standard in long term glaucoma monitoring.Early detection of progression tendency in glaucoma patients is crucial. Purpose of this study was to assess an alternative fast and convenient method compared to GPA (Humphrey Perimeter, Carl Zeiss®) for detecting glaucoma progression shortly after diagnosis-24 months.
Methods
We studied in a longitudinal manner 41 eyes from 41 patients with early open angle glaucoma forms, followed in the first 24 months after diagnosis. Glaucoma was defined according to EGS criteria and a minimum of 5 valid visual fields were required form each patient. All specific glaucoma clinical data were recorded and progression was verified by two distinctive methods: Glaucoma Progression Analysis (GPA) software from Hymphrey Visual Field Analyzer and a non parametric analysis (NPA) according to Wesselink protocol.
Results
In GPA analysis, a positive „event" (progression) was detected in 11/ 41 eyes, 26.82%. NPA confirmed progression in all GPA cases, but additionally detected 8 moreprogression cases (46.34% eyes). The concordance between tests was good (k=0.596, p=0.000), with positive correlation (Mc Nemar test r=0.652, p=0.008). In the first 2 years after diagnosis, GPA sensitivity was 26.82% and a specificity of 73.33%, whereas NPA sensitivity was 46.34% and comparable specificity 72.41% to GPA. Likelihood ratio for progression (LR) in GPA was 1.00 vs 1.51 for NPA analysis.
Conclusions
NPA tends to overestimate progressor number in a cohort, but its purpose is to allert and orient the clinician on the progression profile of the followed patients. In the first years, the GPA analysis can be highly inaccurate, therefore combining two methods with similar specificity might aid this purpose and ease the glaucoma care management.

• 1127

Prospective comparison of global visual field indices and cluster progression in glaucoma and their relationship to structural changes

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(2) Glaucoma & Retinal Neurodegeneration Research Group- Visual Neuroscience, UCL Institute of Ophthalmology, London, United Kingdom

Purpose
Glaucoma diagnosis and follow up of progression is often based on structural and functional assessments. This study aimed to assess clustered progression in comparison to global indices and structural measures from HRT and OCT.
Methods
16 eyes of OHT and glaucoma patients with a minimum of 5 visual fields (HFA II i 24-2) over a year were assessed prospectively. MD and VFI rates of progression were used for trend analysis. Linear regression of clusters defined by the Glaucoma Hemifield Test (GHT) was performed based on the mean threshold in each cluster. Rim Area (HRT 3) and mean parapapillary RNFL(SD-OCT) analysis were assessed and correlated with functional clustered measures. Rates of progression were flagged as statistically significant if the gradients over time were negative with $p<0.05$.
Results
Cluster analysis showed significant progression: 11 of 16 eyes in at least 1 cluster (68.75%) with an average rate of progression of -2.18 ± 2.2 dB/year. RNFL thinning was found in 12 of 16 eyes with an average rate of progression of 2.58 ± 1.43µm/year. 7 out 16 eyes were progressing at HRT RA (43.75%) while 5 of 16 and 6 of 16 were progressing at VF VFI (31.25%) and VF MD (37.5%) respectively. The agreement between GHT Cluster and VF VFI and VF MD was 0.34 and 0.2, respectively. The best agreement was found between GHT Cluster and OCT RNFL (k= 0.61).
Conclusions
Visual field clusters well detected spatial locations of sensitivity loss showing greater sensitivity than global indices (MD; VFI) and better concordance with structural changes .This suggests GHT clusters to be a sensitive method for the early identification of glaucomatous visual field loss.

• 1128

Reproducibility of angle metrics in children using hand-held spectral domain optical coherence tomography: intra-observer and inter-observer variability

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Purpose
To evaluate intraobserver and interobserver agreements of anterior chamber angle measurements in children using hand-held spectral domain optical coherence tomography (HH-SDOCT).
Methods
HH-SDOCT (Leica Microsystems Ltd) was used to scan the anterior chamber of 30 normal children (mean age = 5.12 ± 3.5 years, range: 2 days to 12 years). Two independent observers analysed the same B-scan showing both clear nasal and temporal angles using ImageJ. They identified iridocorneal angle landmarks: scleral spur (SS), Schwalbe`s line (SL) and angle recess (AR) and used them to calculate parameters such as trabecular meshwork length (TML), SS angle opening distance (SSAOD), SL angle opening distance (SLAOD), SL angle (SLA), SS limbal distance (SSLD), SL limbal distance (SLLD), trabecular iris surface area (TISA500), nasal to temporal SS distance (SS-SSD) and pupil diameter (PD). The reproducibility of measurements were assessed using interclass correlation coefficients (ICC) and Bland-Altman plots.
Results
Repeated measurements of anterior chamber were calculated in 141 images. Both intra-observer and inter-observer agreements of most measurements ranged from fair to excellent (0.66 to 0.97). Intra-observer and inter-observer ICC for SSAOD, SLAOD, SLA, SSLD, SLLD, TISA500, SS-SSD and PD were 0.74, 0.78, 0.81, 0.72, 0.80, 0.76, 0.96, 0.96 and 0.83, 0.85, 0.77, 0.91, 0.89, 0.83, 0.84, 0.97, respectively. TML reproducibility was poor, ICC were 0.42 and 0.33, respectively. Bland Altman plots showed no significant difference between repeated measurements (P value were >0.05) for parameters with ICC reproducibility ≥ 0.7.
Conclusions
Reproducible quantitative measurements in children using HH-SDOCT was possible with ICC of up to 0.97. Anterior segment OCT could be a potential method in understanding the normal and abnormal ocular development of children.

• 1131

Pathophysiology of uveitis

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Summary

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

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Summary

Classification of uveitis is important for diagnostic reasons. The first step in developing a differential diagnosis for patients with an intraocular inflammation is to classify the uveitis in detail. Proper classification is also essential if one is to avoid confusion and misinterpretation among multiple ophthalmologists caring for a given patient.
Different types of classification are used: The anatomic classification
should not be confused or overlap with the etiologic
classification. Both classifications are required and important,
but they are distinct and different.

• 1133

Signs and symptoms of uveitis

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Summary

Uveitis can be a sight-threatening disease. In ammation of uveal tract can be divided into: anterior, intermediate, posterior, and panuveitis. Blurred vision, ocular pain, photophobia and oaters are some of the symptoms complained by those who are a ected by uveitis. e onset of uveitis can be either acute or insidious, bilateral rather than unilateral. Posterior uveitis is usually associated with vitritis. Anterior chamber cells and are should be graded according to standardized uveitis nomenclature (SUN) working group. Binocular indirect ophthalmoscopy (BIO) score is used to evaluate the severity of vitritis. Vitreous changes may comprehend: vitreous hemorrhage, vitreous strands, and vitreous traction. A further classi cation of posterior uveitis depends on the primary site of in ammation, which can identify: retinitis, choroiditis, retinochoroiditis, and chorioretinitis. Posterior pole uveal involvement can be: focal, multifocal, and placoid. Retinal vasculitis can be present. Uveitis might be complicated by 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

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Summary

Making the correct diagnosis of a specific uveitic entity is critical to appropriate management. The likely diagnosis can be derived from medical history, anatomic type and clinical characteristics of uveitis, and results of ocular imaging in selected cases. Laboratory testing then is performed to look for an infectious cause or an underlying systemic disease, that cannot be identified on a clinical basis. A comprehensive work-up is costly and unnecessary. It may also give misleading positive results. Laboratory investigations should rather be tailored to epidemiological data and clinical findings. In cases of suspected intraocular infections, intraocular fluids may be evaluated for specific antibody production or polymerase chain testing. In case of negative history and absence of findings suggestive of a particular diagnosis, a minimal work-up should be performed, including complete blood count, erythrocvyte sedimentation rate, Mantoux test, interferon-gamma release assay, chest X-ray, and serology of syphilis. A more extensive work-up may be required in cases of severe uveitis, recurrences, resistance to treatment or worsening under therapy.

• 1135

Imaging in uveitis: modalities and applications

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Summary
Uveitis has become a precise clinical science, in part thanks to the development of performing imaging methods. Laser flare photometry (LFP), although not an imaging method "stricto sensu", measures back-scattered photons from the anterior chamber produced by a laser beam and so establishes the exact level of intraocular inflammation at any time and allows precise monitoring of uveitis. Fluorescein angiography (FA) has been used for more than 50 years and gives indications on inflammation of superficial structures of the fundus, optic disc and the retinal pigment epithelium. Indocyanine green angiography (ICGA) became available in the early 1990ties and is essential in the precise investigation of the inflammatory, otherwise occult reaction in the choroidal compartment, giving panfundal information that is otherwise not available. Optical coherence tomography (OCT) analyses both the retina and choroid (in the enhanced depth mode - EDI) of the posterior pole. Ultrasound biomicroscopy (UBM) is useful to analyse inflammation in the retro-iridal space. Other imaging methods such as fundus autofluorescence (FAF) or OCT-angiography are still being evaluated for their utility in uveitis.

• 1136

Therapeutic management of uveitis

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Summary
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 immuneresponse 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

Measurement of retinal blood flow using Doppler OCT in diabetic retinopathy

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Summary
Purpose: To determine factors of importance for quantitating retinal blood flow in patients with diabetic retinopathy using bi-directional Doppler OCT.
Methods: Retinal blood flow was measured by bi-directional Doppler OCT in 20 diabetic patients with different diabetes type, age and retinopathy stage.
Results: It appeared that age above 40 years was a significant limiting factor for obtaining suitable signals to measure retinal blood flow, which was due to lens opacities and insufficient mydriasis. Quantitative measures of blood flow in the studied patients below the age of 40 years will be reported.
Conclusion: Bi-directional Doppler OCT offers a new principle for quantitating retinal blood flow, but the principle has not yet been fully developed to be suitable for routine clinical practise.

• 1142

Retinal oximetry in central retinal vein occlusion

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Summary
Purpose: To determine the significance of retinal oxygen saturation for visual acuity at diagnosis and after anti-VEGF treatment of central retinal vein occlusion (CRVO).
Methods: Retinal oximetry was performed in 91 patients with CRVO at the Department of Ophthalmology, Aarhus University Hospital, and the predictive value of the retinal oxygen saturation in larger retinal vessels for the visual prognosis after anti-VEGF medication was studied.
Results: At baseline the oxygen saturation in larger retinal vessels was significantly increased in arterioles and decreased in venules in the affected eye. Best corrected visual acuity (BCVA) showed a significant negative correlation with the oxygen saturation in retinal arterioles and a positive correlation with the oxygen saturation in retinal venules. Multiple linear regression showed that BCVA, but not oxygen saturations, contributed significantly to predicting visual outcome after treatment.
Conclusion: Measurement of retinal oxygen saturation may help understanding haemodynamic and visual changes in the acute stages of CRVO. However, retinal oximetry cannot replace measures of retinal function as a predictive parameter for the visual outcome in CRVO after intravitreal anti-VEGF therapy.

• 1143

Retinal microvascular imaging with adaptive optics

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Summary
The human eye provides an accessible, transparent "window" to its retinal structures that can be examined in vivo. Retinal images obtained with conventional modalities such as optical coherence tomography (OCT), scanning laser ophthalmoscopy (SLO) and fundus imaging are degraded because even an emmetropic eye is optically imperfect and fraught with aberrations.
By implementing adaptive optics (AO) to the aforementioned imaging modalities (AO-OCT, AOSLO, AO flood-illumination camera, respectively) we are able to measure and compensate for these aberrations in the living human eye in real time. Retinal structures including (but not limited to) the capillary vasculature, photoreceptors, the retinal pigment epithelium, the nerve fiber layer and -recently- the ganglion cell layer have been succesfully resolved with AO systems down to a cellular scale.
Here the focus is AOSLO systems and imaging techniques currently available in 1) visualising the retinal microvasculature and 2) quantifying blood flow. Both confocal and non-confocal AOSLO detection schemes will be discussed.

• 1144

Static vessel parameters in health and disease

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Summary
Non-invasive observation of the retinal circulation in vivo has seen more and more interest in clinical applications in recent years, not only because of ease of acquisition but also due to improved analysis software. Standardized semi-automatic analysis of vessel calibers are useful markers in systemic vascular disease and have been shown to be linked with disease progression and future cardiovascular events. In recent years new vessel segmentation algorythms and analysis software has made it possible to assess not only vessel calibers but also parameters such as tortuosity, vessel density and branching patterns.
In summary these vessel parameters in conjunction with measurements of retinal metabolism, vessel dynamics and retinal structure allow us to gain a better insight into normal retinal physiology and retinal pathophysiology due to systemic vascular disease.

• 1145

Assessment of retinal blood flow using Laser Speckle Flowgraphy

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Summary

Laser speckle flowgraphy (LSFG) is a promising technique for the two-dimensional, non-invasive assessment of ocular blood flow. We set out to investigate the use of this technique in healthy Caucasians. First, we evaluated the validity of retinal perfusion measurements by direct comparison with dual-beam Doppler optical coherence tomography (D-OCT). Relative flow volume (RFV), the main output parameter of LSFG, was in significant agreement with absolute blood flow measurements as obtained from D-OCT in arteries ($r=0.69$, $P=0.001$) and veins ($r=0.74$, $P<0.001$). We also found that most of LSFG-derived parameters were age-dependent in a healthy population.

In addition, retinal blood flow autoregulation during isometric exercise was studied using LSFG. Retinal blood flow started to increase significantly at ocular perfusion pressure levels that were 45% over baseline. These findings are comparable to data obtained in previous studies.

The presented results show that LSFG can be applied to study ocular blood flow in healthy Caucasian subjects. The technique may also be used in patients with ocular diseases associated with vascular dysregulation such as glaucoma, age-related macular degeneration or diabetic retinopathy in the future.

• 1151

Using biomarkers in clinical trials in ophthalmology

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Summary
Detailed investigations of the composition and changes in the composition of the tears of the ocular surface have provided new ways of evaluating patient outcomes. This intimate knowledge comes from the ability to very accurately quantify proteins found in the tears. As such proteomics as a method is rather similar to performing hundreds or thousands of ELISA assays (which would be an impossible task as the tear volume is insufficient). Moreover, the results using only a few microliters of tears are reproducible so that patients can be statistically evaluated for examining outcomes. Tear proteins can be evaluated in some cases according to their source: for example, lacritin, and lysozyme are secreted from the lacrimal gland while the pro-inflammatory proteins S100A8 and S100A9 are secreted by PMNs and ocular surface epithelial cells. The ability to indicate which proteins support ocular surface and which are inflammatory can reveal how a therapeutic treatment is changing or has not changed the basic pathology.
Conflict of interest
Any consultancy arrangements or agreements:
Santen
Allergan
Any research or educational support conditional or unconditional provided to you or your department in the past or present:
Santen

• 1152

Executing clinical proteomic studies using mass spectrometry

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Summary
Biomarkers are tools of personalized medicine and potentially valuable end points for clinical studies. They can be used to measure a patient's risk to certain disease and the severity of the disease, and to predict and/or measure the patient's therapeutic response to treatment. Mass spectrometry (MS) enables simultaneous detection and quantification of most proteins, and therefore has become an attractive method for biomarker discovery in the recent years. It can be used to detect changes in cellular functions and metabolism in a more comprehensive way than the traditional immunoassays. In this presentation, the techniques used in sample preparation and MS will be demonstrated in a practical way. The presentation will cover methods used through the different phases of clinical proteomic studies from planning to discovery and validation of discovered biomarkers.

• 1153

Bioinformatic analysis of experimental and clinical proteomic data

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Summary
Proteomics, along with other omics, can be utilized as a tool of personalized medicine in order to understand the individual needs of patients better based on their expression levels of proteins. This type of personalized approaches are likely to be much more common in the future, since new diagnostic and therapeutic methods are constantly being developed and there is already currently a great need to select the most cost-effective ones for each patient. For these reasons, a lot of effort is currently going into finding potential biomarkers through discovery studies. In addition to sample processing and advanced equipment, proteomic research also requires the work of statisticians and bioinformaticians as the research methods produce a growing amount of statistical data. Hence, methods of analyzing big data are also increasingly important and therefore researchers in bioinformatics field are both developing new methods and utilizing old ones in order to tackle the growing data. This course will focus on some of the most basic aspects of bioinformatics analysis of proteomic data and is aimed to provide clinicians and other researchers alike better understanding of the aspects important to the analysis.

• 1154

Practical examples of proteomic studies

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Summary
Proteomics, along with other omics, is a potentially valuable tool of personalized medicine and thus helping in selecting the most cost-effective diagnostic and therapeutic options for each patients. This type of personalized approach is becoming more common in the future, since new diagnostic and therapeutic methods are constantly being developed. On the other hand, processing and analyzing of the proteomic samples is becoming easier, more accurate and also cheaper. Tear fluid and ocular surfaces are important and easily available source of samples reflecting not only the state of the anterior segment of the eye but also eye and even human body in general. This presentation is based on the previous ones describing methods of sample processing and mass spectrometric analysis methods of this type of samples as well as on aspects of bioinformatics analysis of proteomic data. It is aimed to provide basic scientists and clinicians an overview of the aspects that are important by using practical examples of this type of research. These examples are covering clinical studies on dry eye, glaucoma medication, glaucoma surgery and refractive surgery.

• 1161

Neural retina identity is specified by lens-derived BMP signals

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Summary
During early development of the CNS, the anterior neural domain becomes restricted into different regions as: the telencephalon, the optic cup and the diencephalon. Simultaneously, lens progenitors are specified in the neural plate border. The molecular mechanisms that regulate the induction and maintenance of eye-field cells, and the specification of neural retina cells in relation to other forebrain domains have been poorly defined. If prospective lens cells affect the early development of retinal progenitors have been debated. We have analysed these issues in intact chick embryos and explant assays. Our results show that BMP signals emanating from the lens ectoderm maintain eye-field identity, inhibit telencephalic character and induce neural retinal cells. This highlights a novel role for BMP signals during the early development of the retina that is distinct from previously described roles in dorso-ventral patterning and fate choice between neural versus RPE cells. Our findings link the requirement of the lens ectoderm for neural retina specification with the molecular mechanism by which cells in the forebrain become specified as neural retina by BMP activity.

• 1162

The role of Meis genes is lens and retina development

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Summary
While significant insights into the functional role of some transcription factors for eye formation have been accomplished, much less is known about the intricate wiring of the gene regulatory network (GRN) that controls the earliest stages of eye development. Here we focus on the role of Meis homeobox genes in mammalian lens and retina development. It is well established that Pax6 represents a key node in the GRN governing lens induction. Meis1 and Meis2 were proposed to be essential upstream regulators of Pax6 during lens morphogenesis. This hypothesis is corroborated by the fact that Meis1/Meis2 double-deficient mice phenocopy Pax6 mutant mice at the lens placode stage. We demonstrate that Meis1 and Meis2 homeoproteins regulate Pax6 gene via two redundant (shadow) enhancers, EE and SIMO. Simultaneous genetic ablation of EE and SIMO enhancers demostrates their requirement for lens induction. Using conditional gene targeting in mice at optic cup stage we provide evidence of a role of Meis genes in the process of retina development. Combined, our data indicate that Meis1 and Meis2 genes are required for normal lens and retina development.

• 1163

Neural crest FGF signaling controls lacrimal gland development

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Summary
NEURAL CREST FGF SIGNALING CONTROLS LACRIMAL GLAND DEVELOPMENT

Neural crests are multipotent progenitors that migrate from the neural tube to populate the entire body, differentiating into diverse cell types in many organs. FGF signaling is one of the key regulators of neural crest development, but the downstream signaling mechanism is not well understood. Here we show that conditional knockout of Shp2 disrupted migration, survival and differentiation of neural crests, culminating in the loss of Fgf10 into the periocular mesenchyme. This results in abrogation of lacrimal gland development. These phenotypes are reproduced by genetic ablation of Fgfr, adaptor protein Frs2 and downstream kinases Mek and Erks in the neural crest, and rescued by constitutive activation of Kras, establishing a FGFR-Frs2-Shp2-Ras-MEK-ERK cascade. By RNAseq analysis, we showed that Shp2 deficiency causes significant changes in the neural crest transcriptome and identified critical regulator of Fgf10 expression in the periocular mesenchyme. These results demonstrate that neural crest FGF signaling is essential for lacrimal gland induction.

• 1164

Genes and regulation of eye development

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Summary
Developmental ocular disorders have a strong genetic component. Our laboratory has been applying whole exome sequencing (WES) to identify novel human genes associated with abnormal eye development for many years. WES provides the opportunity to simultaneously screen coding regions of all genes in order to identify causative mutations. While this comprehensive examination greatly improves the chances of mutation detection, interpretation of the large volume of data is complicated. Since many developmental processes are conserved in vertebrates, studies of zebrafish orthologs of human disease genes can provide critical information about their embryonic function and determine other genes involved in the same pathway. With this, studies of zebrafish mutants help to identify an additional pool of relevant gene candidates for corresponding human phenotypes. Moreover, zebrafish model allows for rapid in vivo testing of promising human variants by overexpression and/or rescue experiments. Our utilization of this approach in studies of zebrafish orthologs of several transcription factors, such as PITX2, PITX3 and FOXE3 associated with Axenfeld-Rieger syndrome, anterior segment dysgenesis, cataracts and microphthalmia, will be presented.

• 1165

Transcriptional dynamics, denucleation, and gene regulation in embryonic lens development

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Summary

Transcription of genes occurs in apparently irregular pulses of activity termed transcriptional bursts. In contrast, cellular differentiation is marked by coordinated gene expression of batteries of genes required for cellular specialization. Ocular lens is comprised of two compartments: the lens epithelium and lens fibers. Position of individual cells within the lens is directly related to their differentiation status, marked by expression of individual crystallin genes. Another hallmark of lens fiber cell differentiation is organized degradation of their organelles. It is currently not known how transcription is terminated in the disintegrating lens fiber cell nuclei and what are the external and internal components of this process critical for lens transparency. Onset of expression of different crystallins follows the temporal pattern Cryaa > Crybb1 > Cryga in differentiating lens fibers. Surprisingly, expression of Cryaa is terminated in "normal" fiber cell nuclei while expression of Cryga persists even in highly condensed nuclei just about to be disintegrated. Differentiation influences both transcriptional burst size and frequency as well as spatial pairing of different chromosomes that carry crystallin genes.

• 1171

Scanning laser ophthalmoscopy – basic optical principles

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Summary
Scanning Laser Ophthalmoscopy (SLO) produces an ocular fundus image by moving a focused laser beam via scanning mirrors over the retina in a grid pattern and registering the reflected light from each scanned point. In confocal SLO, a pinhole is placed in front of the detector to cut off scattered or defocused light coming from outside the point of interest, which otherwise can blur the image. This results in a focused, high-contrast image of a single tissue layer located at the focal plane. Tomographic information can be extracted by moving the plane of the pinhole. The use of various wavelengths allows for different applications, such as fluorescein angiography, indocyanine green angiography, and autofluorescence imaging. This lecture will present the basic principles of SLO, as well as discuss notable applications and variants of the technology.

• 1172

Optical coherence tomography – basic optical principles

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Summary
Optical Coherence Tomography (OCT) is an optical analogue to ultrasound imaging. The much higher speed of light compared with sound allows for finer cross-sectional views of the retina and anterior segment. Since it is extremely difficult to directly detect the shorter "echo" times it takes light to travel from different structures at axial distances within the eye, interferometry is used. Incident light is thus split into two beams, and the beam backscattered from the ocular tissue is then compared ("interfered") with the beam that has traveled a known time from the reference mirror. Broadband (i.e., low "coherence") light sources are used, because they produce a wider band of wavelengths, and thereby enable greater sensitivity in comparing the travel time differences of the two beams. In time-domain OCT, the reference mirror position is altered, so that interference patterns are generated whenever the two beams have traveled almost the same amount of time. In spectral-domain OCT, the reference mirror position is fixed and the mixed interference patterns are separated via spectral wavelength analysis. This lecture will explain underlying concepts of OCT with a discussion of cutting-edge technological developments.

• 1173

Optical coherence tomography – machine learning

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Summary
Machine learning is a method of data analysis. It gives computers the ability to learn from data and to build models from which predictions can be made. Even though OCT is mainly used to visualize retinal structures and compute thickness maps, it conveys information on subtle changes within the retina before structural ones can be identified. Exposing the machine learning model to a set of examples allows it to build a model from which predictions can be made on new data and explain differences between groups. This lecture will explain the underlying principles of machine learning and discuss potential applications in ophthalmology and CNS disorders through the imaging of the retina.

• 1174

Adaptive optics – basic optical principles

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Summary
Adaptive Optics (AO) refers to a technique to compensate for distortions caused by optical aberrations in the media between the camera and the object being imaged. It was originally developed for use in astronomical telescopes to compensate for optical distortions induced by the inhomogeneous earth atmosphere. It has since evolved to become a powerful clinical tool in ophthalmology. In the eye, a "wavefront sensor" (aberrometer) measures the distortion of incoming light induced by inhomogeneities within the cornea and crystalline lens, which is then "undistorted" via reflection by a deformable mirror. AO thus enables imaging of the human retina with unprecedented resolution in vivo, such as revealing individual photoreceptors or the walls of blood vessels. One should note that AO by itself does not provide an image; rather an AO subsystem is incorporated into an existing imaging device. AO subsystems have thus far been successfully integrated into three ophthalmic imaging devices: fundus cameras, scanning laser ophthalmoscopes, and the OCT device. This lecture will introduce the basic principles of AO, illustrate its value with state-of-the-art clinical examples, and discuss potential future applications in ophthalmology.

• 1181

Omega-3 fatty acids supplementation: therapeutic potential in a mouse model of Stargardt's disease

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Purpose
To evaluate the therapeutic effects of omega-3 (ω-3) fatty acids in the ABCA4-/- model of Stargardt's disease. Monitoring the blood level of eicosapentaenoic acid (EPA) and arachidonic acid (AA), served to adjust the treatment dosage (AA/EPA = 1-1.5).
Methods
Eight-month-old mice were allocated to different groups: A) wild type (129S1), B) ABCA4-/- untreated, C) ABCA4-/- treated with ω-3. Treatment was daily administered by gavage for 3 months. Eye cups from each group were histologically examined using confocal and transmission electron microscopy. Proteomic analysis and N-retinylidene-N-retinylethanolamine (A2E) quantification was carried our using liquid chromatography mass spectrometry (LC-MS/MS). Blood and retinal fatty acids analysis was performed using gas chromatography (GC).
Results
A significant decrease in melanolipofuscin granules in the retinal pigment epithelium (RPE) was observed in the treatment group, in parallel with a reduction in A2E level, a major component of RPE lipofuscin. Proteomic analysis indicated decreased levels of complement 3 (C3) in the treated group. The outer nuclear layer (ONL) thickness was significantly greater in group C (75.66 ± 4.8 μm), compared to group A (61.40 ± 1.84 μm) and B (56.50 ± 3.24 μm). Increased EPA and decreased AA levels were observed in both blood and retinas in the treatment group.
Conclusions
Supplementation with ω-3 fatty acids (when AA/EPA = 1-1.5) suggests a protective mechanism in the ABCA4-/- animal model of Stargadt's disease.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Dr T. Georgiou has a patent on omega-3 and eye diseases

• 1182

Vision improvement in dry and wet Age-Related Macular Degeneration (AMD) patients after treatment with new corneal CPV procedure for light redirections onto the retina

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Purpose
To evaluate in two clinics vision improvement in AMD patients treated with a new corneal elastic modulus-altering procedure (CPV) for light redirections onto multiple retinal areas.
Methods
Ten eyes (6 wet, 4 dry), with best-corrected near and distance visual acuities (CNVA and CDVA) between 20/80 and 20/400, without pathological retinal morphology completely affecting the central 10° (3 mm) on OCT, were given a single treatment of CPV and were examined for 12 months post-CPV.
Results
LogMAR Mean CNVA and CDVA in treated eyes improved ($p < 0.01$) from pre-CPV 0.957 and 0.942 to 0.512 and 0.638, 0.544 and 0.602, 0.531 and 0.672 at 1, 6 and 12m, respectively. The number of ETDRS letters gained in mean binocular CNVA/CDVA were 22/15, 25/19, 25/18 at 1, 6, and 12m, respectively. Administered NEI VFQ-25 at 3m improved from pre-CPV. No CPV complications or adverse events occurred.
Conclusions
CPV effectively, safely, rapidly and comfortably redirects light onto functional retinal areas after a single treatment to provide, without visual training, significantly improved monocular and binocular near and distance vision without causing peripheral field restriction or diplopia in patients with atrophic or neovascular AMD with poor vision, including after anti-VEGF therapy to which CPV is complementary and for which CPV may improve compliance because of improved vision restoration.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
patent assignment agreement OAC

• 1183

Optical coherence tomography angiography in occlusive retinal vasculitis

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Purpose
Fluorescein angiography (FA) has been the gold standard for the evaluation and management of occlusive retinal vasculitis. Our purpose is to describe swept-source optical coherence tomography angiography (OCTA) findings in eyes with occlusive retinal vasculitis.
Methods
This prospective study included 15 patients (25 eyes) diagnosed with occlusive retinal vasculitis involving the posterior pole or the periphery. All patients were evaluated using FA, spectral domain optical coherence tomography, and OCTA.
Results
The causes of occlusive retinal vasculitis included Behcet disease in 12 patients (21 eyes), ocular tuberculosis in 1 patient (2 eyes), West Nile virus infection in 1 patient (1 eye) and rickettsiosis in one patient (1 eye). OCTA was superior to FA in evaluating perifoveal microvascular changes. It showed in twenty eyes (80%) areas of retinal capillary nonperfusion/hypoperfusion with or without associated rarefied, dilated, or shunting vessels. The deep retinal capillary plexus was more severely affected than the superficial capillary plexus.
Conclusions
OCTA allowed better evaluation of macular ischemia than FA in eyes with occlusive retinal vasculitis. The deep capillary plexus appeared to be more severely involved than the superficial capillary plexus.

• 1184

Choroidal thickness assessed by swept-source optical coherence tomography in patients with diabetes

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Purpose
To measure choroidal thickness (CT) in diabetic subjects and to correlate it to the severity of diabetic retinopathy (DR) and diabetic macular edema (DME).
Methods
Prospective study using swept-source optical coherence tomography. Choroidal thickness maps of 117 eyes of 60 diabetic patients were compared to 45 eyes of 24 healthy controls. The type of DR (no retinopathy: n = 18 eyes; non proliferative DR – NPDR: n = 62 eyes, proliferative DR – PDR: n = 37 eyes), the type of DME (no DME: n = 39 eyes, diffuse: n = 36 eyes, cystoid: n = 36 eyes, mixed: n = 6 eyes), the duration of diabetes, blood hemoglobin A1C (HbA1C) level and hypertension (HT) were recorded, and their relation to CT was evaluated using multiple regression models.
Results
No significant difference in central subfoveal and mean overall CT was observed between diabetic patients and controls ($p>0.05$). A significantly thinner choroid was measured in PDR eyes compared to NPDR group ($p<0.01$). CT did not show any correlation with type of DME ($p>0.05$). Analysing the whole cohort, the decrease of CT was assessed in subjects with HT ($p<0.05$). Aging showed significant correlation with choroidal thinning (30 μm/10 years; $p<0.001$) after adjustment for HbA1C level and HT. In diabetic patients the duration of the disease significantly correlated with choroidal thinning (15 μm/10 years; $p<0.05$) after adjusting for the effect of age, HbA1C level and HT.
Conclusions
The thinning of the choroid is affected more significantly by the age and HT, than the presence of diabetes. In diabetic patients the duration of the disease is an independent predictor of choroidal thinning.

• 1185

Bilateral quantification of vascular density in diabetic patients using optical coherence tomography angiography

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Purpose
To measure capillary vessel density (VD) using optical coherence tomography angiography (OCT-A) in both eyes of diabetic patients and to evaluate its correlation with systemic risk factors.
Methods
A total of 103 eyes of 61 diabetic patients underwent OCT-A imaging (RTVue-XR Avanti; Optovue, Fremont, CA, USA). The control group included 92 eyes of 46 individuals without diabetes mellitus. In diabetic patients the duration of diabetes, insulin therapy, blood pressure, HbA1C, dyslipidemia and the presence of diabetic retinopathy was recorded. VD was examined in the central macula with a radius of 3 mm. The effect of risk factors on VD was assessed bilaterally using multivariable regression analysis.
Results
Vessel density was significantly decreased in diabetic patients compared to controls (47.26 vs. 50.88%; p<0.001). In control subjects, VD significantly decreased with age (r=-0.54; p<0.001), while in diabetic patients VD was associated only with the duration of diabetes among the risk factors (r=-0.15/year, p=0.03). VD was also significantly decreased in diabetic patients without clinically detectable diabetic retinopathy compared to control subjects (48.19 vs. 50.88%, p<0.001). Between-eye difference in VD were significantly higher in diabetic patients with retinopathy (4.46±2.95%) and without retinopathy (4.19±2.40%) in comparison to the controls (2.74±2.24%; p=0.02 for both comparisons).
Conclusions
Significantly decreased retinal vessel density and increased between-eye asymmetry can be measured in diabetic patients compared to control subjects even before the presence of clinically detectable diabetic retinopathy. While in control subjects vessel density decrease with aging, in diabetic patients both vessel density and between-eye asymmetry are significantly associated with the duration of diabetes.

• 1186

Differential diagnosis of cystoid macular edema by optic disc thickness in optical coherence tomography

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Purpose
The differential diagnosis between Irvine-Gass Syndrome (IGS) and Diabetic Macular Edema (DME) is currently established by angiography, which is an invasive and time-consuming tool.
The aim of this study is to evaluate differences in optic disc's nerve fiber layer thickness (RNFL) in patients with macular edema associated with IGS and Diabetes Mellitus (DM).
Methods
Retrospective case control study of 28 eyes of 28 patients with macular edema divided into 2 groups. Group 1 included 14 eyes with IGS diagnosed by clinical and angiographic criteria and group 2 included 14 eyes with cystoid diabetic macular edema (DME) without previous ocular surgery. A control group (group 3) of 14 eyes of 14 healthy patients paired by age and gender were also included. Ophthalmologic examinations included visual acuity (VA) measurements, slit-lamp examination, Goldmann applanation tonometry, Spectral-Domain Optic Coherence Tomography (SD-OCT) and fluorescein angiography.
Results
Forty two patients (21 females and 21 males), with a mean age of 66.57 ± 10.80 years were included in this study. Optic disc nasal and temporal RNFL thicknesses as well as central macular thickness were significantly higher in group 1 and 2 compared with control group (p<0.05). Nasal RNFL thickness was higher in IGS than in patients with DME (p<0.001). To detect IGS (Group 1), comparative to DME (Group 2), using Nasal RNFL thickness, the area under the curve was 0.842 p<0.002. A cut-off criterion of 82.50 µm resulted in 92,9 % sensitivity and 71,4 % specificity.
Conclusions
Optic disc SD- OCT imaging might be a useful diagnostic tool to differentiate IGS from DME.

• 1188

27-Gauge vitrectomy – the smaller the better?

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Purpose
To evaluate anatomic, functional and refractive outcomes after 27-gauge vitrectomy in a prospective study.
Methods
The study was designed to include patients presenting with vitreoretinal disorders (epiretinal membrane [ERM], macular holes, asteroid hyalosis and vitreomacular traction [VMT]) with or without coexisting significant cataract. Exclusion criteria were (a) patients with rhegmatogenous or tractional detachment, (b) previous vitreoretinal surgery, and (c) the need for silicone oil tamponade. Surgical conditions using a scaled questionnaire, complication rates, IOP, functional and refractive outcomes were evaluated. All surgeries were performed by one surgeon (F-R CI).
Results
Up to now, 60 patients, 41 females and 19 males with a mean age of 72 years, have completed the 3 months follow-up. The vitreoretinal diagnosis was ERM in 36 eyes, macular holes in 9 eyes, VMT in 2 eyes, and asteroid hyalosis in 13 eyes. In 47 eyes cataract surgery was combined with vitrectomy. Intraoperative conditions were graded good to excellent. However, a slightly increased time needed for core vitrectomy was noted and particularly in hyperopic and left eyes the 27 gauge instruments were graded to be more flexible. No wound leakage was found and the IOP was stable in all eyes. Complication rates included a mild postoperative vitreous hemorrhage in one patient which spontaneously resolved during follow-up. Visual acuity improved in all patients and the refractive results in the combined cases were excellent.
Conclusions
These results suggest that 27 gauge vitrectomy with or without combined cataract surgery results in excellent wound architecture and offers promising functional and refractive results.

• 1189

Bidirectional cross talk between uveal melanoma cells and hepatic myofibroblasts promotes inflammation-induced chemokines expression

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Purpose
Uveal melanoma (UM) is the most common primary ocular neoplasm in adults. Its cause is largely unknown, and no risk factors have yet been identified. The metastatic disease develops in up to 50% of patients, usually involving the liver. Treatment only rarely prolongs survival, because metastases are highly resistant to most chemotherapeutic agents. Tumor cells may modulate the functions of surrounding cells to facilitate their own growth, survival, invasion, and metastasis. This study was conducted to investigate the role of hepatic microenvironment on UM cells (UMC).
Methods
Here, we utilized metastatic (Omm2.3) and non-metastatic (Mel270) UMC in coculture with hepatocyte-stellate cells (HSC) LX2. The transcriptomic study was performed by microarray assay. Expression of relevant genes was measured by qPCR. Cytokines were quantified by Elisa test. Cell proliferation was assessed by MTT staining. Extracellular matrix components were evaluated by quantitative cell adhesion assay.
Results
Hepatic microenvironment increased the expression of numerous genes. However, the number of genes overexpressed in metastatic co-cultures is three-times higher than in non-metastatic cocultures, demonstrating that hepatic microenvironment has more impact on metastatic UMC. Over-expressed genes in coculture were linked to inflammation and included several interleukins. In addition, UMC-HSC crosstalk generated expression of cell adhesion receptors, particularly by increasing fibronectin. In contrast, hepatic microenvironment had no effect on cell proliferation.
Conclusions
Our results provide evidence for an important role of inflammation in the progression of metastatic UM. Therefore, the inflammatory characteristics of the tumor microenvironment might offer therapeutic opportunities.

• 1190

Intraconal hybrid neurofibroma - schwannoma of the orbit

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Purpose
Among peripheral nerve sheet tumors, an orbital hybrid neurofibroma-schwannoma has been described twice. We describe a third case of orbital tumor with features of both a neurofibroma and a schwannoma.
Methods
Case report. A 39 year old man presents with diplopia and decreased vision (0.6) in the left eye. He has a proptosis of 7 mm, with mechanical restriction of elevation and horizontal eye movements. MRI shows a well-defined lesion (2,5 x 1,9 x 2,3 cm) in the superotemporal intraconal space, displacing the globe, optic nerve and superior and lateral rectus muscles. The tumor demonstrates heterogeneous contrast enhancement, and is diagnosed as a probable cavernous hemangioma. Through a transconjunctival approach a red-blueish lesion was found with a thin capsule and without lateral adhesions. The tumor could be extracted in 2 parts and consisted of a yellow/white coherent soft mass.
Results
Patient had complete recovery of visual acuity, and only diplopia in extreme lateral gaze. The pathology revealed a tumor composed of small spindle cells arranged in fascicles. The cells showed no atypia and there was no mitotic activity. There were also less cellular areas with a myxoid component. At places we could recognize a fibrous capsule surrounding the tumor. The tumor cells were strongly and diffuse positive with S100. In a few enclosed axons there was focal reactivity with neurofilament. The image is that of a neural tumor with features of both a neurofibroma and a Schwannoma.
Conclusions
This is the third reported orbital hybrid neurofibroma-schwannoma. Although this type of tumor elsewhere in the body is often associated with schwannomatosis and neurofibromatosis, our patient did not show signs of systemic involvement.

• 1191

Alternated intra-arterial and intravitreal chemotherapy: successes and failures of advanced intraocular retinoblastoma treated without systemic chemotherapy

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Purpose
To report the efficacy of combined intravitreal chemotherapy (IViC) and intra-arterial chemotherapy (IAC) for the treatment of advanced stage retinoblastoma.
Methods
The medical records of twenty patients affected by unilateral advanced retinoblastoma (Reese-Ellsworth stage Vb/D of ABC classification). After clinical and ophthalmoscopic evaluation, they underwent MRI to exclude local and CNS dissemination. The IAC was given to treat retinal masses and intravitreal injections to treat vitreous seeding. Patients had received two cycles (six infusions) of IAC, and from six up to ten melphalan injections into the vitreous, with an interval of 7-10 days between them.
Results
All patients underwent to bimonthly MRI examination, during treatment and every 3 months for 1 year after last injection, to exclude orbital dissemination. Successful control (57.8 %) of tumor masses and vitreous seeds was achieved in all cases at 12 up to 60 months follow-up. No permanent complications have been reported. Transient omplications disappeared throughout the months. No intraocular or orbital tumor recurrence or retinoblastoma metastases were observed.
Conclusions
Sequential IAC and intravitreal melphalan for advanced retinoblastoma is a good tool to provide retinal and vitreous seed control.

• 1192

Nanostructured hydroxyapatite used as an augmenting material to expand the orbit

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Purpose
To test the nanostructured hydroxyapatite as an augmenting material to expand the orbit after initial placement of a porous implant.
Methods
Nanostructured hydroxyapatite powder mixed with blood was surgically introduced in the scleral sac of 6 eviscated rabbits (Oryctolagus cuniculus europaeus) after previous placing of a porous hydroxyapatite integrated implant (proved by CT scan). CT scans were done at 1, 2 and 3 months postsurgical to demonstrate the integration of the injected material in the porous implant. The scleral sac wes removed after 3 months and histopathologic examination plus CD31+ (as a marker of neovascularization and osteosinthesis) were performed.
Results
CTscans performed at 1, 2 and 3 months postoperatively and the rapid development of CD31+ osteoclasts and vascular tissue pleade for a good integration of the new material in the previous porous hydroxyapatite implant.
Conclusions
This method can be used for enhancing the volume of a small scleral sac with a previous hidroxyapatite implant. Further studies should be performed.

• 1193

The advantages of serological tests of blood and tears for the diagnosis and the follow up of corneal rickettsiosis

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Purpose
Serological tests were rarely performed in the first intention in the diagnosis of corneal rickettsiosis in patients from an endemic area. The purpose is to elucidate the advantages of serological tests for rickettsiosis in the atypical cases of corneal infections
Methods
Case series study included 03 patients. immunofluorescent-antibody tests were performed to detect rickettsiosis in the blood and in the tears
Results
2 patients with atypical disciform keratitis, 1 patient with panuveitis with corneal involvement. Rickettsiosis was suspected because of skin palpebral lesions in 2 patients and in chronic uveitis in the 3rd patients. Serological tests were positive in the blood and in the tears. Treatment with tetracyclin was effective in the three cases without use of corticotherapy. In the follow up, good evolution of corneal signs and negative serological tests were noted.
Conclusions
Rickettsiosis should be considered in the etiology of atypical cases of corneal infection and serological blood and tear testing should be performed firstly in patients from an endemic area.

• 1311

Principles and techniques; pearls and pitfalls

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Summary
The contrast generated between static and non-static tissue results in a vascular signal. This principle stands at the base of OCT-Angiography (OCT-A), a novel imaging technique that allows to visualize the retinal and choroidal perfusion in a depth-resolved approach. Clinical investigations of OCT-A have demonstrated its potential in a wide variety of retinal and macular diseases. Dye angiographies maintain several advantages mainly related to the larger imaging field. Moreover OCT-Angiography needs some learning time to interpret the images, in order to distinguish new imaging features of a well know clinical entity from artifacts. Motion errors, improper software correction or shadowgraphic flow projection can lead to severe artifacts, which influence and sometime interfere with the imaging assessment.
Purpose of this lecture is to highlight the role of OCT-A in clinical practice: describing its principles, pearls and pitfalls may help the clinician to integrate this innovative approach in common patient care.

• 1312

OCT-A et critères d'activité

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Summary
Optical coherence tomography angiography (OCT-A) might be a useful tool to describe different morphological findings in treatment-naive exudative AMD (eAMD) before and after VEGF-trap intravitreal injections. Trough a prospective case series of 60 consecutive treatment naïve eAMD eyes diagnosed with different types of CNV a micro-structural analysis, based on 5 Activity Criteria (shape, branching pattern, presence of anastomoses, vessel's termini and presence of perilesional halo) was performed. Treatment-induced changes in choroidal neovascularization, CNV area and greatest linear dimension were assessed along with the variation in subretinal and/or intraretinal fluid. After treatment tiny branching vessels, anastomoses and peripheral arcades reduced from 100% of the cases to 40%, 50% and 30% respectively. Considering still-active lesions, persistent tiny vessels were observed in 75% of the cases, anastomoses in 60% of the cases and a residual activity of CNV was associated with a peripheral arcade in 100% of the cases. OCT-A Activity Criteria and quantitative findings, may help in the diagnosis of CNV, guiding decisions for treatment, as well as in monitoring the evolution of CNV and its response to treatment.
Conflict of interest
Any consultancy arrangements or agreements:
Allergan, Heidelberg, Novartis, Bayer

• 1313

OCT-A and assessment of CNV retreatment

COSCAS F, Coscas G, Souied E H
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Correlations in retinal vein occlusion (RVO) patients between macular vascular densities in the superficial and deep capillary plexuses obtained using OCT-Angiography (OCTA) and the data from conventional examination (visual acuity and peripheral retinal non perfusion on fluorescein angiography) might reveal new insights in the pathogenesis of vascular damage. Through a retrospective, observational study of RVO patients with who underwent a comprehensive ophthalmic examination including FA and OCTA a significant correlation between automatically quantified macular vascular density on OCTA and peripheral non-perfusion on FA was demonstrated; OCTA could help in identifying high-risk RVO patients who may benefit from further evaluation using FA.
Conflict of interest
Any consultancy arrangements or agreements:
Allergan, Bayer, Novartis

• 1314

OCT-A A in CSC and in MacTel type 2

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Summary
OCT-A with OCT « en face » allow a good imaging and location of vessel abnormalities in MacTel2. OCT-A reflects the progressive transformation of the perifoveolar capillaries and detects the presence of CNVs. There are still difficulties to analyse the link between the different layers of the retina & the choroid due to the frontal section of OCT-A. There is a need for 3D imaging.
A new symptomatology is described on OCT A in CSC as abnormal dark and white lesions. OCT B, C and multimodal imaging are mandatory in addition to OCT A to diagnose non neovascular retinal and choroidal CSC lesions. However, OCT A is very helpfull in the detection of abnormal choroidal neovascular membrane in CSC patients In CSC, signs on OCT-A must be interprete with caution and compare with multimodal imaging OCT « En-Face ». The main contribution in CSC of OCT-A is for CNV detection.
Conflict of interest
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
BAYER
NOVARTIS
SANOTEK

• 1315

OCT-A in ocular oncology

ZOGRAFOS L
Prof. Leonidas Zografos, Ophtalmology, Lausanne, Switzerland

Summary

OCT-A allows the visualization of various capillary plexusses located in front of the retinal pigmented epithelium. In case of partial depigmentation or metabolic modifications of the retinal pigmented epithelium, vascular networks located in the choroid can also be observed. This new imaging technique is currently used mainly in the diagnosis, the follow-up and the prognostication of irradiation induced maculopathy. The presence of a vascular network in pigmented and unpigmented small choroidal tumors visible in selected cases on OCT-Angiography offers new diagnostic perspectives which are currently under investigation.

• 1316

OCT-A: Diagnosis and management of surgical macular pathologies

POURNARAS C
Hirslanden, Centre Ophtalmologique de la Colline, Genève, Switzerland

Summary

The aim of the coarse is to demonstrate, using OCT-A, the most frequent clinical issues for various pathologies of the macular vitreoretinal interface et their typical evolution following an appropriate surgery.

OCT angiography (OCT-A) enable the simultaneous monitoring of the macular anatomic changes, the macular micro-circulation and flow, allowing the correlation of the functional to the anatomical outcomes during the progression of the anatomical damage as well as their recovery following surgery.

OCT-A indicate and improvement or the resolution the macular contour, associated with the improvement of the perifoveal capillary arcade distortion. The preoperative intraretinal cystoid changes, associated to ischemic changes mainly of the deep capillaries plexus, regresses following surgery. In addition the regression of the associated cystoid inner retinal cystoid changes is associated with the recovery of the superficial and deep capillaries integrity.

OCT-A evaluation following vitrectomy, demonstrated the transient anatomical and ischemic changes of the inner retina, reversible following an appropriate surgery.

• 1317

OCT-A and Diabetic maculopathy; automated assessement

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(2) *Paris, France,*

Summary

A fully automated quantitative assessment of OCT-Angiograms is a useful imaging system for detecting diabetic-induced focal vascular impairment both in retinal and choroidal layers. Through a retrospective case series of 48 DM eyes and 47 healthy controls evaluated by Spectralis HRA-OCT2 (Heidelberg Engineering, Heidelberg, Germany) it was shown that capillary density values were significantly lower ($p<0.05$) in all retinal vascular layers and choriocapillaris of DM patients compared with healthy subjects. Moreover retinal and choroidal vascular networks, although distinct entities, seem functionally interconnected: varying the degree of perfusion may be a mutual compensatory mechanism in response to an ischemic injury.

• 1321

Doctor is there anything else that I can do for my glaucoma?: Alternative therapy for glaucoma, what is the evidence?

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Summary
The usual algorithm for the treatment of glaucoma consists of medical or/and laser therapy, followed by surgical intervention if the IOP does not lower to the target or the disease progresses despite maximal medical therapy. Understandingly, just as for many other chronic diseases, patients are willing to do more for their glaucoma in order to prevent progression and ultimately blindness. The question: "Doctor is there anything else that I can do for my glaucoma?" is therefore often asked. Several studies have suggested that some lifestyle habits or alternative therapies may influence glaucomatous neuropathy and many patients admit using them either in conjunction or as replacement of their prescribed glaucoma medication. This talk will focus on the evidence that is behind these therapies. Education of ophthalmologist and patients is of great importance in order to avoid misleading beliefs and erroneous therapies with the risk to harm patients visual function.

• 1322

Do we need to treat?

MEIER-GIBBONS F
Rapperswil, Switzerland,

Summary
Abstract SIS EVER 27.9.17
"Do we need to treat?"
The gold standard for treating glaucoma patients has always been a reduction of the intraocular pressure with medical therapy, laser or surgery. But despite reaching a defined target intraocular pressure, many glaucoma patients still progress and show a deterioration of their optic nerve or their visual field. Using examples of glaucoma patients, we will discuss if we should treat patients with other therapeutic options besides intraocular pressure control.
Conflict of interest
Any consultancy arrangements or agreements:
Alcon, Allergan, Santen
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
Alcon, Allergan, Santen
Any Lecture fee paid or payable to you or your department:
Alcon, Allergan, Santen

• 1323

Is it feasible to treat?

LEVIN L
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Summary
If we assume that a neuroprotective therapy for glaucoma exists and is truly effective, what are the barriers to making it available to clinicians for use in their patients? This talk will discuss four specific processes that need to take place before neuroprotection can become clinically available:
1) Presence of a neuroprotective effect in a well-designed and powered proof-of-concept clinical trial.
2) Demonstration of a clinically meaningful effect in two or more Phase 3 clinical trials acceptable to regulatory agencies.
3) Pricing and clinical effectiveness that meets national/regional standards for incremental cost-effectiveness ratios.
4) Integration of clinical effectiveness, patient acceptability, and adverse effect profiles into care guidelines that are promulgated by ophthalmology specialty societies and key opinion leaders.
The critical issues underlying each of these four steps will be analyzed.

• 1331

B27-associated uveitis, Fuchs uveitis

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Summary
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

• 1332

Infectious posterior uveitis

MARKOMICHELAKIS N
OCULAR INFLAMMATION CENTER, Athens, Greece

Summary
Several infectious agents (parasites, bacteria, fungi, and viruses) can invade the eye and lead to ocular inflammation. Infectious causes should always be considered and ruled out in all patients with posterior uveitis.
Toxoplasma gondii is by far the most common cause of infectious posterior uveitis in all ages, while Toxocara canis infects typically children. Onchocerciasis and other parasitic diseases may also cause posterior uveitis, more commonly in developing countries. Nowadays, old bacterial diseases, tuberculosis and syphilis, emerged as common causes of posterior uveitis. Bartonella henselae and Borrelia burgdorferi are other bacteria that can also cause posterior uveitis.Fungal posterior uveitis usually occurs in immunosuppressed patients or in intravenous drug users. Herpes viruses (HSV, VZV, CMV) are also associated with infectious retinitis, in immunocompromised as well as immunocompetent patients, with quite destructive clinical course. Recently, more viruses (such as West Nile virus, Rift valley fever, dengue fever, and chikungunya) have been recognized as etiologic factors of posterior infectious uveitis. A rapid and accurate diagnosis is of high importance for the successful treatment and visual outcome of infectious uveitis. Techniques and methods, such PCR and detection of specific antibodies in the intraocular fluids (Goldmann-Witmer coefficient), play a key role towards the detection of the pathogen of posterior infectious uveitis.

• 1333

Behçet's disease, VKH, sarcoidosis

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Summary
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 agents 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. Treatment for acute VKH disease relies on systemic corticosteroids 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 is challenging in the absence of apparent systemic involvement. Treatment of sarcoidosis relies on corticosteroids and immunosuppressive agents, in severe cases.

• 1334

Choroiditis (non-infectious)

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Summary
Choroiditis (non-infectious)
Non-infectious choroiditis is classically subdivided into at least two main categories, including choriocapillaritis and stromal choroiditis. In the latter, the site of inflammation is situated in the choroidal stroma. When inflammation exclusively originates from the choroidal stroma which is the target of an immune reaction such as in Vogt-Koyanag-Harada disease (VKH), sympathetic Ophthalmia (SO) or birdshot retinochoroiditis (BRC), the term of primary stromal choroiditis is used. When the choroidal stroma is a chance and random location of a systemic disease such as sarcoidosis, the term of secondary stromal choroiditis is used. In the choriocapillaritis group the lesion process is an inflammatory non perfusion of the choriocapillaris, a mechanism occurring or suspected to occur in diseases such as multiple evanescent white dots syndrome (MEWDS), (idiopathic) multifocal choroiditis, acute posterior multifocal placoid pigment epitheliopathy (APMPPE). The difference of these two mechanism will be further presented with the help of practical examples presented in the same fashion as the "viva voce" EBO examination.

• 1335

Retinal vasculitis

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Summary

Nearly all etiologies of intermediate, posterior or panuveitis may be associated with retinal vasculitis. The clinical analysis of different inflammatory markers is the first step for diagnostic orientation and further work-up. Different cases will be discussed in an interactive manner in order to highlight the vascular type of involvement, associated vitreous inflammation, macular edema, retinal or choroidal lesions such as granuloma or ischemia. A systemic autoimmune, autoinflammatory or infectious disease have also to be taken into consideration. Therapeutic options remain significantly large, ranging from close monitoring to corticosteroids, different types of immunosuppressors, biolgics, antimicrobials, anti-VEGFs, laser photocoagulation and rarely vitrectomy. Prognosis is variable based on etiology, diagnostic delay and therapeutic efficacy.

Conflict of interest
Any consultancy arrangements or agreements:
AbbVie, Allergan, Santen,
Any research or educational support conditional or unconditional provided to you or your department in the past or present:
AbbVie, Bayer, Novartis

• 1341

Flat-mount preparation of cornea

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Summary
Flat mounting of the whole cornea has two main advantages over conventional cross sections: it provides an overview of the whole tissue while allowing precise subcellular localization. We first described how to improve immunostaining for the analysis of the endothelial cells of flat-mounted corneas, by using fixation with methanol or 0.5% PFA at room temperature, and not the conventional fixation with 4% PFA. We then applied a similar technique for the multilayered epithelium. Flat mounting is essential to study the distribution of rare cells inside large area of cells.

• 1342

Flat-mount preparation of lens epithelium

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Summary
The lens capsule with its attached epithelium is a relatively accessible epithelial model system, suitable for various cell culture assays, histology, and histochemical assays. The optical requirements for imaging of lens capsule-epithelium can be challenging, especially if the tissue is not flat. The lecture will cover various techniques for preparation of flat-mount capsule-epithelium, including differences among species, removal of cortical tissue, and fixation of the capsule-epithelium to various base materials.

• 1343

Flat-mount of retina, including preparation of choroid and iris

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Summary
Flatmount methods have been applied to multiple animal models to grant a panoramic view of specific tissues. Mouse models of retinopathy of prematurity (oxygen-induced retinopathy) and age-related macular degeneration (laser-induced choroidal neovascularization and iodate-induced geographic atrophy) have generally been assayed from whole-tissue flatmount studies. We have recently developed a method for mouse iris flatmounts as a model of rubeosis iridis, a clinical diagnosis associated with proliferative diabetic retinopathy and neovascular glaucoma. The aim for the course is to illustrate technical aspects of mouse retinal, choroidal, and iris flatmounts, as well as methods for analysis and interpretation of results.

• 1351

Mouse case

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Summary
The retina of Down syndrome (DS) patients is thicker than the one from controls, an anomaly reproduced in two murine models of the disease, Ts65Dn and Tg(Dyrk1a) and attributed to the increased dosage of Dyrk1a (Laguna et al. 2013), considered as one of the key genes in the apparition of DS symptoms. As HSA21 genes not triplicated in Ts65Dn may affect the expression/function of DYRK1A, we have analyzed by optical coherence tomography (OCT) the retina of Ts65Dn and Tg(Dyrk1a) mice, and compared the results to those obtained on various additional models, notably Dp(16)1 Yeh mice, which have a triplicated segment of MMU16 longer than Ts65Dn, and crosses between Tg(Dyrk1a) and Dp1 Yah, which carries a triplication of the MMU17 genes orthologue to HSA21. In parallel, we have started to analyze by immunohistochemistry the retinal neuron populations in Tg(Dyrk1a) mice, showing an increase in dopaminergic amacrine cells when Dyrk1a is triplicated. Mirror results were obtained on the retina of Dyrk1a+/-, a model of Mental Retardation 7.
Laguna et al. Triplication of DYRK1A causes retinal structural and functional alterations in Down syndrome. Hum Mol Genet. 2013 Jul 15;22(14):2775-84.

• 1352

Human case

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Abstract not provided

• 1353

Deficiency in the expression of Vps13C is associated with altered retinal and lens development in mice

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Summary
While performing genotyping screening in the German Mouse Clinic we identified the Vps13C mouse mutant with eye phenotype where the homozygous mutant mice show signs of neurodegeneration, indicated by a reduction in the total retinal thickness, additionally the retinal blood vessels showed a pattern with structural alteration. Eye histology revealed the display of lipid-like droplets in the retinal layers and in the anterior lens matrix. VPS 13C is a member of the VPS13 family of vacuolar protein sorting-associated proteins highly conserved throughout eukaryotic evolution. While mutations in VPS13A and VPS13B cause the genetic diseases chorea-acanthocytosis (ChAc) and Cohen syndrome, respectively, VSP13C is reported to be associated with Parkinsons disease and late onset Alzheimer's disease (LOAD). Moreover VPS13C has recently been found to be involved in the protein degradation through the ubiquitin being closely associated with lipid droplets and lysosomes. Human diseases are caused by the dysregulated accumulation of ubiquitinated protein aggregates, including neurodegenerative disorders. We believe Vps13c could open novel avenues for uncovering new treatments of metabolic and neurodegenerative disorders.

• 1354

Human case

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Summary
We will present two cases of early onset, possibly congenital, retinal dystrophies, in children, who do not have Leber congenital amaurosis. Visual acuity is decreased, and the fundus shows serpentine like images, most visible in infrared. OCT evidences abnormal retinal structure. ERG has been performed. Molecular genetics is undergoing.

• 1355

Human case

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Summary

Inherited eye disease cases will be presented with an emphasis on conditions with readily recognisable features that aid precise diagnosis. Cases of monogenic disorders mimicking common, multifactorial disease will also be shown. The value of genomic testing will be highlighted and the role of investigations to exclude/identify extraocular involvement will be discussed.

• 1361

Inflammation in relation to retinal diseases

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Summary

Maintaining tissue and cellular health to preserve vision requires active immune responses to prevent damage and respond to danger. Macrophage polarisation may determine the result of the immune response and subsequent tissue health and TNF–alpha is a central regulator. With respect to an insidious degeneration in atrophic AMD or in neovasular AMD, the ability to attenuate pathogenic immune responses is observed despite known inflammasome activation. The result of immune cell activation is environmentally dependent, for example on retinal cell bioenergetics status, autophagy and oxidative stress, alterations in which skew interaction between macrophages and retinal pigment epithelium (RPE). For example, dead RPE eliciting macrophage VEGF secretion but exogenous IL-4 liberates an anti-angiogenic macrophage sFLT-1 response. Impaired autophagy or oxidative stress drives inflammasome activation, increases cytotoxicity and accentuation of neovascular responses, yet exogenous inflammasome derived cytokines such as IL-18 and IL-33 attenuate responses.

• 1362

Autoimmunity in relation to retinal diseases like glaucoma

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Abstract not provided

• 1363

Role of taurine in cone death

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Summary

Cone photoreceptors degenerate in a number of retinal diseases leading thereby to blindness or low vision as in age-related macular degeneration or retinal dystrophies. However, mechanisms leading to cone photoreceptor death remain enigmatic. In the 70s, taurine depletion was shown to lead to complete photoreceptor degeneration. We have investigated the relative cone/rod sensitivity to taurine depletion and the effect of taurine supplementation on cone degeneration in a model of Usher syndrome type 1.

Using a taurine transporter blocker, we have shown that taurine depletion induces a cone degeneration prior to the rod loss. This cone degeneration affect both blue and green cones throughout the retina. To investigate whether taurine could provide an interesting neuroprotective agent in retinal diseases, we supplemented a mouse model of Usher syndrome type 1 with taurine. This taurine supplementation prevented the cone photoreceptor degeneration and the associated retinal gliosis.

These studies demonstrate that taurine is an essential antioxidant for cone photoreceptor survival. Its supplementation could slow down the degenerative process of cone photoreceptors as in our in animal models of Usher syndrome type 1.

• 1364

Elevation of intraocular pressure in relation to retinal diseases

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Summary

Intraocular pressure remains the only modifiable risk factor in glaucoma, a disease characterized by progressive loss or retinal ganglion cells (RGCs) and visual field deficits leading to blindness. Using two rat models of chronic (COH) or acute (AOH) ocular hypertension we study the response of the general population of RGCs responsible for image-forming visual information and the intrinsically photosensitive population of RGCs responsible for nonimage-forming visual information, identified with Brn3a and melanopsin antibodies, respectively. For AOH the anterior chamber of the left eye was cannulated and connected to saline elevated 1½ meters for 75 minutes. COH was induced by laser-photocoagulation of limbar tissues. In both models prior to OH a single intravitreal injection of brain derived neurotrophic factor (5 µg BDNF in 1% albumin PBS) or vehicle was administered. Re retinas were examined at 12 or 15 days after COH or 3, 7, 14, or 45 days after AOH to identify surviving Brn3a+RGCs and m+RGCs. COH induced comparable loss of RGCs but only Brn3a+RGCs responded to BDNF. After AOH, Brn3a+RGCs died progressively while m+RGCs did not, and BDNF induced a permanent protection up to 45 days after AOH in both types of RGCs.

• 1365

Insult dependent oxidative-induced cell death

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Summary

Mitochondrial dysfunction caused by inhibition of oxidative phosphorylation results both in reduced ATP production and oxidative stress because of a significant elevation of ROS. In the reported studies oxidative stress to cultures of cells (RGC-5 cells) was initiated by inhibition of mitochondrial phosphorylation (blue light, sodium azide) or by use of hydrogen peroxide known to induce superoxide through the activation of cellular NADPH oxidase. While all insults resulted in cell death and attenuated by the antioxidant EGCG differences occurred in various measured biochemical parameters implicated in cell death. For example, blue light-induced apoptosis was attenuated by the presence of the mitochondrial the uncoupler M3778 but potentiated by the presence of cobalt. In contrast, hydrogen-peroxide-induced apoptosis was unaffected by M3778 but attenuated by cobalt. Also, blue light-induced cell death occurs via necroptosis, in that it was inhibited by necrostatin-1 and was caspase-independent. This was not the case for sodium azide, where the death process was caspase-dependent, occurred via apoptosis and was unaffected by necrostatin-1.

• 1371

Phenotype of human corneal stroma-derived cells obtained by different isolation techniques from various corneal regions

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Purpose
Investigating the effect of isolation technique and location upon the phenotype of human corneal stroma-derived cells (CSCs).
Methods
Cells were obtained from the center and periphery of the corneal stroma using the explant and enzymatic digestion methods. The native tissue was stained for markers of functionality, stemness, proliferation, adhesion and matrix proteins. Surface immunophenotyping was performed on ex vivo cultured CSCs obtained by the different methods by three-colour fluorescence-activated cell sorting (FACS) analysis. Finally, RT qPCR was used to determine the expression of corneal stroma-specific genes and to verify the results of immunostaining.
Results
Cultures of human CSCs were established by explant and enzymatic techniques from the central and peripheral corneal stroma regions. The corneal stroma, in situ was positive for a-actinin, ALDH1A1, CD31, CD34, Collagen I and Vimentin, while ABCG2, ABCG5, fibroblast marker, CD73, CD90, CD105, Collagen IV, Fibronectin, Ki-67, Nestin and VE-Cadherin were not detected. Ex vivo cultured CSCs expressed CD73, CD90, CD105, CD51, Nestin, CD49a, CD49d, ABCG2, CD47, while CD34 and CD31 were absent. RT qPCR analysis revealed a significant downregulation of ALDH1A1, AQP1, ITGB4, ALDH1A1 and CD34 in cultured versus native cells, with the upregulation of ABCG2, ITGAV, Nestin, CD73, CD90, CD105 and Vimentin. KLF4, GPC4 and CD31 were not significantly different.
Conclusions
The present study finds no significant difference between the phenotype of the CSCs generated by the explant or enzymatic digestion technique from the central or peripheral part of the stroma. For research purposes, any type of corneal stroma tissue may be used, however the change in cultivated cells' surface marker and genotype prolife during ex vivo expansion needs to be considered.

• 1372

The role of p62/SQSTM1 in IL-1β-mediated cytokine production in retinal pigment epithelial cells

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Purpose
p62/SQSTM1 is a selective autophagy substrate being added to ubiquitinated proteins directed to lysosomal degradation. Its levels increase inside the retinal pigment epithelial (RPE) cells when proteasomal activity and autophagic clearance decline during aging. p62/SQSTM1 can also contribute to the activation of pro-inflammatory nuclear factor kappa B (NF-κB) or mitogen-activated protein kinase (MAPK) pathways. According to our previous studies, reduced intracellular clearance promotes the NLRP3 inflammasome-mediated release of IL-1β, which subsequently stimulates RPE cells to produce other pro-inflammatory mediators, such as IL-8. In the present study, we have investigated, whether increased levels of p62/SQSTM1 play a role in the IL-1β-induced response.
Methods
Upregulation of p62/SQSTM1 was induced by bafilomycin A1 or the over-expression vector, or prevented by p62/SQSTM1-specific small interfering RNA (siRNA) transfection. Thereafter, the cells were exposed to IL-1β. The release of IL-6 and IL-8 were detected using the enzyme-linked immunosorbent assay (ELISA) method. In addition, the autophagy markers p62/SQSTM1 and LC3 were determined using the western blot technique.
Results
IL-1β resulted in low IL-6 and high IL-8 production in human RPE cells. p62/SQSTM1 and its absence were verified but they did not affect the cytokine profiles.
Conclusions
Our data suggest that p62/SQSTM1 does not play a role in the IL-1β-induced production of pro-inflammatory cytokines in human RPE cells.

• 1373

Mitochondrial impairment regulates inflammasome activation in human retinal pigment epithelial cells

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Purpose
Dysfunctional mitochondria and excessive inflammasome activation have been shown to play a role in age-related macular degeneration. The aim of the present study was to investigate whether release of mitochondrial reactive oxygen species (ROS) by impaired mitochondria leads to inflammasome activation and further secretion of IL-1β in human retinal pigment epithelial cells.
Methods
ARPE-19 cells were primed with IL-1α and exposed to mitochondrial electron transport chain III inhibitor, Antimycin A, after pretreatment with caspase-1 inhibitor, Ac-YVAD-CMK or mitochondrion-specific ROS scavenger, mito-TEMPO. Pro and mature forms of IL-1β were measured from cell lysates and cell culture supernatants by enzyme linked immunosorbent assay (ELISA) method. Cytotoxicity was determined by commercial lactate dehydrogenase (LDH) assay.
Results
Antimycin A induced secretion of mature form of IL-1β in IL-1α primed ARPE-19 cells. However, secretion of IL-1β was significantly declined by Ac-YVAD-CMK and further by pretreating cells with mito-TEMPO. AC-YVAD-CMK or mito-TEMPO had no impact to the cell viability.
Conclusions
In conclusion, the present study reveals that impaired mitochondria increases release of bioactive IL-1β through the inflammasome activation in human retinal pigment epithelial cells.

• 1374

National diabetic retina screening programme: Identifying non-diabetic eye disease

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Purpose
The Irish Diabetic RetinaScreen Service offers Nationwide screening to all diabetics over the age of 12. It is internationally unique given the integrated nature of its screening and treatment arms. It is now well established, demonstrating impressive uptake with considerable clinical impact. The aim of this study is to explore the significant and increasing number of referrals from the Diabetic RetinaScreen Service with non-diabetic eye disease. We determine the individual contributions of pathology sub-groups and their respective outcomes.
Methods
We retrospectively examined a 12-month referral assessment database from the Mater Misericordiae University Hospital treatment center from January 2016 to 2017. Non-diabetic eye disease referrals were identified and analysed with respect to their frequency of referral and outcome.
Results
One thousand nine hundred and ninety-three patients seen in the MMUH during the 12-month period were included in the study. Diabetic eye disease referrals comprised 1250/1,993 (63%) referrals, with 743/1,993 (37%) referred for assessment of non-diabetic eye disease. Substantial pathology sub-groups included retinal artery and vein occlusions; Arterial emboli; Cataract; Glaucoma; Age Related Macular Degeneration; and Pigmented retinal lesions. We discuss the relative contribution from each pathology and the subsequent assessment outcomes.
Conclusions
Several non-diabetic, sight threatening ocular pathologies, which are often asymptomatic in their early course, are being identified and referred for appropriate treatment. The referral volume is increasing. Quantifying this promotes a more informed discussion on increased service demands, helping predict its practical and financial impact, and influencing strategies on future service provisions.

• 1375

Loss of Nrf-2 and PGC1-alpha genes changes macromorphology of the eye and evokes microstructural and pigmentation pattern changes of the retinal pigmented epithelium

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Purpose
Nrf2 (NF-E2-related factor 2) and PGC1- α (peroxisome proliferator-activated receptor-gamma coactivator 1-alpha) regulate oxidative stress response in cells. Nrf-2 and PGC1-alpha double-knock-out (dKO) mice were used to monitor macro and morphological changes of eye, retina and retinal pigmented epithelium (RPE), respectively.
Methods
The mMRI and mCT imaging were carried out for mice aged at 6 weeks (mCT), 12 weeks and 12 months (mMRI). The retinal and RPE microanatomy and pigmentation were studied from HE-stained thin wax and toluidine blue-stained epoxy sections. Finally, cellular proliferation and pigmentation patterns were studied in the primary cell cultures.
Results
The dKO samples showed smaller body parameters and weight. mMRI, mCT assays indicated size differences and dysmorphic body features in the dKO mice. Moreover, dKOs exhibited reduced retinal full tickness joined with retained RPE morphology. The melanosomes of dKO RPEs were heterogeneous in shape morphology, but comparable in size to aged matched wild type melanosomes, respectively. However, there was a striking trend of increase in the density of melanosomes in RPE of dKOs that was convinced by the primary RPE cultures.
Conclusions
Nrf-2/PGC-1α knockout mice provide a novel model to study degenerative changes in retina and RPE.

• 1376

Effects of HSP90 inhibitor TAS-116 on the inflammasome activation in ARPE-19 cells

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Purpose
Chronic inflammation is one of the key characters of Age-Related Macular Degeneration (AMD), the leading cause of blindness in the Western countries. The NLRP3 inflammasome contributes to the induction of inflammation. The heat shock protein, Hsp90 protects NLRP3 prior to its activation, and its removal releases the receptor protein for degradation. In this study, we tested the effect of the Hsp90 inhibition on the regulation of NLRP3 inflammasome in human ARPE-19 cells.
Methods
The experiments were carried out using IL-1α-primed ARPE-19 cells. Proteasomal degradation and autophagy were blocked with MG-132 and Bafilomycin A, respectively. TAS-116 was used as an Hsp90 inhibitor. The cytokine levels of IL-1β, IL-6, IL-8, and MCP-1 were measured from cell culture medium using the ELISA method. In addition, the activity of caspase-1 was measured by a commercial assay, and the levels of Hsp70 and Hsp90 were determined by the western blot technique from cell lysates. The toxicity of TAS-116 was assessed by measuring lactate dehydrogenase (LDH) levels from cell culture medium and using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay.
Results
According to our data, TAS-116 showed no toxic effects on ARPE-19 cells. TAS-116 decreased the secretion of IL-1β and IL-8 from IL-1a-primed RPE cells with dysfunctional intracellular clearance. The caspase 1 activity decreased along with the IL-1β levels. No changes were seen in the levels of IL-6 and MCP-1.
Conclusions
Our results suggest that TAS-116 is capable of reducing the NLRP3 inflammasome activation and the subsequent release of IL-1β and IL-8 in human RPE cells.

• 1377

The supportive role of interferon-γ in retinal differentiation of mesenchymal stem cells

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Purpose
Retinal disorders represent a serious health problem causing a decreased quality of vision or even blindness. There are currently no effective treatment protocols for these disorders. The promising approach for the treatment of retinal disorders is stem cell-based therapy. Mesenchymal stem cells (MSCs) are a perspective candidate due to their possibility to migrate to the site of injury, differentiate into multiple cell types and produce a number of trophic factors. In this study we analysed the potential of murine bone marrow-derived MSCs to differentiate into cells expressing retinal markers and tested the possibility to express neurotrophic factors by differentiated MSCs.
Methods
Flow cytometry was use to characterize the phenotypic markers of murine MSCs isolated from bone marrow. The retinal extract were prepared by homogenization of posterior segments of the mouse eyes and the supernatants were prepared by stimulation of spleen cells with Concanavalin A. MSCs were cultured with retinal extract and supernatants simulating the environment of retinal damaged for 7 days. The expression of genes for retinal markers and growth factors by MSCs was detected using real-time PCR.
Results
MSCs cultured with retinal extract and supernatant differentiated to the cells expressing retinal cell markers. To identify a supportive molecule in the supernatant from activated spleen cells, MSCs were cultured with retinal extract in the presence of various T-cell cytokines. The expression of retinal markers was enhanced only in the presence of IFN-γ, and the supportive role of spleen cell supernatants was abrogated with the neutralization antibody anti-IFN-γ.
Conclusions
The results show the supportive role of IFN-γ in differentiation of MSCs to the cells expressing retinal cell markers and the enhanced ability of differentiated cells to express growth factors.

• 1378

Remote ischemia affects the diameter of larger retinal vessels in normal persons

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Purpose
Remote ischemic conditioning (RIC) implies that repeated episodes of ischemia in one organ can protect another remote organ from the adverse consequences of ischemia. It remains to be elucidated whether the diameter response in retinal vessels can be used as a marker of RIC in general and whether the response can be used to predict the effect of RIC on the visual prognosis in diseases characterized by retinal ischemia.
Methods
In twenty normal persons aged 20-31 years the Dynamic Vessel Analyzer (DVA) was used to measure the resting diameter and diameter changes during isometric exercise and flicker stimulation before, immediately after, and one hour after RIC induced by transient ischemia in the left arm.
Results
The baseline diameter of retinal venules was reduced non-significantly immediately after ($p=0.07$) and significantly one hour after RIC ($p<0.009$), whereas the baseline diameter of arterioles was unaffected by the intervention ($p>0.61$). Arterial constriction induced by isometric exercise was significantly reduced immediately after RIC ($p<0.04$), but not one hour after RIC ($p>0.99$). None of the other diameter responsese were affected by RIC ($p>0.22$ for all comparisons).
Conclusions
The diameter of large retinal vessels is affected one hour after controlled transient ischemia in the left arm. This indicates that the diameter response of retinal vessels could be a potential marker of ischemic conditioning in the body in general. The potential of remote ischemic conditioning as an intervention on vision threatening retinal diseases where ischemia is a part of the pathogenesis should be investigated.

• 1381

When OCT angio can help us: from diagnosis to follow-up

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Abstract not provided

• 1382

OCT A from anatomy to imaging, vascular remodeling in macular diseases

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Abstract not provided

• 1383

OCT angiography in diabetic retinopathy: what for?

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Abstract not provided

• 1384

Adaptative optics: the optical Stiles-Crawford effect in the clinics

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Abstract not provided

• 1385

Diabetic retinopathy screening and deep learning

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Abstract not provided

• 1511

Fluorescence lifetimes of drusen in age-related macular degeneration

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Purpose
Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO) allows non-invasive in vivo measurement of fluorescence lifetimes of natural fluorophores of the retina upon excitation with a laser light. FLIO in different retinal diseases showed that the technique is useful to detect early metabolic changes and can differentiate between retinal deposits. The aim of this study was to characterize fluorescence lifetimes in retinal drusen due to age-related macular degeneration (AMD).
Methods
FLIO imaging was performed using a Fluorescence Lifetime Imaging Ophthalmoscope (Heidelberg Engineering, Germany). Autofluorescence was elicited with a 473 nm laser and decay times were measured in a short (498–560 nm) and in a long (560–720 nm) spectral channel. Fluorescence lifetime data was compared with autofluorescence intensity images, optical coherence tomography (OCT) and color fundus images. Soft drusen and reticular pseudodrusen were analysed and compared to an age matched control group.
Results
64 eyes from 64 patients with AMD and retinal drusen (age: mean±SD 78±8.5 years) were investigated and compared to 20 age matched healthy controls. Mean fluorescence lifetime in patients with AMD was significantly prolonged compared to the healthy control eyes (mean±SEM; SSC 486±18ps vs 332±11ps, p>0.0001; LSC: 493±9ps vs 382±17ps, p>0.0001). Areas of drusen featured a broader range of fluorescence lifetime values. Long lifetimes were identified in areas of atrophy and intraretinal hyperreflective deposits. Areas of short lifetime corresponded to deposits within the photoreceptor outer segment band.
Conclusions
Mean retinal autofluorescence lifetimes in AMD were significantly prolonged compared to healthy control eyes. Intraretinal deposits caused prolonged lifetimes whereas deposits in the area of the outer photoreceptor segments lead to short fluorescence lifetimes.
Conflict of interest
Any research or educational support conditional or unconditional provided to you or your department in the past or present?:
Heidelberg Engineering (non financial)

• 1512

Deep learning to screen for referable diabetic retinopathy

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Purpose
Diabetes patients worldwide are at risk for diabetic retinopathy (DR). High performance informatics technologies, such as deep learning, are envisioned to achieve acceptable sensitivity for detecting referable retinopathy and appear to be cost-effective alternatives to manual scoring, allowing for large-scale, cost-effective DR screening. The purpose of this work was to develop a deep learning computer model and evaluate its performance.
Methods
An ensemble of two deep convolutional neural networks (resp. 25 and 26 layers; high resolution (512x512 pixels); different filter sizes) was trained to detect the presence of signs of DR using labeled fundus images from the Kaggle dataset. The computer model has been evaluated with the public Messidor-2 dataset for referable DR. Next, the model has been evaluated "in the field" in the context of the Qatar Biobank initiative. Study participants undergo fundus imaging. These images have been graded by retinal specialists in the context of this study.
Results
All 190 patients in the Messidor-2 database with referable DR (moderate non-proliferative DR or worse) have been detected by the trained computer model (sensitivity 100%, 95% CI: 98,1%-100%). The software labeled 444 of the 684 diabetes patients without referable DR accordingly (specificity 64,9%, 95% CI: 61,2%-68,5%). A total of 385 participants of the Qatar Biobank were examined, with 23 individuals having referable DR. The model identified them with 100% sensitivity (90% CI: 85,2%-100%) and 88% specificity (95% CI: 84,3%-91,3%).
Conclusions
The deep learning network obtains high sensitivity combined with a good specificity. The model is conservative while screening for the presence of referable DR, allowing users to focus their attention on patients in which signs of referable DR are detected by the automated screening.

• 1513

Macular changes in patients with multiple sclerosis – A texture analysis of optical coherence tomography data

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Purpose
In this work, a novel approach is used to assess macular changes in patients diagnosed with multiple sclerosis. The vast majority of the studies, if not all, do use the capacity of the optical coherence tomography (OCT) to detect changes along the optical path to identify the different retinal layers and the detection of these to measure the thickness of the retina and the different layers. In particular, the measurement of the retinal nerve fibre layer (NFL) has played a fundamental role in related studies. In this work, we computed a fundus image for the NLF, the ganglion cell layer (GCL), the inner plexiform layer, the inner nuclear layer, the outer plexiform layer and the out nuclear layer and analysed the texture of these fundus images to find their relative differences to the healthy control group.
Methods
A total of 152 eye scans, from 38 healthy controls (age (m/sd): 36.3/9.2 yrs) and 39 multiple sclerosis patients (age (m/sd): 38.8/7.3 yrs) were performed by the Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA) and exported to be segmented by the OCT Explorer (Retinal Image Analysis Lab, Iowa Institute for Biomedical Imaging, Iowa City, IA, USA). The segmentation was further analysed and corrected when necessary.
Results
Each of these images was analysed using first and second order statistics. A support vector machine (SVM) classification process was used to assess the capacity to discriminate between healthy controls and patients to find that the layer presenting the highest difference between the control and the patient group is, surprisingly, the GCL, with over 10% in classification accuracy compared to the NFL layer.
Conclusions
This finding points to the need for further analysis of retinal changes beyond that of the thickness measurement and only in the nerve fiber layer.

• 1514

Structural Bscan OCT correlation with OCT angiography biomarkers of activity in neovascular age related macular degeneration

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Purpose
Fluid on structural B scan OCT is currently the most important sign among all imaging modalities of neovascular AMD. Recently, OCT angiography biomarkers of activity of nAMD have been described. The aim of the study is to compare the appearance of OCT angiography of eyes with wAMD with intraretinal or subretinal fluid against those without fluid on Bscan OCT.
Methods
Retrospective cross sectional study.Fluid on Bscan OCT was classified as intraretinal fluid such as cysts and subretinal fluid as fluid under the retina. OCT angiography biomarkers of activity of nAMD were presence of secondary small vessel branching, peripheral arcades with anastomoses and presence of a dense net (DN). Inclusion criteria were: presence of neovessels on OCT angiography and sufficent images quality on both modalities. Presence of degenerative cysts and/or PED was an exclusion criteria.
Results
59 eyes of 55 patients naive or treated for wet AMD were included (average age: 80 (SD ±7), min-max: 63-95). Subretinal fluid was present in 20% eyes (12/59), intraretinal fluid in 25% (15/59), a combination of both in 10% (6/59) and absence of subretinal or intraretinal fluid in 44% (26/59). DN was present in 30% (18/59), LN in 69% (41/59). Dense net was present in statistically significantly more of the uncontrolled eyes 45% (15/33) (p=0.009, fisher exact test.) Peripheral arcades with anastomoses were evident in 46% (12/26) of controlled eyes and 61% (20/33) of uncontrolled eyes. Small vessel branching was evident in 0% (0/26) of the controlled eyes and in 36% (12/33) uncontrolled eyes.
Conclusions
Dense net are significantly more prevalent in eyes with uncontrolled AMD; small vessel branching and peripheral loops are also more prevalent in these eyes. This suggest that OCT-A provides imaging of the morphology of choroidal CNV in AMD patients associated with disease activity.

• 1515

Cross-sectional static retinal vessel analysis in routine optometric practice

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Purpose
Do retinal vessel calibres provide the same conclusions regardless of which eye was assessed?
Methods
A cross-sectional sample of patients seen in routine optometric practice [n=225] underwent a standard eye examination including subjective refraction and slit-lamp biomicroscopy. Undilated optic nerve-centred fundus photographs were obtained (camera angle: 50 degrees). Red-free photographs were analysed using iFlexis software (Vito, Belgium) to give objective retinal vessel calibre measurements (central retinal artery/vein equivalents; CRAE/CRVE), as described by Knudtson et al.
Results
The mean age of the cohort was 59 years (range: 16-90 years ±15) and comprised of 137 women and 88 men. BMI ranged between 17.6 – 37.3 kg/m2. Average systolic blood pressure (BP) was 131mmHg ±20 and diastolic BP was 82mmHg ±12. Refractive error (MSE) ranged from -10.00 to +7.00D. CRAE was found to be 142AU ±16 (RE) and 143AU ±18 (LE). CRVE was 210AU ±23 (RE) and 209AU ±22 (LE). Paired t-test showed no difference between RE and LE calibres. There was good agreement of both vessel calibres in both eyes, as shown by Bland-Altman plots. (CRAE: bias: -0.88; upper/lower limits: 27.81/-29.57; CRVE: bias: 0.08; upper/lower limits: 33.43/-33.26). Stepwise forward multiple regression analysis found a significant (all $p<0.001$) decrease in both CRAE and CRVE with increasing myopia and age; CRVE also increased with increasing BMI. Analysis was run on all RE, all LE and randomly selected eyes to test if the same conclusion could be drawn regardless of eye selected.
Conclusions
Established associations between age, refractive error and BMI with retinal calibres were in agreement with the sample used. The impact of refractive error on retinal vessel calibre measurements highlights its importance as a co-variate in larger studies, especially when assessing systemic vascular disease.

• 1516

Ophthalmoscopic and video OCT methods to detect spontaneous venous pulsation in individuals with apparently normal intracranial pressure: the rebirth of the SVP?

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Purpose
Purpose: To compare the efficiency of high magnification binocular indirect ophthalmoscopy and direct ophthalmoscopy in detecting the spontaneous venous pulsation (SVP) at the optic nerve head, and to demonstrate the utility of video optical coherence in detecting the phenomenon in patients with normal intracranial pressure.
Methods
Methods: The SVP of the right eye of 54 consecutive clinic patients presenting without neuro-ophthalmic symptoms and with BMIs under 30 were dilated and examined by one ophthalmologist using a 66D handheld Volk lens, then examined by a second blinded ophthalmologist using direct ophthalmoscopy. Immediately the patient was assessed by a third blinded ophthalmologist via vOCT for the presence or absence of SVP.
Results
Results: The population included 20 males and 34 females and were corrected for VA (M 0.127 LogMAR, SD 0.22, SE 0.036), IOP(M 16.5 SD 4.02 SE 0.558), phakia, age (M 68.3, SD 15.15, SE 2.062), C:D ratio (M 0.48 V 0.58 H, SD 0.19 V 0.18 H, SE 0.035 V and 0.033 H), BP (M 136/79, SD 17.71 Sys 12.04 Dia, SE 2.410 Sys, 1.639 Dia) and weight (M 75.48, SD 15.92, SE 2.486). SVPs were detected in 32 of 54 patients using direct ophthalmoscopy, and in 33 of 54 patients using a 66D lens and slit lamp. The ophthalmologists using direct ophthalmoscope and the 66D lens agreed in 49 of 54 cases, giving an inter-rater reliability of 91%. All patients were found to have SVP on vOCT.
Conclusions
Conclusions: Ophthalmoscopically-assessed SVP has a high inter-observer agreement in normal subjects. However, 26% of patients with apparently normal ICP had no ophthalmoscopically detectable SVP. Conversely, SVP was detectable in all patients with apparently normal ICP by vOCT, suggesting it may be a more useful clinical assessment than ophthalmoscopically assessed SVP-detection.

• 1517

Inner retina changes in hydroxychloroquine patients

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Purpose
To study if hydroxychloroquine (HCQ) patients with apparent no retinal toxicity will show lower retinal thickness in inner layers as compared to healthy controls.
Methods
Retrospective study of 43 patients (86 eyes) evaluated for HCQ macular toxicity with spectral-domain OCT (SD-OCT) and with no OCT signs of maculopathy were subdivided into two groups: 1) no blunting of the foveal contour (foveal splaying), 2) with foveal splaying. Age and sex-matched controls were used for comparison. Automated retinal layer segmentation at the center of fovea and at a radius of 3 (parafoveal) to 6mm (perifoveal) from the superior, inferior, temporal and nasal sectors was performed. Statistical analysis using two sample t-test was made to calculate significant results between groups.
Results
Center macular and internal retinal layers thickness in all parafoveal sectors, particularly in the retinal nerve fibre (RNFL) and ganglion cell layer (GCL), was statistically reduced when compared to control group ($p<0.05$) and differed between group 1 and 2. RNFL thickness was also reduced in all perifoveal sectors but temporal sector ($p<0.05$) and inner plexiform layer and inner nuclear layer thickness showed only significant reduction in foveal and nasal parafoveal sector ($p<0.05$) in HCQ eyes. No significant differences in outer layers was observed between groups.
Conclusions
Small changes in inner retinal layers thickness have been described with HCQ use and conflicting correlation with HCQ toxicity is present in the literature. This study supports that inner retina at the fovea and parafovea is thinner in patients with no outer retinal OCT signs of HCQ toxicity. Further investigation is needed to assess if an inner retinal thickness reduction threshold could serve as valuable tool for identifying patients with increased risk of HCQ maculopathy.

• 1518

Idiopathic retinal vasculitis, arteriolar macroaneurysms and neuroretinitis (IRVAN): Case series of three patients with multimodal imaging.

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Purpose
To describe the clinical presentation, disease progression, treatment and complications of IRVAN.
Methods
Retrospective review of three patients with a diagnosis of IRVAN seen at the Birmingham and Midland Eye Centre between 2010 and 2017. Multimodal imaging investigations included wide-field fluorescein angiography, optical coherence tomography, and indocyanine green angiography.
Results
A total of 6 eyes from 3 patients with bilateral disease were included. All six eyes were treated with panretinal photocoagulation (PRP). One eye received a dexamethasone implant for refractory macular oedema and exudation. One eye was treated with Avastin injections for persistent optic disc neovascularization. All 3 patients were treated with oral steroids at some point in the course of their disease and one was subsequently immunosuppressed with mycophenolate mofetil.
Visual outcomes varied. One patient maintained excellent visual acuity of 6/6 in both eyes at 72-months follow-up.
The second patient experienced progressive visual loss from 6/9 right eye, 6/6 left eye at presentation; to 6/18 right eye, 6/60 left eye at 12 months follow-up due to macular exudation despite aggressive PRP and intravitreal Ozurdex.
The third patient deteriorated from 6/5 right eye, 6/4 left eye at presentation to 6/60 right eye at 6 months, despite aggressive PRP. He had recurrent vitreous haemorrhages in the right eye secondary to NVD despite further interventions with Avastin injections; seven years after presentation, vision remained at 6/60 right eye and 6/18 left eye.
Conclusions
The cadence of progression of IRVAN can vary greatly, despite aggressive treatment with PRP, intravitreal steroids, and anti-VEGF agents. We observed variation in disease progression both among patients as well as within the same individual, supporting an individualized approach to therapy.

• 1521

Summary of main clinical trials

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Abstract not provided

• 1522

Evidence for successful treatment in glaucoma: who to treat and when?

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Summary
Treating glaucoma successfully means avoiding the occurrence of visual disability in the individual patient. Since the rate of vision loss can be extremely variable among patients, an accurate phenotyping is essential in planning the proper therapy for each patient. Besides, the recent inclusion of patients' reported outcomes (PROs), in the glaucoma therapeutic algorithm, is increasing the complexity of the scenario.
This presentation will focus, then, on (a) the available tools to phenotype the glaucoma patient(s), (b) the criteria for assessing the intensity and the timing of different treatment modalities and (c) the state-of-the-art in the evaluation of PROs in glaucoma.
Conflict of interest
Any post or position you hold or held paid or unpaid:
late summary submission, COI YES

• 1523

The three P's of testing new drugs in glaucoma: Pilot, POC and Pivotal

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Abstract not provided

• 1524

Outcomes and endpoints in glaucoma

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Summary
Clinical trials in glaucoma have historically relied in IOP. However, the emergence of neuroprotection in glaucoma ghas lead to a need for new measures of trial success. Several potential outcomes exist including autoimmune and genetic biomarkers, brain and retina imaging, clinical signatures of RGC disease and structural and functional endpoints. These will be covered in this talk including DARC – detection of apoptosing cells.
Conflict of interest
Any research or educational support conditional or unconditional provided to you or your department in the past or present:
Grant/Research Support: Allergan Novartis VISUfarma Annexon Dompe
Employment/Honoraria/Consulting Fees/Travel expenses: Visufarma Allergan Novartis GSK Santhera Thea Santen Sooft
Patent – named inventor on UCL-owned DARC patents

• 1531

Misunderstanding laboratory evaluation

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Summary

Intraocular inflammations always represent a diagnostic challenge for ophthalmologists. It is often tough to make a precise etiological diagnosis in certain subsets that very often appear atypical. Recently, several advances in the investigations for uveitis have been introduced. Such scientific achievements have significantly helped uveitis specialists in the management of such clinical conditions. Although the approach to laboratory diagnosis of uveitis should be directed by the history, patient's symptoms and signs, and clinical examination, very often the ophthalmologist can be confused if such method is not rigorously followed. The matching of clinical pattern and the tests should be always considered in order to reach the goal of a correct interpretation. This review summarizes various modalities of laboratory investigations and their role in the diagnosis of uveitis, furthermore paying attention to the most common mistakes in their interpretation.

• 1532

Mistaking infection for inflammation

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Summary

Among the first steps in diagnosing any patient with uveitis is to identify infection. Common infections that may masquerade as autoimmune disease include herpes simplex virus, varicella zoster virus or cytomegalovirus (CMV) anterior uveitis, chronic post-surgical endophthalmitis, endogenous endophthalmitis, acute retinal necrosis, CMV retinitis in immunocopme patients, syphilis, atypical toxoplasmosis and tuberculosis. Patient history and clinical exam can often make the diagnosis. The utility of diagnostic tests such as treponemal tests, quantiferon testing, Mantoux skin test, and toxoplasmosis serology will be covered. Case series of polymerase chain reaction (PCR) testing of anterior chamber and/or vitreous aspirate for anterior segment and posterior segment uveitis will be reviewed, with an emphasis on demonstrated clinical utility. More invasive biopsy such as vitreous biopsy via pars plana vitrectomy or chorioretinal biopsy may be necessary in some settings. Appropriate treatment and criteria for treating specific infections will be covered. Cases of polymicrobial infection will be reviewed as well. Emphasis will be placed on distinguishing infection from autoimmune disease.

• 1534

Over-interpreting white dots

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Summary

The white dot syndromes are a group of inflammatory chorioretinopathies of unknown etiology which have in common a unique and characteristic appearance of multiple yellow-white lesions affecting multiple layers of the retina, retinal pigment epithelium (RPE), choriocapillaris, and the choroid.

They also have overlapping clinical features. For example, multifocal choroiditis and punctate inner choroidopathy target the same essential structures in the same phenotypic manner and, when active, are treated the same way, and thus there seems to be limited clinical utility in trying to differentiate them.

Transitions between the individual diseases have also been described, and when a prolonged progressive clinical course and widespread distribution of lesions is present, the term "relentless" is now applied.

Neither the trigger mechanism nor the pathogenetic development is known with certainty for any of these diseases. Immunological reactions to previous viral infections coupled with a genetic predisposition seem to be a common denominator. Some of these conditions share an association with systemic infectious diseases.

• 1535

Choosing the wrong imaging modalities

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Summary

The diagnosis of uveitis often requires careful clinical examination of the peripheral retina. Ultra-wide-field angiography could prove useful in the clinical evaluation and treatment such patients. However, its use is often restricted to intermediate and posterior uveitis. There are instances in which ultra-wide-field FA can be paramount in evaluating the peripheral angiographic expression of the retina in anterior uveitis.

Fundus autofluorescence (FAF) is a novel noninvasive imaging technique that assess the health and viability of the RPE/photoreceptor complex. Characteristic fundus autofluorescence patterns have been described in eyes affected by inflammation of the posterior segment, and these patterns have provided insights into the pathogenesis of posterior uveitis entities. In addition, preliminary data indicate that fundus autofluorescence characteristics may serve as markers of disease activity, allow prediction of visual prognosis, and may help determine the adequacy of therapy.

Indocyanine green angiography (ICGA) provides the clinician with a powerful adjunctive tool in choroidal inflammatory disorders. It still needs to be determined if ICGA can prove to be a follow up parameter to evaluate disease progression.

• 1536

Fear of the correct treatment dose

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Summary

Fear of the correct treatment dose
Underdosing valacyclovir
Underdosing immunosuppressive therapy
Uveitis can occur in all age-groups and often has devastating effects on vision. The visual loss can have a variety of causes including cataract formation, vitritis, optic nerve damage and macular edema. In patients with active inflammatory disease resulting in reduced vision, corticosteroids are a very important part of the management, and uveitis specialists have learnt a long time ago that their use should be optimized. Even if serious side effects are associated with chronic use of systemic steroids, the correct full-dose should be employed. The concept of optimizing the treatment by using the correct dose, then lower it to the minimum effective dose that controls inflammation, should be applied as well to the second step of uveitis treatment, immunomodulatory agent. Tailored treatments must also be extended to infectious uveitis, for which there is a low level of awareness of recommended guidelines to control the diseases. A perfect example is anti-viral treatment in cases on herpes uveitis, which should be tailored when the causing herpes virus is identified.

• 1541

Sicca syndrome - disease continnum. Anatomical, functional and systemic assessment

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Purpose

To evaluate objective findings in the ophthalmologic examination and search for patterns of association with the clinical and laboratory characteristics in patients with Sicca Syndrome (SiS).

Methods

Cross-sectional study of 80 eyes of 80 patients with SiS divided into four groups. 20 patients with pSS for more than 10 years (group1), 20 patients with pSS for less than 2 years (group 2), 20 patients with SiS associated to undifferentiated connective tissue disease (UCTD) (group 3) and 20 patients with SiS without UCTD (group 4). Demographic, clinical and immunologic data were recorded. Ophthalmologic examinations included Schirmer test, break up time (BUT), Corneal Staining Score (CSS), tear meniscus evaluation in Anterior Segment – Optical Coherence Tomography (AS-OCT) and corneal sub-basal nerve plexus (CSNP) measurements with in vivo Confocal Microscopy (IVCM).

Results

Group 1 had an early diagnosis when compared with group 2. Group 1 presented a higher frequency of positivity for anti-SSA, anti-SSB, Rheumatoid Factor and ANA titers compared to groups 2-4 ($p<0.05$). Patients in group 1 presented more frequently systemic manifestations compared to groups 2-4 ($p<0.05$). Sjogren Syndrome Activity Index (SSDA1) correlated positively with positive anti-SSA ($r=0.470$, $p<0.0005$). Group 1 showed a higher CSS and a lower BUT, tear meniscus height and area compared to group 2 and 3 ($p<0.005$). CSNP's length and density were significantly smaller in group 1 compared to group 2 and 3 ($p<0.05$).

Conclusions

CSNP's density and length, as well as tear meniscus area and height are smaller in advanced pSS compared to pSS with recent diagnostic and SiS-UCTD. AS-OCT and IVCM may be useful for risk stratification in SiS.

• 1542

Estimating basal rear osmolarity in normal and dry eye subjects

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Purpose

Tear osmolarity (tOsm) is used as a measure of severity in dry eye disease (DED) and has also been proposed as an index of body hydration. Currently in DED the level of tear hyperosmolarity is compared with that of a normal population. We propose that a more valid reference point for both DED and body hydration could be acquired by measuring tOsm after a period of evaporative suppression.

Methods

Eight normal (N) and eight DED subjects were recruited and their tOsm measured with a TearLab® osmometer in uncontrolled environmental conditions. They then entered a controlled environment chamber (CEC) set to 23°C and 0.08 m/s airflow and, either: 1) had tOsm measured after 45 minutes of eye closure and then at 15 minute intervals for a further 45 minutes at 45% relative humidity (RH), or 2) had tOsm measured every 15 minutes for 45 minutes, at 70% RH, to suppress evaporation.

Results

Tear osmolality was significantly reduced after eye closure in both N and DED subjects, to levels in the range of plasma osmolarity, between 285-295 mOsm/L (N $p = 0.03$; DED $p = 0.006$). The tOsm rose towards the start value on eye opening. In subjects exposed to 70% RH, which was not expected to suppress evaporation completely, a fall in tOsm also occurred, but to a lesser extent than achieved with eye closure. This was significant in DED patients ($p = 0.026$) but not in N subjects ($p = 0.12$).

Conclusions

As predicted, total suppression of tear evaporation resulted in a fall in tOsm. We hypothesise that complete suppression of evaporation, for a sufficient period, drives down tOsm to a basal tear osmolarity value that will be a better measure of body hydration than tOsm measured in open eye conditions. It will also provide a personal baseline against which to gauge the severity of tear hyperosmolarity in DED patients.

Conflict of interest

Any Stocks or shares held by you or an immediate relative?:

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Interest: Instrumentation for Ms Willshire's research was provided by the TearLab Corporation. Professor Bron has served on the Advisory Board of TearLab and was the recipient of share options. Professor Buckley declares .

• 1543

Ocular chronic graft-versus-host disease after allogeneic haematopoietic stem cell transplantation in Denmark (1971-2011): - Incidence and risk factors in adults

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Purpose

Ocular chronic graft-versus-host disease (cGVHD) is a bothersome complication to allogeneic hematopoietic stem cell transplantation (HSCT). The objective of this study was to assess incidence and risk factors of developing ocular cGVHD.

Methods

A retrospective study of 1021 consecutive patients who underwent HSCT at a single institution. The patients were examined by an ophthalmologist before HSCT, annually up to five years after HSCT and more frequently if ocular symptoms occurred. Ocular cGVHD was diagnosed using the criteria proposed by The International Chronic Ocular GVHD Consensus Group. Myeloablative(MA) and non-myeloablative(NMA) transplants were analysed separately due to great differences in patient age, conditioning regimen and stem cell source.

Results

Out of 1021 patients 99 (9.7%) had dry eye disease before HSCT. The 5-year cumulative incidence of ocular cGVHD was 0.16(95%CI 0.13-0.19) in the MA group and 0.30(95%CI 0.25-0.36) in the NMA group. In adjusted cox regression models, we identified five risk factors of developing ocular cGVHD in the MA group: Schirmer's test ≤10 mm/5 min before transplantation; malignant disease; peripheral blood as stem cell source; female donor and the use of an unrelated donor. Risk factors in the NMA group were: Schirmer's test ≤10 mm/5 min before transplantation, higher recipient age and the use of an unrelated donor.

Conclusions

The 5-year cumulative incidence of ocular cGVHD was 16% after MA conditioning and 30% after NMA conditioning. A low Schirmer's test before transplantation is a potential predictive factor of ocular cGVHD. Surprisingly, many of the patients had dry eye disease already before transplantation. Special attention should be directed toward patients with malignant disease, older age and patients receiving graft from peripheral blood and the use of a female donor or an unrelated donor.

• 1544

Preclinical validation of an innovative corneal bioreactor versus organ culture for long term storage: a randomized controled study

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Purpose

The organ culture (OC) is a passive corneal storage, gold standard in Europe for decades. The bioreactor (BR) is a sterile transparent device that allows active storage: transcorneal pressure gradient and fluid renewal. Aim: To compare quality of human corneas stored for 1 month in our BR versus (vs) OC.

Methods

Randomized controled preclinical study, authorized by the French Biomedicine Agency and an IRB, including only fresh scientific paired human corneas >2000cells/mm2 and <10% difference between both corneas at day (D)2. Immediately at retrieval, one cornea was randomized and stored in OC and the other in BR, both with the same commercial medium (CorneaMax). At D26 only OC corneas were transferred to a deswelling medium (CorneaJet). We calculated that 49 pairs were needed to show a difference of 500 viable cells/mm2 between groups. Assessments were performed at D2, 26, 28. Main criterion: viable ECD (vECD) determined by triple staining Hoechst/Ethidium/Calcein at D28, blind of storage method. Secondary criteria: average transparency (T), central corneal thickness (CCT) and microbiology.

Results

We retrieved 60 pairs, included 52 pairs at D2, analyzed 50 pairs (1 contamination per group). At D2 ECD in BR was 2607±340 vs 2576±357cells/mm2 in OC (p=0.243). At D26 ECD was >2000cells/mm2 for 92% of corneas in BR vs 58% in OC (p<0.001). At D28 vECD was higher in BR 2188±379 vs 1687±389cells/mm2 in OC, with 76% of corneas >2000 viable cells/mm2 in BR vs 22% in OC (p<0.001); T didn't differ and CCT was higher in BR with 684±52 vs 608±53µm in OC (p<0.001).

Conclusions

Restoring IOP and renewing medium significantly improves endothelial cell survival while avoiding deleterious deswelling necessary in OC: after 1 month-storage, the BR provides much more corneas suitable for transplantation and higher quality grafts that could survive longer in recipients.

• 1545

Efficacy of a RARγ selective agonist eye drop formulation on improvement of tear production and corneal fluorescein staining in the BTX-B mouse model of dry eye disease

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Purpose

Multiple studies have demonstrated the potential beneficial effects of retinoids on dry eye disease. Retinoic acid receptors (RAR) α, β and γ are widely distributed in ocular tissues. In vitro data suggest that the beneficial effects of retinoids on ocular health are mediated via RARγ (Kimura 2015). The purpose of this study was to evaluate the in vivo effects of palovarotene (PVO), a RARγ selective agonist, in a dry eye animal model.

Methods

The efficacy of a PVO ocular formulation was tested in the botulinum toxin type B (BTX-B) mouse model which involves injection of BTX-B into the lacrimal gland of the right eye with contralateral control. Eye drop formulations at 3 doses of PVO (low, mid, high) with vehicle, were administered by daily topical instillation for 28 consecutive days and compared to current standard of care, Restasis®. Endpoints included ophthalmic examinations, tear production measurement (TPM) by phenol red-impregnated cotton threads, corneal fluorescein staining (CFS) using a scoring system of 0 to 4, and histopathology.

Results

At Day 28 post BTX-B injection, the mean (SD) TPM and CFS score in the untreated group were 1.5 (0.3) mm and 2.0 (0.7), respectively. In comparison, PVO eye drop treatment significantly improved dry eye signs (p<.0001) at all doses tested – TPM was increased by 132, 166 and 188% at low, mid and high dose, respectively, while CFS score was decreased by 70, 85 and 85%, respectively. PVO treatment effects were greater than Restasis® (113% increase in TPM, 50% decrease in CFS). All PVO doses were tolerated for 28 days. Histopathology evaluation revealed no effects on the Meibomian glands.

Conclusions

These results indicate a beneficial therapeutic effect of PVO in the BTX-B animal model and support further development of a PVO ocular formulation for the treatment of human dry eye disease.

Conflict of interest

Any post or position you hold or held paid or unpaid?:
Presenter and co-authors are employees of Clementia
Any Stocks or shares held by you or an immediate relative?:
Presenter and co-authors have Clementia stock options

• 1546

Graft blues: case report

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Purpose

To describe unusual inadvertent persistent staining of stromal structures by trypan blue (TB) after penetrating keratoplasty (PK) and Descemet membrane endothelial keratoplasty (DMEK) performed in patients suffering from lattice corneal dystrophy (LCD)

Methods

Case report of patients suffering from LCD and having received intracamerular TB. Series 1: retrospective study on 85 consecutive triple procedures (PK+cataract+IOL) performed by a single surgeon (PG) in a tertiary care university hospital during 7 years. 0.4% TB was systematically used. Series 2: case report of a DMEK (stained with TB) performed after a late endothelial failure of a previous PK realized 5 years before for advanced LCD. Six weeks after DMEK, the patient was hospitalized for acute rejection that appeared unusual

Results

Series 1: Only patients with LCD (n= 18 eyes in 17 patients) presented an isolated intense blue staining of the graft host interface (blue ring). It persisted during 18-24 months and had no consequence. Series 2: during the acute rejection, intense blue staining was observed in spindle shaped small structures located in the first third of the whole stroma. The DMEK was partially detached. Stromal edema almost completely resolved after intense steroid therapy but the stromal blue staining persisted (9 month follow-up) with impaired vision.

Conclusions

Abnormal amyloid protein characterizing LCD can be stained by TB in vivo. In PK it stains a ring in the recipient stroma and has no consequence. However, during DMEK performed after a PK, TB may also stain the protein accumulated in the graft stroma during slow recurrence of the disease. TB-stained DMEK should therefore be avoided in late endothelial failure of a PK initially performed for LCD.

• 1551

Modulation of Muller cell membrane organization by 24S-hydroxycholesterol

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Purpose

Muller glial cells (MGC) are involved in the retinal homeostasis and they are sustaining cholesterol homeostasis. A lack or an excess of cholesterol in neurons can cause neurodegeneration. Cholesterol is eliminated from the retina mainly as 24S-hydroxycholesterol (24S-OHC). 24S-OHC is produced by 24S-hydroxylase (CYP46A1) in retinal ganglion cells (RGC) and is overexpressed during glaucoma. the objective of this study was to determine whether 24S-OHC triggers MGC membrane dynamics involving lipid rafts and contribute to gliosis at early and late time points.

Methods

MGCs were grown in vitro from retinas of young rats. They were treated with 24S-OHC (10 µM) for 2 min or 6h. Lipid rafts of MGC membranes were obtained after 1% lubrol lysis and 20h-ultracentrifugation at 180,000 g in a sucrose gradient. The expression of caveolin-1, Flotillin-1, GFAP, Vimentin, Connexin-30, Connexin-43, phosphorylated and non phosphorylated p38 and p42-44 MAPK was analyzed by Western-blotting. High-performance liquid chromatography coupled with mass spectrometry (LC-MS) was used to estimate the levels of ganglioside GM3 (monosialodihexosylganglioside), and protein pathways were analyzed by nanoLC-MS/MS in raft and non raft fractions from MGCs after treatment with 24S-HOC.

Results

Cholesterol, sphingomyelin and saturated fatty acids C15:0, C16:0, C17:0 and C18:0 were enriched in the rafts fractions in MGCs. Structural proteins, Caveolin-1 and flotillin-1, and functional proteins, Connexin-30 and -43, were localized in the MGCs rafts. Ganglioside GM3 showed a characteristic enrichment in the raft fractions. Protein implicated in adhesion or oxidative stress pathways in the raft and non-raft fractions were up and down-regulated by treatment with 24S-OHC.

Conclusions

Our data showed that 24S-OHC induced early changes in protein distribution in raft microdomains.

• 1552

Plasmalogens and cell-cell communication between retinal glial cells

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Purpose

Plasmalogens are glycerophospholipids containing a vinyl-ether bond at sn-1 position of their glycerol backbone and polyunsaturated fatty acids (PUFAs) at sn-2. We have previously shown that plasmalogens are involved in the regulation of perinatal retinal vascular development and particularly in astrocyte template formation (Saab et al, PLoSONE 2012 9(6):e101076). Since retinal Müller cells and astrocytes can communicate through calcium waves and connexin 43-rich gap junctions, the aim of our study was to determine whether a reduction of plasmalogen levels affects communication between retinal glial cells.

Methods

Primary Müller cells and astrocyte were isolated from retinas of 9-days old and cerebral cortex from 21-days old Wistar rats, respectively. SiRNA against DHAPA-AT -the key enzyme of plasmalogen biosynthesis- were used to decrease plasmalogen content of Müller cells before they were co-cultured with naïve astrocytes. Calcium waves initiated in Müller cells by topical application of ATP were monitored by Fura-2 calcium imaging. Expression levels of cellular proteins involved in calcium metabolism, including connexin 43, were evaluated by proteomics and Western-blotting in reponse to Si RNA treatment.

Results

Treating Müller cells with SiRNA against DHAP-AT led to a reduction of plasmalogen content of about 60% and to a remodelling of PUFA distribution in cell membranes. The expression of connexion 43 was reduced by more than 50% in Müller cells treated with SiRNA. This was associated with an alteration of calcium waves originating from Müller cells as well as a slowed propagation to neighbouring astrocytes.

Conclusions

These data suggest that membrane plasmalogens content influences cell-to-cell communication between retinal Müller cells and astrocytes. Altered coupling between these cells might be one of the factors influencing perinatal vascular development.

• 1553

Gene therapy strategies for hypoxia-inducible angiogenesis in ocular neovascularization

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Purpose

Our previous results have associated HIF expression in RPE cells to CNV progression, and we have shown that gene transfer of prolyl hydroxylase domain (PHD)2 in the mouse model of nAMD resulted in mitigation of HIF-mediated angiogenesis. Here, we investigate the function of hypoxia-regulated molecular elements in modulating the expression of transgenes in retinal pigment epithelium (RPE) cells, with putative use in gene therapy strategies for the treatment of nAMD.

Methods

Hypoxia-mediated RPE-specific expression vectors were generated using the minimum mouse Rpe65 promoter (pRpe65), while hypoxia-mediated expression was achieved using hypoxia-response elements (HRE) and oxygen-dependent degradation peptides (ODP). Hypoxia-dependent regulation of transgenes in ARPE-19 cells was determined by green fluorescence protein (GFP) expression. Expression pattern analyses of transgenes in response to hypoxia and reoxygenation were assayed by western blot and RT-PCR.

Results

Use of pRpe65 resulted in RPE-specific expression of GFP. Hypoxia-enhanced expression of GFP was achieved with HRE-driven pRpe65, and GFP expression patterns were regulated at the transcriptional level. Fusion of ODP to GFP resulted in hypoxia-mediated expression, under pRpe65 regulation, and GFP protein expression was subject to hypoxia-dependent protein expression.

Conclusions

Our data shows that transgenes can be expressed specifically in RPE cells and be regulated by hypoxia, both by transcriptional and post-translational regulation, limiting the therapeutic gene expression to pathologic hypoxic RPE cells. These results may have implications for the clinical treatment of ocular vascular pathologies, such as nAMD, particularly regarding the use of gene therapy to negatively regulate neoangiogenesis.

• 1554

A holistic dynamic concept on dry eye disease identifies several different interacting self-enforcing vicious circles of disease progression

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Purpose

Dry Eye Disease (DED) is a complex alteration of the ocular surface. Typical are self-enforcing mechanisms that drive the condition are termed ´Vicious Circles´ (VC). It is generally believed that ´a vicious circle´ occurs in DED that is driven by inflammation .

Methods

A NLM PubMed based review of the literature review was performed and pathogenetic mechanisms were analyzed according to patho-physiology.

Results

This approach in DED indicates that Basic primary causative factors are (A) deficiency of tear SECRETION by the ocular secretory glands (aqueous lacrimal gland, oily Meibomian glands, single conjunctival goblet cell mucin glands) and (B) deficiency in FORMATION of a stable tear FILM by the eye lids & blinking. The two main pathologies are (1) tear film deficiency and (2) tissue damage. Several VC in DED were identified: One important VC is destruction of the surface epithelium by insufficient wetting due to a deficient tear film which, in turn, further reduces the tissue wettability and thus tear film stability. Surface destruction leads to induction of inflammatory pathways that drive VS for progression of disease. Since the destruction of the tissue also impairs the ocular glands, large VC of gland destruction (Pathological Carousels) occur wherein tissue destruction increasingly impairs gland secretion which, in turn, drives further surface destruction. Other VC are hidden in the gland pathology of Meibomian Gland Dysfunction (MGD) and Lacrimal Gland Dysfunction (LGD).

Conclusions

A holistic dynamic analysis of DED can identify, In contrast to present over-simplified models, that Vicious Circles do not necessarily depend on inflammation and that there are in fact several, different, interacting vicious circles instead of just one. The relevant VC must be identified in the individual patient to allow an effective therapy.

• 1555

A novel in vivo model of puncture-induced iris neovascularization

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Purpose
To assess iris neovascularization by uveal puncture of the mouse eye and determine the role of angiogenic factors during iris neovascularization.
Methods
Uveal punctures were performed on BalbC mouse eyes to induce iris angiogenesis. VEGF-blockage was used as an anti-angiogenic treatment, while normoxia- and hypoxia-conditioned media from retinal pigment epithelium (RPE) cells was used as an angiogenic-inducer in this model. Iris vasculature was determined in vivo by noninvasive methods. Iris blood vessels were stained for platelet endothelial cell adhesion molecule-1 and vascular sprouts were counted as markers of angiogenesis. Expression of angiogenic and inflammatory factors in the puncture-induced model were determined by qPCR and western blot.
Results
Punctures led to increased neovascularization and sprouting of the iris. qPCR and protein analysis showed an increase of angiogenic factors, particularly in the plasminogen-activating receptor and inflammatory systems. VEGF-blockage partly reduced iris neovascularization, and treatment with hypoxia-conditioned RPE medium led to a statistically significant increase in iris neovascularization.
Conclusions
This study presents the first evidence of a puncture-induced iris angiogenesis model in the mouse. In a broader context, this novel in vivo model of neovascularization has the potential for noninvasive evaluation of angiogenesis modulating substances.

• 1556

Modulation of the rod outer segment aerobic metabolism diminishes the production of radicals due to light absorption

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Purpose
Oxidative stress is a primary risk factor for inflammatory and degenerative retinopathies. Irradiation with blue light of eye explants was shown to cause an oxidative stress, higher in the rod outer segment (OS) than in the inner limb, ultimately impairing the extra-mitochondrial aerobic metabolism of the OS. Here, to establish a correlation between the energy metabolism and phototransduction, the aerobic metabolism of purified bovine rod OS was assayed in function of exposure to either ambient or dim light.
Methods
Isolated bovine rod OS, purified by Fycoll/sucrose gradient were utilized. Production of Reactive Oxygen Intermediates (ROI) was evaluated by citofluorimetry, with dihydrorhodamine 123 (DHR) probe; ATP synthesis and oxygen consumption were assayed by luminometry or oximetry, respectively. When necessary, isolated OS were preincubated with 30 μM Resveratrol, for 15 minutes, or 5 mM Metformin, for 2 hours.
Results
Upon exposure to ambient light for 1 h, a significant increase in oxygen consumption as well as ATP synthetic ability by rod OS was observed, along with a consistent ROI production, with respect to dim light, i.e. the physiological rod conditions. Pretreatment with resveratrol, inhibitor of F1Fo-ATP synthase, or metformin, inhibitor of the respiratory complex I, significantly diminished the ROI production in vitro.
Conclusions
Data show for the first time the relationship between light and the rod OS metabolism. A production of ROI by the OS in vitro was also observed, positively correlating to light exposure. A beneficial effect of metformin and resveratrol was found, as modulators of ROI production, consistently with their inhibitory action on the complexes I and V of respiration, respectively. Data shed new light on the prevention of the cone loss secondary to rod damage due to oxidative stress.

• 1557

Protective effects of sulforaphane on STZ-induced diabetic retinopathy via activation of Nrf2/HO-1 antioxidant pathway and inhibition of NADPH oxidase

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Purpose
To investigate the protective effects of sulforaphane, an Nrf2 activator, on streptozotocin (STZ)-induced diabetic retinopathy.
Methods
8 wk male C57BL/6 mice were intraperitoneally injected with streptozotocin (STZ, 45 mg/kg) for 5 consective days. Animals with fasting blood glucose higher than 13.89 mmol/L were considered diabetes and used for further study. Two weeks after STZ injection, animals were intraperitoneally injected with sulforaphane (12.5 mg/kg) for 8 wks, 3 times per week and retinas were harvested at the tenth-week. Reactive oxygen species (ROS) in retina were detected by DHE staining. The expression of heme oxygenase-1 (HO-1) and Nox2 in retina was detected by Western blotting. Immunofluorescent staining was used to detect the expression of RNA binding protein with multiple splicing (RBPMS) and choline acetyl transferase (ChAT), which could specifically mark the retinal ganglion cells (RGCs) and amacrine cells (ACs), respectively. Acellular capillaries in retina were observed by using periodic acid-Schiff and hematoxylin staining.
Results
The fasting blood glucose of the mice injected with STZ was increased rapidly, accompanied by significantly decreased body weight. STZ-injection induced increased ROS generation, increased RGCs and ACs loss, and increased formation of acellular capillaries, which could all be reversed by SF treatment. Meanwhile, HO-1 and Nox2 expression were increased by STZ-injection. SF treatment could further enhance STZ-induced HO-1 expression, whereas decreased STZ-induced Nox2 expression.
Conclusions
SF treatment could protect mice retina from STZ-induced oxidative stress and cellular damage, possibly through the activation of Nrf2 antioxidant pathway and inhibition of Nox2 expression.

• 1558

The 8-fold quadrant dissection method for ex vivo human interventional retinal experimentation

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Purpose
Retinal research relies on animal and in-vitro models which lack many of the characteristics of human retina. We have instead established a reproducible ex-vivo model of primary retinal explants derived from human donor eye cups.
Methods
A dissection strategy performed independently by two investigators was designed to maximize retinal tissue whilst maintaining experimentally reproducible fragments of retina suitable for experimental purposes. The retina was divided into 4 quadrants through the fovea and equivalent distribution of photoreceptors between quadrants was confirmed with CD73 staining in 7 pairs of donor eyes with flow cytometry. In the 8 quadrants from each of the 7 donors, the standard error in proportion of photoreceptors was 0.8-2.3%.
Results
Cellular composition of free floating retinal explants were followed for 2 months in 10 retinas with quadrant dissection and 8 with random dissection. Explants could be maintained for 2 months with live populations of photoreceptors, ganglion cells and Müller cells detected by flow cytometry. In contrast, amacrine and horizontal cells, decreased by 90% at 7 days. Only quadrant dissection from the same patient showed reproducible and reliable proportions of cell populations between dissections at any time point. There was no statistically significant relationship between the proportion of any cell population and donor age, time after death, time to storage or time in storage.
Conclusions
The 8 fold quadrant dissection method from a single donor forms an attractive human experimental model for interventional testing in retinal research. We demonstrate the utility of this model in a simple neuroprotection study, showing that insulin protected against CoCl2 induced hypoxia in human photoreceptors.

• 1561

Biological model of Zebrafish- a new research trend in ophthalmology, for an antiangiogenic treatment

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Purpose
Zebrafish is an ideal biological model for studying human diseases because of many similarities with the human genome. The structure of zebrafish eye is also very comparable to the human eye. We focused on new therapies for wet age-related macular degeneration (wAMD) and proliferative diabetic retinopathy (PDR). The aim of the study was to present the influence of dopamine's agonist on the angiogegesis of Zebrafish larvae in comparison with anti-angiogenic effect of bevacizumab
Methods
3 substances were used: bromocriptine, pergolide, cabergoline in concentrations from 1nmol to 2,5 umol. Process of angiogenesis was observed for 5 days in larvae of genetically modified Zebrafish Fli with labelled, luminescent blood vessels. Photo documentation was taken under the fluorescent microscope Stereo discover v8, fluorescence 200c hxp. Carl Zeiss Microscopy GmbH.
Results
Tested substances had inhibitive impact on process of angiogenesis in Zebrafish larvae. The strongest one was pergolide. We observed the diferences in Zebrafish vessels . Patological vessels were observed not only in the retina but also in the whole body of Zebrafish.
Conclusions
Zebrafish is getting more and more common model for pharmacologic research. Inhibition of angiogenesis by dopamine's agonist may be new therapeutic option in treatment of diseases, complicated by neovascularization like AMD and proliferative diabetic retinopathy.

• 1562

Importance of cellular factors in the retention of melanin-binding drugs in pigmented ocular tissues

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Purpose
Many clinical drugs bind to melanin pigment in ocular tissues, affecting their pharmacokinetics in the eye. Drug-melanin binding is frequently studied in vitro with isolated or synthetic melanin. The effect of other factors, such as permeability of melanosomal and plasma membrane, dissociation rate from melanin, melanin content of the tissue and ion trapping in melanosomes, are poorly understood. This study aims to probe the impact of the above-mentioned factors together with melanin binding on drug retention in the pigmented retinal pigment epithelium (RPE) and choroid by kinetic simulations.
Methods
We simulated drug retention in the RPE-choroid after intravitreal and systemic administration of a high and a moderate melanin-binding drug using a bottom-up approach with Stella software. The model parameters were based on realistic values from experimental studies and the model integrated these parameters together allowing the exploration of their interplay.
Results
The high melanin binder was retained in the pigmented but not in the non-pigmented RPE-choroid after both intravitreal and systemic administration. Lowering the cell membrane permeability increased retention, but changes in dissociation rate from melanin had minimal effect. Ion trapping in melanosomes increased retention. The moderate melanin binder was not retained considerably in the pigmented RPE-choroid, although the concentrations increased compared to the non-pigmented RPE-choroid. Lowering the permeability values and dissociation rate lengthened the retention in the pigmented RPE-choroid.
Conclusions
Melanin binding can accumulate high-binding drugs into pigmented tissues, but other factors, including melanosomal and plasma membrane permeability, ion trapping in melanosomes, and dissociation rate from melanin, play an important role in drug distribution to pigmented ocular tissues.

• 1563

Optic nerve cupping and lamina cribrosa sclerae depth as a resultant of translaminar pressure difference

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Purpose
The aim of the research was to evaluate correlation between translaminar pressure difference (TLPD) and optic nerve head (ONH) morphology parameters: lamina cribrosa sclerae depth (LCD) and optic nerve cupping (ONC).
Methods
Study included 42 eyes of 25 patients qualified to undergo lumbar puncture (LP) due to neurological circumstances. LCD, ONC and intraocular pressure (IOP) were measured 1-3 hours prior to LP during ophthalmic examination. IOP was measured using Goldmann applanation tonometry. ONH morphology parameters: LCD and ONC were assessed using enhanced depth imaging optical coherence tomography (EDI-OCT). CSFP was measured during lumbar puncture. TLPD was calculated as a difference between IOP (mmHg) and CSFP (mmHg).
Results
20 female eyes and 22 male eyes were included in the study. Mean age of female subjects was 44,1 ±18,00 while the mean age of male subjects was 54,73 ± 13,57. LCD was revealed to be significantly deeper in male population (mean 365,83µm vs. 296,07µm). Statistical analysis revealed a strong positive correlation between LCD and TLPD ($p<0,0001$, $R=0,78$) and between LCD and ONC ($p<0,0001$, $R=0,71$).
Conclusions
There is a strong positive correlation between TLPD and ONH morphology parameters. LCD and ONC should therefore be viewed as a resultant of two pressure compartments: IOP and CSFP. Intraocular pressure is since many years a confirmed modifiable risk factor for development and progression of glaucomatous neuropathy. CSFP was also proved to be significantly lower among primary open angle glaucoma subjects. In future LCD and ONC as a resultant of TLPD could therefore play a role in assessing the risk of glaucomatous neuropathy progression. According to significant correlation between TLPD and ONH morphology parameters, combined LCD and IOP measurement could moreover play a role as a non-invasive CSFP assessment tool.

• 1564

Alzheimer's disease: can the retina be a window to the brain?

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Purpose
The diagnosis of Alzheimer's disease (AD) is difficult. Since AD patients have visual problems, even before AD diagnosis, and retina is part of the CNS, we aim to understand whether retina could be used as a window to the brain, and for earlier and better diagnosis of AD.
Methods
To achieve this, we are performing a longitudinal study to evaluate potential changes in several molecular, cellular, structural and physiological parameters in the retina of a triple transgenic mouse model (3xTg-AD), comparing to age-matched wild-type (C57BL6/129S) mice, at 4, 8 and 12 months (M) of age, by Western blot, immunohistochemistry, TUNEL assay, ERG, PERG and OCT.
Results
In 3xTg-AD mice, at 8 and 12 M, the retinal thickness decreased significantly, and at 4, 8 and 12 M the scotopic b-wave and photopic flicker amplitude increased. No differences were detected in PERG recordings. Amyloid beta protein was not detected in the retina of 3xTg-AD at 4 and 8 M. The p-Tau protein levels increased at 4 M, but not at 8 M. At 4 and 8 M, amyloid precursor protein, beta-secretase 1, choline acetyltransferase, syntaxin and synaptophysin levels remained unchanged in the retina of 3xTg-AD. Apoptotic cells (TUNEL+ cells) were not detected. Also, no alterations were detected in the immunostaining of vimentin in 3xTg-AD, but GFAP immunostaining decreased at 8 M.
Conclusions
These results show that retinal thickness and function are early affected in a mouse model of AD. However, no molecular and cellular correlates were found in the majority of parameters evaluated in the retina, with the exception of p-Tau and GFAP, at least in early timepoints.
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• 1565

Electrical direct current stimulation affects retinal vessel diameter and vasodilation in healthy subjects

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Purpose
Electrical stimulation (ES) of the human eye is an emerging technique in the treatment of ophthalmic diseases since several studies showed improvements of visual functions in patients. Neuroprotective effects are assumed to cause beneficial impacts of ES. We investigated the acute effects of ES on retinal vasculature in healthy subjects using dynamic vessel analysis (DVA). This method enables continuous measurements of vessel diameters and assessment of flicker-induced vasodilation.
Methods
DVA was performed in 7 healthy subjects (5 females, 25.7±1.7 years, one eye) to examine retinal vessel behavior. Two primary vessel segments were analyzed in each eye (temporal artery (tA) and vein (tV)) regarding baseline vessel diameter (BLD) and vasodilation provoked by flicker (VD). For non-invasive ES a ring-shaped rubber electrode surrounding the eye and a square rubber electrode at the occiput were used. Positive direct current (800µA) was applied for 20min at the eye. Each subject participated in two experimental trials in random order, applying real and sham ES (rES/sES) once. DVA was conducted before and immediately after rES/sES to observe changes in BLD and VD. Results were analyzed using paired t-test to check for changes in BLD and VD due to rES/sES on a level of p=0.05.
Results
All subjects showed retinal vessel reactions to flicker in DVA. BLD decreased significantly after rES for tA (-3.4±1.7%; p=0.003) but not for tV (-0.2±1.6%; p=0.814). In contrast, VD of tA showed an upward trend (+0.7±1.2%; p=0.162), while VD of tV was reduced after rES (-0.4±1.6%; p=0.547). For sES no significant changes of BLD and VD were observed.
Conclusions
Real ES affects both arterial BLD and VD by narrowing tA in resting state and enhancing vessel reaction to flicker provocation. These results provide evidences for beneficial effects of ES on circulatory processes.

• 1566

Influence of metabolic control in patients with refractory diabetic macular edema treated with Ozurdex

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(2) IOBA, Retina, Valladolid, Spain
(3) Hospital Universitario de Burgos, Retina, Burgos, Spain

Purpose
To analyze the relationship between glycemic, lipid, and blood pressure control following the American Diabetes Association(ADA) goals, and the response of refractory diabetic macular edema (DME)in patients treated with Ozurdex.
Methods
A retrospective, descriptive and observational study was conducted on patients with refractory DME treated with Ozurdex® in the University Hospital of Burgos, Spain, between 2012 and 2015.
Results
21 patients were included. Almost all (95%) patients had type 2 diabetes mellitus (DM), and 81% were treated with insulin. The mean time of evolution of DM in this series was 16 years (± 12). The mean HbA1c was 7.22 ± 1.06. The mean initial best corrected visual acuity (BCVA) was 0.72 (log Mar ±0.33) and improved to 0.58 (log Mar ±0.31) after 6 months of follow up. The initial central macular thickness (CMT) was 506µ ±99, and a reduction to 384µ ±128 was observed after 6 months of follow up. Taking into account the overall metabolic control of the patient, a statistically significant difference was found in the improvement in BCVA after 3 months of follow up in patients with good metabolic control. A greater central macular thickness reduction was observed in patients with a better metabolic control at six months of follow up. This study also suggests that patients with an optimum HbA1c control have a tendency to achieve a better visual acuity after an Ozurdex implantation. No statistical differences were found between blood pressure and lipid parameters, and the anatomic or functional response to Ozurdex.
Conclusions
Ozurdex is an effective and safe treatment in the treatment of DME in patients that did not respond or poorly responded to other therapies. The overall metabolic control of the patient following the criteria of the ADA is related to the success of the treatment with Ozurdex.

• 1571

Critical points in scientific retinal imaging

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(3) University of Kuopio, A. I. Virtanen Institute for Molecular Sciences, Kuopio, Finland
(4) University of Kuopio, SIB laboratory, Kuopio, Finland
(5) University of Kuopio, Institute of Clinical Medicine- Department of Ophthalmology- Kuopio University Hospital, Kuopio, Finland

Summary
Images obviously are one of the most important category among the available data in everyday clinical ophthalmology and the visualization of different layers of retina. In experimental eye research it also play pivotal role in understanding of different biological processes of retina. This talk will focus on image capturing and analysis of mouse retina with different genetic background. In our project, we have focused on retinal pigmented epithelium (RPE) obtained from different degenerative mouse models mimicking cellular changes observed in Age-related Macular Degeneration (AMD). The 2D and 3D of RPE images were acquired through different types of microscopy. We deliver results on modern methods of absolute nucleic acid or protein quantification (q-PCR, WB, ELISA), but highlight the importance of imaging of the bio-molecular processes by a range of powerful imaging weapons (stereo/light/confocal/EM/microMRI). We have carried out do novo, in and ex vivo analyzis at micro and ultrastructural level to describe the molecular fingerprints of mouse RPE features in AMD.

• 1572

Different light spectra to better visualize retinal detail

UUSITALO H (1), Lensu L (2), Hauta-Kasari M (3)
(1) University of Tampere, Department of Ophthalmology, Tampere, Finland
(2) Lappeenranta University of Technology, Machine Vision and Pattern Recognition Laboratory, Lappeenranta, Finland
(3) University of Eastern Finland, Computational Spectral Imgaing, Joensuu, Finland

Summary
Retinal imaging provides a unique opportunity to directly visualize central nervous system and its blood vessels and analyze their structural and functional changes with modern technologies. Retinal imaging has been used for the diagnosis and follow-up of various eye diseases like glaucoma and age-related macular degeneration. Also in many systemic diseases like diabetes retinal imaging has been developed as the state of art diagnostic tool. It is one of the most sensitive tools to detect diabetic complications and screening programs to detect retinal complications has been set-up worldwide. To provide a proper care for increasing numbers of patients is an enormous burden to the health care and will need a new thinking and technologies. Personalized health care, individualized follow-up and automated self-testing technologies will neccesary tools to beat these challenges. Re-engineering retinal imaging with photonics and computational science is a multidisciplinary approach based on spectral imaging and analysis of human retina. It has realized a spectral eye fundus imaging device, spectrally tunable light source device and spectral image database of eye fundus images with clinical expert markings.

• 1573

Old and new retinal imaging techniques in research and differential diagnosis of retinal diseases

PETROVSKI, Goran(1)*
University of Szeged, Department of Ophthalmology, Szeged, Hungary

Abstract not provided

• 1574

What is the meaning of autofluorescence in retinal diseases?

KAARNIRANTA K
University of Kuopio, Department of Ophthalmology, Kuopio, Finland

Summary
The fluorophore is fluorescent chemical compound that absorbs light energy of a specific wavelength and re-emits light at a longer wavelength. The absorbed wavelengths, energy transfer efficiency, and time before emission depend on both the fluorophore structure and its chemical environment, as the molecule in its excited state interacts with surrounding molecules. Excitation energies range from ultraviolet through the visible spectrum, and emission energies may continue from visible light into the near infrared region. Recently, fundus autofluorescence (FAF) imaging has got more role in retinal diagnosis. FAF imaging is a quick and non-invasive method. It provides information also from inside of the cells (RPE cells). For example lysosomal lipofuscin is highly autofluorescent compound.
FAF is useful for monitoring disease progression, estimate age of lesions or severity level. However, FAF imaging is unspecific and observations must be combined with other diagnostic methods. In this course we discuss benefits and limitations of FAF in retinal diseases.

• 1575

Histological analysis with OCT

PATERNO I

Kuopio University Hospital, Ophthalmology Clinic, Kuopio, Finland

Summary

Each distinct retinal layer is visible on the optical coherence tomography (OCT). In clinic, the OCT has been part of diagnostics of retinal disease over 25 years, and due the technical advances, state-of-the-art OCT technique provides an impressive non-invasive tool for evaluating retinal anatomy in vivo, corresponding well to histological studies. This talk will discuss the current use and future of OCT in retinal disease research and disease models.

• 1581

Retina assessment: Imaging or function?

*SCHMETTERER, Leopold(1)**
University of Vienna, Clinical Pharmacology, Vienna, Austria

Abstract not provided

• 1582

3D surgery: new tool or just a toy?

*CREUZOT, Catherine(1)**
Prof. Catherine CREUZOT, Dijon, France

Abstract not provided

• 1583

Glaucoma: structure assessment and imaging

*BRON, Alain(1)**
Dpt of Ophthalmology, Dijon, France

Abstract not provided

• 1584

OCTA Predictive factors of CNV re treatment

*COSCAS, Florence(1)**
Université Paris XII, CHI de Creteil, Creteil, France

Abstract not provided

• 1585

Corneal nerves: from imaging to disease

*ROUSSEAU, Antoine(1)**
Hôpital de Bicetre, Ophthalmology, Le Kremlin Bicêtre, France

Abstract not provided

EVER 2017
THURSDAY
SEPT 28

• 2111

Acute retinal ischemia

AMBRESIN A
Jules-Gonin Eye Hospital, Medical Retina Unit, Lausanne, Switzerland

Summary

Retinal ischemic injuries may occur in various clinical conditions. Untill recently, funduscopy and dye angiography were the only exams to evaluate the extention of occlusive damages. Acute arterial occlusive disorders can be clinically obvious such as in branch or central arterial occlusion but in more localised ischemic injuries, these exams can be silent. Recently, Bscan OCT allowed visualisation of hyperreflective lesions in various retinal layers suggesting ischemia of the related retinal plexus. The recent advance of OCT angiography allows us today to differentiate various depths of retinal ischemic injuries. Illustrations of paracentral acute middle maculopathy will be discussed.

• 2112

OCT-A: guided treatment of diabetic retinopathy

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(1) Univ. Paris XII, Ophtalmologie, Creteil, France
(2) University of Perugia, Biomedical and Surgical Sciences- Section of Ophthalmology, Perugia, Italy

Summary

Diabetic retinopathy (DR) is the leading cause of blindness in working-age individuals in the developed world, affecting approximately 75% of patients with diabetes mellitus after 15 years. One of the early changes in diabetic eyes is loss of pericytes and proliferation of endothelial cells leading to the development of microaneurysms. Pericyte loss impairs the blood–retinal barrier, thereby leading to venous dilation and beading. The gold standard to screen for DR is dilated biomicroscopic fundus examination, where microaneurysms in the posterior pole are typically the first sign on ophthalmoscopy. Although fluorescein angiography is more sensitive than examination to detect early DR, it is invasive, costly, and time consuming, and therefore, is not appropriate as a screening test for DR. Optical coherence tomography angiography (OCT-A) is a fast, noninvasive imaging technique that uses motion contrast to create OCT-angiograms by comparing the decorrelation signal among sequential OCT B-scans. Optical coherence tomography angiography may be a valuable screening tool for DR, useful as a clinical trial endpoint, and efficient in guiding early treatment decisions in the future.
Conflict of interest
Any consultancy arrangements or agreements:
Heidelberg, Allergan, Bayer, Novartis

• 2113

OCT-A based management and treatment of RVO

COSCAS F, Coscas G, Souied E H
Université Paris XII, CHI de Creteil, Creteil, France

Summary

Correlations in retinal vein occlusion (RVO) patients between macular vascular densities in the superficial and deep capillary plexuses obtained using OCT-Angiography (OCTA) and the data from conventional examination (visual acuity and peripheral retinal non perfusion on fluorescein angiography) might reveal new insights in the pathogenesis of vascular damage. Through a retrospective, observational study of RVO patients with who underwent a comprehensive ophthalmic examination including FA and OCTA a significant correlation between automatically quantified macular vascular density on OCTA and peripheral non-perfusion on FA was demonstrated; OCTA could help in identifying high-risk RVO patients who may benefit from further evaluation using FA.
Conflict of interest
Any consultancy arrangements or agreements:
Allergan, Bayer, Novartis

• 2114

OCT-A evaluation and treatment of the macular surgical pathologies

POURNARAS, Constantin(1)*
Centre Ophtalmologique de la Colline, Genève, Switzerland

Abstract not provided

• 2115

Irradiation induced retinopathy: OCT-A in the management and treatment

ZOGRAFOS L

Prof. Leonidas Zografos, Ophtalmology, Lausanne, Switzerland

Summary

Irradiation induced maculopathy is a major complication of conservative management of intraocular tumors. Risk factors include an irradiation dose of more than 20 Gy with proton beam or Gy with brachytherapy and co-existing diabetes and high blood pressure. In irradiation induced maculopathy, we observe a disruption of the inner B/R barrier, a disruption of the outer B/R barrier and a progressive vaso-occlusive microangiopathy. In a prospective trial, based on more than 150 cases of irradiation induced maculopathy, examined with fluoresceine angiography, OCT-angiography, B-mode OCT and OCT "en face", the status of the deep capillary plexus in OCT-A had the best correlation with the residual visual acuity. Intravitreal anti-VEGF applied in cases with disrupted deep capillary plexus contribute to the maintain of the visual function and reduced the progressive perifoveal capillary loss.

• 2116

AMD type I and II: OCT-A based management and treatment

*LUMBROSO, Bruno(1)**

Centro Macula, Rome, Italy

Abstract not provided

• 2121

Tube surgery techniques

GANDOLFI S
University of Parma, Department Ophthalmology, Parma, Italy

Summary

Tube surgery has has moved from the bottom line in the glaucoma treament stepladder, to be more conveniently placed as a surgical first-line option.

This presentation will focus on (a) the mechanisms of action of tubes, (b) the most recent scientific evidences on efficacy and safety of tube surgery and (c) the technical still unmet needs to be addressed in the near future.

Conflict of interest

Any consultancy arrangements or agreements:

Santhera, Alcon-Novartis, Santen, visufarma, Ivantis, Glaukos, Allergan

Any research or educational support conditional or unconditional provided to you or your department in the past or present:

Alcon-Novartis, Ivantis, Allergan, Bayer, Visufarma

Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:

Alcon-Novartis, Allergan

Any Lecture fee paid or payable to you or your department:

Santen, Allergan, Visufarma, Alcon-Novartis

• 2122

Tube surgery in scarry eyes!

AHMED F
Western Eye Hospital Imperial College Healthcare NHS Trust, Glaucoma, London, United Kingdom

Summary

The use of glaucoma drainage devices (GDD) has been a vital advancement in the management of patients with refractory glaucoma. However, GDD implantation can be difficult- due to either the disease pathology or scarring from previous surgery.

The aim of this presentation will be to show examples of implanting GDD in eyes in which conventional GDD surgery is difficult.

The second part of the presentation will be looking at approaches on how to manage eyes with uncontrolled intra-ocular pressure even after glaucoma drainage device implantation.

• 2123

Pars plana & ciliary sulcus drainage tubes

BLOOM P (1,2)
(1) Western Eye Hospital, Ophthalmology, London, United Kingdom
(2) The Hillingdon Hospital, Ophthalmology, London, United Kingdom

Summary

Primary glaucoma surgeries, whether minimally invasive or trabeculectomy, are usually effective in lowering intra-ocular pressure. However, in a proportion of cases the initial procedure is ineffective or the procedure fails; in this eventuality, comprehensive glaucoma specialists need to be skilled in a number or other surgical strategies.

Glaucoma drainage devices ('tubes') have long been used in complex or advanced cases, and are increasingly being used earlier on in the glaucoma treatment paradigm. In this part of the symposium, consideration will be given to instances where drainage tubes inserted into the anterior chamber are unlikely to be effective or have a high risk of failure. In such situations, there may be advantages for the drainage tube to be implanted through the posterior limbus or the pars plana.

Consideration will be given to the indications, techniques, advantages and complications of posterior tube implantation. Clinical case scenarios will be described using anterior segment photography and video presentations, so that skills and knowledge will be transferred effectively; this will allow assimilation of these techniques into the clinical practice of glaucoma specialist participants.

• 2124

ECP - limbal & pars plana techniques

BLOOM P
Western Eye Hospital, London, United Kingdom

Summary

Cyclo-photocoagulation is a well-recognised and powerful therapeutic modality for the reduction of intraocular pressure. Externally applied laser treatment (TransScleral Cyclo-Photocoagulation, TSCP) may cause collateral destruction of local tissue and can induce considerable inflammation so until recently the use of diode laser cyclo-photocoagulation was restricted to poorly sighted eyes.

Endoscopically applied diode laser (Endoscopic Cyclo-Photocoagulation, ECP) is a newer, more controlled, titratable, minimally destructive treatment that treats only the target tissue. One of the first MIGS procedures, ECP allows for a quick and simple additional step to be added to routine cataract surgery (Phaco-ECP), offering the potential to treat cataract and glaucoma simultaneously.

In addition, ECP is of considerable value in treating cases of advanced, refractory glaucoma; this area will be discussed in detail during this part of the symposium, via both limbal and pars plana approaches. ECP may be used before or instead of drainage device surgery, or afterward to further augment IOP control.

• 2131

Ocular angiography: dual FA/ICGA scoring of posterior uveitis

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

Summary
In the recent past uveitis has become an exact clinical science thanks, among others, to the availability of performing imaging methods. The SUN process (standardization of uveitis nomenclature) should have been the forum where these new imaging modalities should have been integrated. However SUN did just the opposite, perpetuating old and obsolete measurement methods. For the evaluation of posterior uveitis they recommended the more than 30 year old vitreous haze scoring system comparing vitreous haze to a set of 4 pictures with increasing grades of vitreous haze, recommending it as the gold standard and main outcome measure for clinical trials on new treatments in posterior uveitis. This method is subjective and has a scale of only 4 grades, improper to reach statistical significance even in cases with pronounced vitritis. Dual FA/ICGA angiography allows scoring of both retinal and choroidal inflammation with scales of respectively 40 for each. Such a numbered measurement modality is by far more adequate to measure posterior uveitis as it scores both the retinal and choroidal inflammation in entities that mostly have limited vitreitis. Several studies will illustrate the central role of FA/ICGA in monitoring posterior uveitis

• 2132

Ocular fluid analysis to pin down the cause of inflammation

NERI P, Gorgoni F, Pirani V, Pelliccioni P, Nicolai M
Polytechnic University of Marche, Eye Department, Ancona, Italy

Summary
The accuracy for the diagnosis of inflammatory eye diseases is a crucial step for an appropriate treatment strategy and their management in general. In most of the cases, non-invasive techniques, such as fluorescein angiography, indocyanine green angiography and optical coherence tomography, can lead to a correct diagnosis. In addition, blood tests and neuro-imaging can be strongly contributory. However, it has been estimated that in 8% of cases with uveitis, approximately, the clinical presentation can be atypical and, moreover, systemic medical evaluation might be non-conclusive. In order to minimize such ambiguities, diagnostic sampling of ocular fluids can help in determining the etiology of the disease, and can provide sufficient evidences for the treatment management. The diagnostic tests for atypical or uncertain uveitis subsets include: anterior chamber tap, vitreous biopsy and chorioretinal biopsy. This lecture will focus on the indications, techniques, reliability and limitations of vitreous biopsy for ocular inflammatory or pseudo-inflammatory diseases.

• 2133

The place of OCT-angiography in uveitis

KHAIRALLAH M, Khochtali S, Abroug N
Fattouma Bourguiba University Hospital, Ophthalmology, Monastir, Tunisia

Summary
Optical coherence Tomography (OCT) angiography is a newly developed, dye-less, imaging method that provides high-resolution, depth-resolved en face images of the retinal and choroidal microvasculature. OCT angiography has shown to be helpful in evaluating retinal vasculitis. It is better than fluorescein angiography in detecting perifoveal retinal ischemia and other microvascular changes. In such cases, the deep capillary plexus appears to be more severely involved than the superficial capillary plexus. On the other hand, OCT angiography may play a critical role in the differential diagnosis, evaluation, and monitoring of various choroidal inflammatory diseases involving the macula. It may show evidence of choroidal flow reduction. In these conditions, the choriocapillaris seems to be the primary site of a reversible or persistent ischemic process. OCT angiography is also useful for noninvasive detection of inflammatory choroidal neovasculization, and for monitoring of its response to therapy. Further studies are needed to definitely establish the role of OCT angiography in the diagnosis and management of retinal and choroidal inflammatory conditions and in assessing predictive factors for visual outcome.

• 2134

The potential impact of new OCT technology for the measurement of ocular inflammation

PICHI F (1,2)
(1) Cleveland Clinic, Cole Eye Institute, Cleveland, United States
(2) Cleveland Clinic Abu Dhabi, Eye Institute, Abu Dhabi, United Arab Emirates

Summary
One of the greatest challenges when caring for patients with sight-threatening uveitis is the lack of objective markers of disease activity, whether in the context of routine clinical practice (to direct treatment) or for use in clinical trials (to establish efficacy of new therapies and standardization of care). For example, the use of slit-lamp microscopy to grade anterior chamber cells is quiet subjective, depending on the empirical ability of the grader, thus nowadays spectral domain-OCT can be used to highlight cells in the anterior chamber, and new automated algorithm are being developed to measure the number of cells in a 3D volume scan.
In the anterior segment the iris tissue bed would also be a desirable site to monitor the progression of acute anterior uveitis, in which it is well known that the iris vessels dilate. OCT angiography is a novel technique that uses motion-contrast imaging to non-invasively create depth-resolved angiographic maps of the vasculature. As such, OCT angiography can be used to analyze the iris vasculature in acute anterior uveitis, and new software are available to isolate the iris vessels, create a 3D rendering and measure the vasculature volume.

• 2141

New protein drugs for retinal diseases: Attributes, efficacy, and safety

BEHAR-COHEN F
INSERM U 598, Ophthalmology, Paris, France

Summary

New protein drug delivery for retinal diseases: Attributes, efficacy and safety

One of the major challenge in the field of retina is to reduce the need for frequent re-injections of proteins in the vitreous. Sustained release of proteins is the eye remains an unmet need. To prolong the duration of protein efficacy, higher doses are injected , carrying the risk of off target effects and toxicity. Solid non biodegradable implants, dispersed polymeric systems, micro-pumps have been proposed. Gene therapy has also appears as an appealing strategy to produce secreted proteins. Beside viral vectors, non viral vectors are also developped with this purpose in mind. We will detail the advantages and drwabacks of each technology and present the latest development of ciliary muscle electroporation of plasmid encoding therapeutic proteins, from pre clinical development to first in man. The regulatory developement and safety issues will also be described.

Conflict of interest

Any Stocks or shares held by you or an immediate relative:

I am a founder of Eyevensys which is developing non viral gene transfer technology

• 2142

New biomaterials and ocular drug delivery

SHEARDOWN H , Muirhead B , Zhang J
McMaster University, Chemical Engineering, Hamilton, Canada

Summary

The need for new methods of delivering pharmacologically active agents to the eye has never been greater with the growing incidence of ocular disorders. Polymeric drug delivery methods show great promise for enhancing drug residence time as well as convenience for the patient. This talk will focus on three novel polymer based drug delivery systems developed in our labs. A mucoadhesive micelle system has been developed using acceptable polymers and has been shown to enhance the on eye residence time and the delivery of cyclosporine A in the treatment of dry eye disease. A transparent, in situ gelling injectable system has been examined to enhance the delivery of various drugs for treating diseases of the back of the eye. Finally, a Vitamin E based system is injectable, gelling upon exposure to aqueous conditions will be described. The potential of these systems as well as their limitations will be discussed and next steps in their development with a goal of creating a clinically viable drug delivery system will be described.

Conflict of interest

Any Stocks or shares held by you or an immediate relative:

A spin out company based on one of the technologies has been created. I hold one third of the company.

• 2143

Biodegradable implants for sustained drug release: Manufacturing considerations, drug stability, and drug release

KOMPELLA U B
University of Colorado Anschutz Medical Campus, Pharmaceutical Sciences-Ophthalmology- and Bioengineering, Aurora, United States

Summary

Poly(D,L-lactide-co-glycolide) (PLGA) is a biodegradable polymer used in preparing sustained release dosage forms including implants, microparticles, and nanoparticles. Indeed, an intravitreally injectable PLGA implant loaded with dexamethasone, an anti-inflammatory corticosteroid, has been approved for treating retinal vein occlusion, posterior segment uveitis, and diabetic macular edema. The purpose of this study was to determine the influence of implant manufacturing method on release of dexamethasone from PLGA implants. Melt compression and hot-melt extrusion were the two methods employed for implant manufacturing. Drug release from implants was assessed over 10 weeks in phosphate buffered saline (PBS, pH 7.4) maintained at 37 degrees Centigrade. Drug stability in PBS was assessed under the same conditions. The results indicated degradation of dexamethasone to over 10 products in PBS. Drug amounts in release medium were corrected for drug degradation, in order to estimate actual drug release. The two manufacturing methods resulted in different drug release profiles.

• 2144

Ocular pharmacokinetics and pharmacodynamics

URTTI A (1), Del Amo E (2), Pelkonen L (2), Rimpelä A K (1), Kidron H (1), Reinisalo M (2)
(1) University of Helsinki, Faculty of Pharmacy, Helsinki, Finland
(2) University of Eastern Finland, School of Pharmacy, Kuopio, Finland

Summary

Ocular pharmacokinetics is of crucial importance in ocular drug delivery and pharmacodynamics. Posterior segment drug pharmacokinetics is particularly important, since it seriously limits the applicable routes of drug delivery in the retinal treatment. In this presentation, some important aspects of posterior segment pharmacokinetics will be discussed, such as the role of blood retina barrier, drug transporters, and melanin binding. Quantitative and systematic pharmacokinetics approaches will be presented and discussed in the light of pharmacodynamics and drug delivery.

• 2145

Iontophoretic targeting of drug delivery in the eye via the suprachoroidal space

JUNG J H (1), Chiang B (2), Prausnitz M (1)
(1) Georgia Tech, Chemical and Biomolecular Engineering, Atlanta, United States
(2) Georgia Tech, Department of Biomedical Engineering, Atlanta, United States

Summary

Suprachoroidal space (SCS) injection has been developed using a microneedle to increase bioavailability of drugs. For many indications, the site of action is near the posterior pole, so targeting delivery within the SCS toward the back of the eye is of interest. Therefore, we hypothesize applying electric current (i.e., iontophoresis) can drive drugs having charge to specific areas within the SCS.

To test this hypothesis, we injected fluorescent particles using a 30G hollow microneedle into rabbit eyes ex vivo. First, negatively charged particles were infused using the microneedle embedded a Ag/AgCl electrode, and then iontophoresis was applied to generate an electric current (0.14mA for 3min) between the injection site and the optic nerve where the other Ag/AgCl electrode was attached.

After injection of 100µL without iontophoresis, we found 38% of particles were in the most anterior quadrant of the SCS (<3mm from the limbus) and 9% of particles were in the most posterior quadrant of the SCS (>9mm from the limbus). In the presence of iontophoresis, the number of particles found in the most anterior quadrant was almost cut in half to 20% and the number of particles in the most posterior quadrant was almost doubled to 17%.

• 2151

Tips and tricks in grossing & processing specimens

MOULIN A
Jules-Gonin Eye Hospital, Lausanne, Switzerland

Summary
This course will review the modalities to address the specimens for optimal histopathological processing and establishment of a correct diagnosis. It will cover orbital, palpebral, conjunctival and intraocular biopsies as well as larger resections. The course will be illustrated by clinicopathologic correlations from routine specimens.

• 2152

Overview of conjunctival and eyelid tumours

VAN GINDERDEUREN R
UZ St. Rafael, Ophthalmology, Leuven, Belgium

Summary
In this part of the course an overview will be given of the most common and most important conjunctiva and eyelid tumours (basal cell carcinoma, squamous cell carcinoma, sebaceous cell carcinoma, malignant melanoma). For each disease clinical-pathologic correlations will be emphasized. Typical and atypical characteristics will be shown.
In most cases the clinician finds the correct diagnosis, but even then it is important to investigate the section margins and the degree or details of the tumour. In rare cases a surprise in diagnosis is found and some important examples of these will be given, with also the useful consequences on the clinical follow-up of these patients.
Correct diagnosis can also be useful in non-malignant processes and examples will be given.
A short overview will be given of newer techniques and diagnostic possibilities.

• 2153

Overview of adult and paediatric orbital pathology

HEEGAARD S
Ojenpatologisk Institut, Copenhagen, Denmark

Summary
An update of the most important orbital diseases both for adults and for children will be presented.Diagnostic hallmarks for the most important diseases will be shown and correlated to the clinical features.

• 2154

Anterior to posterior “tour” of ocular disease processes

VAN GINDERDEUREN R
UZ St. Rafael, Ophthalmology, Leuven, Belgium

Summary
In this part of the course the most important pathology of the internal eye structures will be explained from front to back side of the eye. The malignant tumours of adults (melanoma, metastasis , lymphoma) and children (retinoblastoma) will be covered, but also the differential diagnosis and important consequences of non-malignant diseases (sympathetic ophthalmia). Newer technologies can be incorporated in the pathologic examination which can have far reaching consequences for the patients. Enucleation and the difference with evisceration specimens will be discussed. Newer methods for fine needle aspiration biopsy (in solid tumours) and vitreo-retinal biopsies in malignant and inflammatory processes will be explained.

• 2155

Molecular techniques in ocular pathology

MOULIN A
Jules-Gonin Eye Hospital, Lausanne, Switzerland

Summary
With the advancement of imaging modalities in ophthalmology encompassing OCT, angio-OCT, confocal microscopy, high definition MRI, the correct diagnosis can often be reached without a biopsy. In ocular oncology, ocular biopsy remains however crucial not only for the diagnosis, but also to assess the possible response to specific therapy. This course will review the recent development in diagnostic and molecular pathology. It will be based on practical routine examples and clinico-pathologic correlations of adnexal, orbital, conjunctival and intra-ocular biopsies.

• 2156

Comparative ocular pathology and animal models used in eye research

HEEGAARD S
Ojenpatologisk Institut, Copenhagen, Denmark

Summary
This lecture dealing with comparative eye pathology will present various interesting animal eyes seen from a basic anatomical point of view but also seen as a potential animal eye model used for research. Anatomical differences in different animal eyes will be presented and nature's way of solving different eye problems is discussed.

• 2161

A review of the nature & role of pre-receptoral, wavelength-selective, ocular filters in vertebrates

DOUGLAS R
City University London, Optometry & Visual Science, London, United Kingdom

Summary

Such filters are widespread in all vertebrates groups, most notably fish. Several species have pigmented corneas, whose density may alter with illumination. Filters within lenses are common, occurring in animals that inhabit well-lit environments as well as the deep-sea. Pigmented humours are rare but have been reported in a few species. Various layers within the retina also contain pigments, including the primate macular pigment, that absorb short wavelength light and the inner segments of many animals, such as birds, contain coloured oil droplets.

While many of these filters are various carotenoids, other substances such as mycosporine-like amino acids, are common. The variety of filtering pigments indicates pigmentation has evolved independently on a number of occasions; a clear testament to its importance.

Most pigments serve to reduce short wavelength light and have a variety of functions including; protection of the eye by removing the most damaging photons, acting as antioxidants, and improving image quality by reducing scatter. In deep-sea fish they enhance the visibility of bioluminescence and in animals with oil droplets they refine the spectral properties of photoreceptors.

• 2162

A review of motion photometry in the assessment of macular pigment distribution profiles obtained over two decades; applications and insights

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Summary

This presentation will review the use of a Moreland anomaloscope, modified for motion photometry, in the assessment of macular pigment (MP) over the last 20 years. Early studies examined the influence of MP on chromatic visual evoked potentials and highlighted the limitations of monitor-based methods of MP quantification, involving the use of carotenoid solutions to simulate MP. Detailed examinations using motion photometry characterised a wide range of MP distribution profiles and revealed a lack of correlation between peak optical density at the fovea and computations of the total complement of MP within the central 15 degrees, corroborated using 2-wavelength fundus autofluorescence measurements. Motion photometry assessments in individuals with widely different MP distribution profiles demonstrated a high degree of stability over periods of up to 19 years, pertinent to studies that aim to monitor MP in disease or modify MP through dietary supplementation.

• 2163

Does ethnicity and foveal morphology play a role in the spatial distribution of macular pigment?

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Summary

While macular pigment optical density typically follows an exponential decline with eccentricity from the fovea, atypical profiles have also been described, including reports of increased prevalence of ring-like and central dip profiles among non-white ethnicities. However, classification of macular pigment (MP) profile phenotypes varies and is often based on subjective visualisation. We present data showing that compared to visual assessment, objective MP profiling (taking into account measurement repeatability) is a more reliable method that should be considered in future observational and interventional studies. We will also describe ethnic variations in MP spatial distribution (among white, black and South Asian individuals) in relation to variations in foveal architecture, including data regarding individual retinal layers, foveal width and pit slope taken from SD-OCT images. Our data suggests that although ethnicity explains around 10% of the variance in MP profile, gender plays no significant role. In addition, although white subjects demonstrate thicker retinal layers than non-whites, the significant differences in the amount and distribution of MP between ethnicities is not explained by variations in foveal morphology.

• 2164

Is macular pigment spatial profile a clinical biomarker in children of AMD parents?

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Summary

A central dip in macular pigment (MP) has shown to be more prevalent with age, in AMD patients, and in smokers. We investigated clinical and genetic biomarkers in non-smoking children of AMD parents (n=131) over 40 years of age without AMD pathology in relation to their MP spatial profile. MP peak and volume were obtained with ARIS (Visual Pathways, Inc, Prescott, AZ USA) while spatial profiles for both eyes were classified visually and objectively. We explored risk factors including serum carotenoids and in-vivo skin carotenoids, and cardiovascular biomarkers including omega-3 fatty acids EPA and DHA, methylenetetrahydrofolate reductase C677T and A1298C in this well-nourished Caucasian study group. Objectively, a central dip appeared more prevalent in children of AMD patients (41%) when compared to a healthy population. Those with central dip showed increased mean MP peak and volume, decreased serum L, Z, EPA and DHA, and decreased skin carotenoids in comparison to no dip. Identifying biomarkers in children genetically susceptible to AMD and introducing lifestyle changes such as nutrient repletion could provide invaluable advice to those associated with increased risk of AMD.

• 2165

Pre-receptoral filters in the eye and their effect on vision

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Summary

Advanced Vision and Optometric Tests (www.city.ac.uk/avot) were employed to study changes in macular pigment optical density and visual performance following three months of daily supplementation with carotenoids. The subject investigated was earlier diagnosed with type 2 diabetes, but recovered through diet and exercise, to the point of being free of diabetes.

Before supplementation, the tests revealed borderline performance for photopic and mesopic visual acuity (VA), functional contrast sensitivity (FCS) and red / green (RG) colour vision. The subject's thresholds for yellow-blue (YB) colour vision and rod sensitivity were, however, just above normal, age-matched limits.

Post supplementation, the results revealed increased macular pigment levels in the central retina. In addition, the results also revealed significant improvements in several, other aspects of vision, particularly at lower light levels. VA and FCS improved, but this outcome depended on whether the stimuli were of positive or negative luminance contrast. Rod and cone mediated vision showed significant changes with large improvements in rod sensitivity. Thresholds for detection of RG and particularly YB colours were also significantly lower post-supplementation.

• 2171

Circadian regulation of outer segments phagocytosis by RPE cells: more complexity than meets the eye

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Summary

Daily clearance of aged photoreceptor outer segments (POS) extremities is one of the main functions of retinal pigment epithelial (RPE) cells. Absence or deregulation of this process leads to early-onset or age-related retinal pathologies. Despite the permanent tight contact between POS and RPE microvilli, phagocytosis occurs only once a day. Over the years, the main molecules implicated in POS tethering and subsequent internalization have been identified. POS tips expose phosphatidylserines on the outer membrane portion to be cleared. Timely recognition of POS tips and phagocytosis synchronization are mediated by the MFG-E8–alphavbeta5 integrin ligand–receptor couple. This triggers intracellular signaling pathways leading to the activation of the MerTK internalization receptor. While this draws a sequential scheme of events, things are far from being that simple. Recently new roles for MerTK and implication of new receptors have been suggested. In contrast to macrophages that share a similar phagocytic machinery, the continuous contact between both cell types requires the strict regulation of phagocytosis launch and stop to ensure lifelong retinal function. Thus, at this point the puzzle is about to get much more complicated.

• 2172

Novel roles for voltage sensitive ion channels in retinal pigment epithelium and phagocytosis

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Summary

Photoreceptors of the retina undergo a daily renewal process where they shed 10% of their outer segment disks that are then digested by the retinal pigment epithelium (RPE). Recent work demonstrated that L-type calcium channels in RPE are important for the diurnal regulation of this process. We investigated the regulatory role of several ion channels of the RPE in phagocytosis using human embryonic stem cell (hESC)-derived RPE and freshly isolated mouse tissue. The ion channels were first characterized by patch clamp recordings. The localization of photoreceptor outer segments (POS) and different ion channels during phagocytosis were studied by incubating hESC-derived RPE with purified POS particles or by dissecting mouse RPE during the physiological peak of POS shedding. Our phagocytosis assays and subsequent immunolabeling showed a promising co-localization between certain voltage sensitive ion channels, opsin and proteins involved in the phagocytosis pathway. Moreover, blocking the activity of these channels significantly reduced the efficiency of the process. Overall, several types of ion channels appear to be involved in the phagocytosis pathway. Yet, more work is required to assess their specific role.

• 2173

The importance of the polarity proteins CRB in the differentiation process of the RPE cells

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Summary

Apicobasal polarity is essential for epithelial cell function, and it is determined by the expression of three polarity protein complexes: Scribble, Par and Crumbs. Both the Par and the Crumbs complex, promote apical membrane identity. Crumbs complex is composed by PALS1, PATJ and the Crumbs homologs (CRB) proteins. We have recently described the expression of one of the Crumbs proteins, CRB2, in the retinal pigment epithelial (RPE) cells. To better understand this process, we have studied the role of CRB2 in human RPE cells during differentiation in vitro and in the mouse retina in vivo. To achieve this goal, we analyzed the temporal sequence of the establishment of the polarity proteins during human fetal RPE cells polarization and knocking-down CRB2, we analyzed the establishment of junctional complexes and features involved in the acquisition of polarization compared to the control RPE cultures. We demonstrate that, in differentiating RPE cells, CRB2 functions, as the sole CRB protein, in the formation of the junctional complex and apicobasal polarity. Additionally, the absence of the CRB2 protein from these cells results in a delay in the formation of cell-cell junctions and in an increase in cell proliferation in RPE cells.

• 2174

Proteomic tools for studying RPE functions

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Summary

Human embryonic stem cell-derived retinal pigment epithelial cells (hESC-RPE) provide a promising cell source for studying retinal development, for disease modelling, and retinal cell replacement therapies. Several research groups, including ours, have demonstrated that hESC-RPE structure, function, and physiology resembles that of native RPE regarding cellular fine structure and expression of many RPE signature genes and proteins. To characterize the hESC-RPE proteome in larger scale, we have compared hESC-RPE protein expression to primary human RPE using isobaric tags for relative quantitation (iTRAQ) technology. The hESC-RPE proteome reflected that of native RPE with a large number of metabolic, mitochondrial, cytoskeletal, and transport proteins expressed. No adverse signs such as increased stress, proliferation, or retinal degeneration-related changes were seen in hESC-RPE, while proteins involved in key RPE functions such as visual cycle and phagocytosis were detected. Proteomics provides valuable tools for validation of hESC-RPE, studying disease mechanisms, and discovery of new biomarkers and therapeutic targets.

• 2181

Ophthalmic ophthalmology

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Summary

How Do Patients Respond to Genetic Testing for AMD?

The goal of this project was to conduct a pilot AMD genomic medicine study. Eligible patients aged 50-65 with no personal AMD history gave informed consent and DNA samples were genotyped for 5 single nucleotide polymorphisms (SNPs) in the CFH gene, 1 SNP in the ARMS-2 gene, 1 SNP in the C3 gene and 1 SNP in the mitochondrial ND2 gene. The study optometrist provided risk scores and counseling for personal protective behaviors. 101 (85%) participated; 78 (77.2%) were female. The smoking status was: 67 (66.3%) never smoked, 31 (30.7%) former smokers, and 3 (3.0%) current smokers. More than half (n=48) of participants said they were motivated to participate because they had a family member with AMD or another eye or genetic disorder. Despite low risk levels, many participants made changes as a result of the genetic testing. Twenty-seven people reported making specific changes, including wearing sunglasses and brimmed hat, or taking vitamin supplements. Another 16 people said that they were already doing the recommended activity(ies). Interest in genetic testing for future risk of AMD was high in this population and led to continuation or improvement of eye health behaviors.

• 2182

A genome-wide association study suggests that the NADPH Oxidase 4 *(NOX4)* gene is associated with severe diabetic retinopathy in a Scottish diabetic population

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Summary

Diabetic retinopathy is one of the devastating eye complications in patients with diabetes. The purpose of this study is to investigate the genetic contributors of severe diabetic retinopathy using a Scottish diabetic population through a genome-wide association approach. In the Genetics of Diabetes Audit and Research in Tayside Scotland (GoDARTS) datasets, cases of severe diabetic retinopathy were defined as type 2 diabetic patients who were ever graded as having severe background retinopathy (Level R3) or proliferative retinopathy (Level R4) in at least one eye according to the Scottish Diabetic Retinopathy Grading Scheme or who were once treated by laser photocoagulation. Controls were diabetic individuals whose longitudinal retinopathy screening records were either normal (Level R0) or only with mild background retinopathy (Level R1) in both eyes. 560 cases of type 2 diabetes with severe diabetic retinopathy and 4,106 controls were identified in the GoDARTS cohort. We revealed that rs3913535 in the NADPH Oxidase 4 (NOX4) gene reached a P value of 4.05 x 10-9. This genome-wide association study of severe diabetic retinopathy suggests that the NOX4 gene might play a role in retinopathy.

• 2183

Ophthalmic ophthalmology

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Abstract not provided

• 2311

Interventions to increase attendance for diabetic retinopathy screening: a systematic review and meta-analysis

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Purpose
Study objectives were to: 1) determine the effectiveness of interventions to improve diabetic retinopathy screening (DRS) attendance; 2) specify intervention content in terms of behaviour change techniques (BCTs); 3) determine whether interventions that included particular BCTs were more effective in increasing attendance.
Methods
We searched the Cochrane Library, MEDLINE, EMBASE and clinical trials registers to February 2017 for randomised controlled trials (RCTs) that were designed to improve attendance for DRS or were evaluating general quality improvement (QI) strategies for diabetes care and reported the effect of the intervention on DRS attendance. We did not use any date or language restrictions in the searches. We identified and categorised component BCTs using an established BCT Taxonomy (BCTTv1).
Results
We included 66 RCTs. QI interventions were multifaceted and targeted patients, healthcare professionals (HCPs) or healthcare systems. Overall, DRS attendance increased by 12% (risk difference (RD) 0.12 [95% CI 0.10-0.14]) compared with usual care, with substantial heterogeneity in effect size. Both DRS-targeted and general QI interventions were effective, particularly where baseline DRS attendance was low. All frequently identified BCTs were associated with significant improvements in attendance. Higher effect estimates were observed in sub-group analyses for the BCTs 'goal setting (outcome)' (0.26 [0.16-0.36]) and 'feedback on outcomes of behaviour' (RD 0.22 [0.15-0.29]) in interventions targeting patients, and 'restructuring the social environment' (RD 0.19 [0.12-0.26]) and 'credible source' (RD 0.16 [0.08-0.24]) in interventions targeting HCPs.
Conclusions
RCT evidence indicates that QI interventions incorporating specific BCT components are associated with meaningful improvements in DRS attendance compared to usual care.

• 2312

A systematic review of the associations between dietary intake and diabetic retinopathy

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Purpose
The evidence linking diet with diabetic retinopathy (DR) is growing, but DR-specific dietary guidelines are still lacking. We conducted a comprehensive systematic assessment of the association between dietary intake and DR, and determined key areas for further research.
Methods
PubMed, Embase, Medline, and the Cochrane Central register of controlled trials were systematically searched for papers published between Jan 1967 and Jan 2017 according to standardized criteria. Interventional and observational studies, investigating nutrient intake, food and beverage consumption, and dietary patterns, were included. Data extraction was performed through a standardized extraction form, and study quality was evaluated using a modified Newcastle-Ottawa scale for observational studies, and the Cochrane collaboration tool for interventional studies.
Results
Of 4265 titles initially identified, 31 studies (3 interventional, 9 cohort, 4 case-control, 15 cross-sectional) were retained. The evidence suggests the intake of dietary fibre, oily fish, and a Mediterranean diet to be protective of DR. Conversely, higher caloric intake was associated with higher DR risk. No significant associations of DR with carbohydrate, vitamin D and sodium intake were found. The association between DR and antioxidants, fatty acids, proteins, alcohol, and other popular beverages such as tea and coffee remains equivocal.
Conclusions
Diet is a crucial aspect of DR management, with dietary components including dietary fibre, oily fish, and a Mediterranean diet being protective of DR, and a high caloric intake associated with greater DR risk. However, further cohort studies to untangle the effects of other key dietary components on DR, such as antioxidants, fatty acids, proteins, alcohol and popular beverages, are needed in order to better inform clinical guidelines.

• 2313

Vitrectomy with fibrovascular membrane delamination for proliferative diabetic retinopathy with or without preoperative Avastin

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Purpose
To describe and compare 1. the changes in intraretinal microstructure using serial spectral domain optical coherence tomography (SD-OCT) preceding and following pars plana vitrectomy and delamination of fibrovascular membranes and 2. Intraoperative and postoperative complications in patients with proliferative diabetic retinopathy (PDR) who had preoperative Avastin (group A) or not (group B).
Methods
This retrospective, interventional case series includes 113 eyes. Outcome measures included LogMAR distance best-corrected visual acuity (BCVA), SD-OCT integrity of photoreceptor inner and outer segments junction (IS/OS), and integrity of external limiting membrane (ELM), intraoperative and postoperative complications.
Results
Pre-operative central macular thickness (CMT) was significantly correlated with the final post-operative LogMAR BCVA in group A. Both groups were also categorised into three sub-groups based on post-operative IS/OS integrity (group 0: IS/OS intact; group 1: IS/OS irregular but not completely disrupted; group 2: IS/OS completely disrupted). Mean BCVA improved significantly and IS/OS integrity and ELM integrity postoperatively, were significantly and positively correlated with final BCVA in group A. Intraoperative complications such as iatrogenic tears and haemorrhage and postoperative such as vitreous haemorrhage and neovascular glaucoma where significantly less in group A compared to group B.
Conclusions
Pre-operative Avastin reduces the risk of intraoperative and postoperative complications and results in better postoperative anatomic and functional outcomes in fibrovascular delamination surgery for patients with PDR.

• 2314

Towards a shared care model for stable diabetic retinopathy patients: a feasibility trial in Singapore

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Purpose
While diabetic retinopathy (DR) is a chronic disease, patients in Asian' health care systems are often managed within hospital settings. Aim of this feasibility study is to assess the quality of care and economic benefits of a shared care model managing patients with stable DR in a primary eye care clinic (PEC) compared with a current tertiary specialist outpatient clinic (SOC) in Singapore.
Methods
A randomized equivalence feasibility trial was performed, to compare a PEC with a SOC. The trial patients included those previously seen at the SOC, and having no DR or stable mild non proliferative (NPDR) with no macular edema, no visual and DR deterioration. Primary outcomes were clinical management. Secondary outcomes were patient satisfaction and cost of consultation. Differences analysis used equivalence testing and generalized odds ratios (GOR).
Results
The trial included 231 patients, 83.1% classified as no DR (PEC: 79.1%; SOC: 87.1%) and 16.9% as stable mild NPDR (PEC:20.9%;SOC:12.9%). DR management at PEC was significantly equivalent to that received at the SOC (rate difference 2.56%; CI:(-1.61%– 6. 74%)) and 4.29%;CI: (0.14%–8.45%), respectively. Patient satisfaction at the PEC was high when compared to SOC (GOR: 1.71; CI: (0.50 – 2.00)). Direct costs per patient visit were 45% lower at PEC compared to SOC.
Conclusions
Our feasibility trial showed that patients with no or stable DR receive similar clinical care and management at a lower-cost PEC setting, are equally satisfied with the service compared to tertiary eye care. A follow-up study is necessary to validate these findings. Managing stable DR patients at a PEC may be a safe and effective shared care model to improve accessibility for patients while enhancing professional collaboration between hospital and community settings.

• 2315

Cost-effectiveness of intravitreal therapy with both anti-VEGF and Dexamethasone implant in patients with Diabetic Macular Edema

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Purpose
The aim of this study was to evaluate the cost-effectiveness of intravitreal therapy (IVT) with both anti-VEGF and Dexamethasone implant in patients with Diabetic Macular Edema (DME) during two years' follow-up.
Methods
A retrospective review of 191 patients (382 eyes) with type I and II diabetes and DME was performed. Pre-IVT and final best correct visual acuity (BCVA), central macular thickness (CMT), intraocular pressure (IOP), number and type of IVT,number of examinations, and fluorescein angiography were assessed. Based on surgery procedure other than IVT, patients were divided into 5 groups. To avoid bias, we analysed only patients who had undergone cataract surgery before (group 1) or during enrolment (group 2).
Results
41 eyes from Group 1 and 48 eyes from group 2 were evaluated. Median BCVA ranged between 20/80 and 20/63 Snellen (P=0.008) in Group 1 and from 20/63 to 20/40 Snellen (P=0.0035) in Group 2, while improvement up to 1 Snellen line was observed in 58.5 and 68.75% of eyes in Group 1 and 2, respectively.In terms of median CMT, a statistically reduction (P=0.0007) was found in Group 2 (-85 µm), whereas no statistical differences were found in Group 1. The two groups showed no statistically significant difference in median IOP. The estimated cost per eye was €7803 in Group 1 and €8988 Group 2, whereas the mean cost per patient was €15190 and €16580 in Group 1 and 2, respectively. Analysis between groups did not show any statistical difference in the considered parameters.
Conclusions
In this study, despite the high treatment cost, vision improvement in DME patients undergoing IVT was disappointing. Our results emphasise the need for a better understanding of the cost-effectiveness of DME treatment

• 2316

Topical betamethasone sodium phosphate, tetracycline hydrochloride and nonsteroidal anti-inflammatory drugs in the treatment of diabetic macular edema: a case report

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Purpose
To report a case of clinically significant diabetic macula edema (DME) cured only with topical Betamethasone Sodium Phosphate, Tetracycline Hydrochloride and nonsteroidal anti-inflammatory drugs.
Methods
A 44-year-old type I diabetic woman was referred to our Unit after a partial tarsorrhaphy procedure for exposure keratopathy in her left eye. OCT examination of her right eye revealed a clinically significant DME with important visual loss (Central Macular Thickness [CMT] 716 µm, Best Correct Visual Acuity [BCVA] 20/100 Snellen). The patient refused the suggested intravitreal therapy (Ranibizumab injections with PRN protocol). Topical treatment with Betamethasone Sodium Phosphate, Naphazoline Nitrate, Tetracycline Hydrochloride (Alfaflor®, Alfa Intest, Italy) and Diclofenac (Voltaren Oftabak®, Thea, France) eye-drops 4 times/day was started.
Results
In the following 10 months, right CMT decreased to 335 µm and right BCVA increased to 20/25 Snellen. However, OCT scans still showed some intraretinal cysts. Topical Diclofenac was then replaced with Bromfenac (Yellox®, Bausch & Lomb, Italy) eye-drops 2 times/day. After 4 months' treatment, right BCVA was 20/20 Snellen and OCT scans showed a normal CMT. This treatment was continued and there was no recurrence of DME in the next 11 months of follow-up. No adverse events were noted.
Conclusions
Topical Betamethasone Sodium Phosphate and Tetracycline Hydrochloride, together with nonsteroidal anti-inflammatory eye-drops, might be an effective alternative for the treatment of newly diagnosed DME in patients not suitable for intravitreal therapy. Future case-control studies are necessary to confirm these results.

• 2321

Leber's hereditary optic neuropathy: the ophthalmologist point of view

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Summary

Leber hereditary optic neuropathy (LHON) is a maternally inherited genetic disorder, associated to mitochondrial DNA mutations, with incomplete penetrance and variable expresivity, usually leading to large bilateral centrocecal scotomas in otherwise healthy young adults. The smaller-caliber fibers of the papillomacular bundle are selectively lost at a very early stage of the pathologic process. Clinically, most patients with LHON go through pre-symptomatic ophthalmoscopic changes before the acute phase, including peripapillary microangiopathy, small vessel tortuosity, swelling of the retinal nerve fi ber layer (RNFL). Once the disease becomes symptomatic, the vascular changes increase with swelling of the superior and inferior fiber arcades and rapid loss of the papillomacular bundle. As the pathologic process progresses, temporal pallor may become evident. Then nerve fiber swelling decreases concomitantly with the extension of optic disc pallor toward complete atrophy; vascular changes follow a similar pattern. By 6 months after onset, optic atrophy is usually evident, and visual loss stabilizes. The chronic phase is reached by 1 year after onset.

• 2322

Leber's hereditary optic neuropathy: the neurologist point of view

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Summary

Leber's hereditary optic neuropathy (LHON) is a neurodegenerative disorder that selectively affects the retinal ganglion cells (RGCs), consequently leading to optic atrophy and loss of central vision. The primary cause is a metabolic dysfunction of mitochondria due to mitochondrial DNA mutations affecting the respiratory complex I. Despite the metabolic defect is systemic and measurable in post-mitotic tissues, the disease is usually limited to the RGCs and leads to profoundly impaired vision. However, adjunctive neurological features may be present in a subset of LHON patients defining the so-called "plus" variant phenotype. The most frequent neurological features may be a multiple-sclerosis-like disease, basal ganglia involvement with dystonia or spastic dystonia and bilateral striatal necrosis, myoclonus, parkinsonism, peripheral neuropathy, migraine and sensorineural hypoacusia. Neurological exam, brain MRI, MR-spectroscopy and other ancillary exams may be needed to well characterize the "plus" phenotype of LHON patients. The genetic bases of these LHON "plus" cases are currently unclear, but private mtDNA mutations and nuclear genetic variants may be relevant.

• 2323

Fluorescence lifetime imaging ophthalmoscopy

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Summary

Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO) allows in vivo measurement of autofluorescence lifetimes of natural retinal fluorophores upon laser excitation. Beyond fluorescence intensity, lifetimes provide further information about the metabolic state of the retina as they are dependent on micro environmental factors.

Fluorescence lifetimes were investigated in healthy retinae and compared with retinal diseases such as retinal artery occlusion, geographic atrophy due to age related macular degeneration, central serous chorioretinopathy, Stargardt disease, and choroideremia.

Retinal autofluorescence lifetimes feature disease specific patterns. They allow identifying differences within retinal deposits and changes of local or systemic metabolic conditions over time. Thereby, FLIO provides a promising tool for investigation of retinal metabolic changes. Especially neurodegenerative diseases associated with intracellular deposits shall be further investigated. As FLIO is a non invasive imaging technique which is easy to apply it might qualify as a screening technique for early detection of retinal changes also in neurodegenerative diseases.

• 2324

AD in the eye

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Summary

Alzheimer's Disease (AD) is the most common form of dementia, however, diagnosis of this condition typically occurs late in the disease process and can only be confirmed post-mortem. Late diagnosis of AD is problematic as considerable damage to the brain has already occurred by the time symptoms present. Timely diagnosis would therefore serve to create a window of opportunity for novel therapeutics designed to slow or prevent AD progression. The retina presents the only portion of the CNS that can presently be readily and non-invasively imaged at the single cell resolution owing to the optically transparent nature of the eye. Visual defects have long been reported in AD patients and there are growing reports that histopathological changes in the brain can also be observed in the retina. This talk outlines recent developments in our understanding of potential retinal manifestations of AD with a view to using these findings to develop novel retinal based diagnostics.

• 2325

MS and optic neuritis

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Summary

Neurodegenerative disorders such as Alzheimer Disease, Parkinson Disease and Multiple Sclerosis present ocular manifestations which could precede general signs and symptoms. This correlation between the eye and the brain has been confirmed by recent advances in imaging technologies.

Hardware and software improvements have given the possibility of examining structures previously inaccessible. The assessments of these structures could lead to novel diagnostic and therapeutic approaches.

The first objective of this SIS is to generate a multidisciplinary discussion between ophthalmologists and non-eye experts; novel synergic approaches to neurodegenerative conditions will be discussed.

The second objective is to explore the current application of retinal imaging in neurodegenerative diseases.

• 2331

Activation of retinal microglia and accumulation of sub-retinal fluid after systemic challenge with Lipopolysaccharide in mice

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Purpose
Retinal pathology such as diabetic retinopathy can be exacerbated by systemic viral illness. However, little is known whether systemic inflammation causes activation of retinal microglia. The aim of the present study was to investigate the effect of a systemic inflammatory stimulus with lipopolysaccharide (LPS) on retinal microglia activation.
Methods
LPS (1 mg/kg) was administered intravenously for 4 days in Cx3cr1gfp/+ mice, specifically expressing gfp in microglia/macrophages. Retinas were examined with optical coherence tomography, fluorescein angiography and autofluorescence imaging before and after the LPS challenge. A group of mice was fed with the colony stimulating factor-1 receptor (CSF-1R) inhibitor PLX5622, which has been shown to deplete retinal microglia after 48 hours, for 7 days and until the end of the experiments. PLX-fed mice were challenged with LPS as above, imaged and euthanized at day 4 of the LPS challenge.
Results
Accumulation of sub-retinal fluid and leakage of fluorescein was observed in the retinas of LPS mice, suggesting disruption of the blood retinal barrier (BRB). In vivo imaging and histology showed increased numbers of gfp+ cells in retinas and brains and accumulation around retinal vessels in the LPS group. Increase of gfp+ cell numbers was partially attributed to proliferation, based on Ki67 staining. PLX attenuated the numbers of gfp+ cells and reversed the effects of LPS on sub-retinal fluid accumulation.
Conclusions
Our data suggest that systemic LPS challenge initiates inflammatory responses in the retina and can lead to disruption of the BRB, whose integrity seems to be highly dependent on retinal microglia and/or invading macrophages. Pathology is completely abrogated in microglia depleted mice, suggesting that novel CSF-1R inhibitors may be a promising target for inflammation mediated retinal diseases.
Conflict of interest
Any Stocks or shares held by you or an immediate relative?:
Martin Zinkernagel is holding equity in Novartis
Any research or educational support conditional or unconditional provided to you or your department in the past or present?:
Despina Kokona receives grant support from Bayer
Martin Zinkernagel received financial support from Allergan, Bayer, Heidelberg Engineering, Novartis
PLX5622 rodent diet was provided without financial support under a Materials Transfer Agreement with Plexxikon Inc., Berkeley, CA, USA.
Any Lecture fee paid or payable to you or your department?:
Andreas Ebneter received honoraria from Bayer for lectures

• 2332

Chronic exposure to TNFα impairs RPE barrier and immunosuppressive functions

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Purpose
The retinal pigment epithelium (RPE) is a monolayer of pigmented cells with important roles in the outer blood-retinal barrier and subretinal immune suppression. Failure of RPE functions and inflammation have both been hypothesized to play a role in the pathophysiology of age related macular degeneration (AMD). We here investigated the long-term effects of TNFα on RPE morphology and function in vitro.
Methods
Primary porcine RPE cells were cultivated until confluence, then recombinant TNFα was added daily in the culture medium (at 0.8, 4, 20 or 100ng/ml=C1,C2,C3 and C4) for 10 days. RPE cell morphology and gene expression, barrier, phagocytosis and immunosuppressive functions were assessed.
Results
Cell morphology and gene expression:TNFα (i) decreased cell number (3653.6,3428,3227,2791 and 2020 cells/mm2 respectively for control,C1,C2,C3 and C4, all $p<0.01$); (ii) increased cell size (+5.3,+12.6,+13.9 and +9.5% of control for C1,C2,C3 and C4, all $p<0.05$); (iii) increased the % of multinucleated cells (5.7,7.7,9.4,9.9 and 15.9% of multinucleated cells for control,C1,C2,C3 and C4, all $p<0.05$); (iv) and decreased OTX2 (a major RPE gene) expression (-11.1, -19.7, -52 and -82.9% of control for C1,C2,C3 and C4, all $p<0.05$). Barrier function: Stimulation by TNFα (i) disturbed Zonula Occludens 1 cellular distribution and actin F distribution and (ii) significantly decreased RPE transepithelial resistance in a dose-dependent manner (-70, -88.5 and -90.8% of control for C2,C3 and C4, $p<0.05$). Immunossupressive function: 10 day pre-stimulation with -TNFα significantly decreased RPE capacity to induce monocyte death after 24h of co-culture ($p<0.05$).
Conclusions
Chronic exposure to TNFα deteriorates major RPE functions that are essential to visual function and might play a key role in the pathophysiology of AMD.

• 2333

Uveitic macular edema : efficacy and safety of subconjonctival triamcinolone injections

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Purpose
Triamcinolone acetonide is a prolonged-release corticosteroid with a maximum effect until approximately 3 months. The aim of this work is to evaluate its effectiveness and side-effects in uveitic macular edema treatment.
Methods
This is a single institution retrospective study. From October 2014 to September 2016, 44 eyes of 44 patients who had subconjunctival triamcinolone acetonide injections for an uveitic macular oedema were included. The main outcome measures were the best corrected visual acuity and the central macular thickness measured in optical coherence tomography (OCT). These parameters were evaluated at baseline, 1 month, 3 months, 6 months and 10 months after first injection. Intraocular pressure, introduction of anti glaucoma medication, and appearance of cataract during follow-up were also noted
Results
A statistically significant improvement of visual acuity was observed as early as one month, and the benefit continuing up to 10 months. Initial visual acuity was 0.59 ± 0.49 logMAR and 0.35 ± 0.43 logMAR at 10 months. Initial macular central thickness was 460 ±124 µm, it significantly decreased to 333 ±78 µm at 1 month. Macular thickness was rapidly reduced to 1 month, and then seems relatively stable up to 10 months. The mean intraocular pressure at baseline was 14.8 ± 3.6 mmHg and significantly increased at 1 month to 17.6 ± 6 mmHg and to 17.2 ± 4,3 mmHg at 3 months. There were 9 intra ocular hypertension cases (20%) treated with glaucoma medication. No filtration surgery was required. There was one case of cataract but no surgery.
Conclusions
Subconjonctival triamcinolone acetonide injections thus provide a visual acuity gain and a decrease of uveitic macular oedema. They appear to be an alternative to intravitreal and subtenon injections, less invasive and easier to achieve.

• 2334

INFLIXIMAB and ADALIMUMAB in uveitic macular edema

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Purpose
To compare the efficacy of infliximab versus adalimumab for the treatment of uveitis related refractory macular edema (ME).
Methods
We included in this retrospective case series patients diagnosed with uveitis related refractory ME and treated with infliximab (IFX) or adalimumab (ADA) at Pitie Salpetriere hospital between 2006 and 2016. All patients were assessed including best corrected visual acuity (BCVA), clinical inflammatory parameters, multimodality imaging, fluorescein angiography, ICG and SD-OCT. Central foveal thickness (CFT) and retinochoroidal architecture were analysed with SD-OCT at baseline, 6 and 24 months after treatment initiation. Findings of patients treated with IFX were compared with those of patients treated with ADA. Success was defined as a decrease of more than 50 microns of CMT.
Results
Twelve patients with a mean age of 40 years and 13 patients with a mean age of 46 years were respectively treated with ADA and IFX. At baseline, the mean BCVA of ADA patients was 0.59 logMar ((0; 1,3); median=0,54; SD=0,41) and the mean BCVA of IFX patients was 1,01 logMar ((0,52; 1,3) mediane=1; SD=0,31). The mean CFT of ADA patients was 417µ ((247; 732); median=350; SD=171) and the mean CFT of IFX patients was 450.4µ ((202; 617); median=521; SD=145). Six of the 12 patients (50%) were sucessfully treated by ADA at 6 months, and 8 of the 13 patients (61%) treated by IFX were successful at 6 months. At 6 months, CFT median decreasing from baseline was 61 microns for ADA groupe [range : 17; 136] showing no significant difference vs 92 microns for IFX [9; 165] showing no significant difference (p=0,32).
Conclusions
Anti TNF alpha therapy seems to be an efficient treatment at 6 month for uveitis related refractory macular edema. No difference in efficacy was observed between IFX and ADA.

• 2335

Results from the SAKURA program: central retinal thickness changes with intravitreal sirolimus in subjects with non-infectious uveitis of the posterior segment and macular edema at baseline

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(2) Santen- Inc., Global Medical Affairs, Emeryville, United States

Purpose
To evaluate the effects of intravitreal (IVT) sirolimus on central retinal thickness (CRT) in subjects with non-infectious uveitis of the posterior segment (NIU-PS) with macular edema (ME) in the SAKURA program.
Methods
The SAKURA program consisted of two Phase 3 international, randomized, double-masked studies evaluating the efficacy and safety of every-other-month IVT sirolimus in subjects with active NIU-PS. Inclusion criteria included vitreous haze (VH) ≥1.5+. Subjects from both studies comprised the integrated intent-to-treat population evaluating IVT sirolimus 440 µg (n=208) vs 44 µg (active control; n=208). Primary endpoint: VH=0 at Month 5 (M5). Change in CRT at M5 was assessed in subjects with baseline ME (CRT ≥300 µm).
Results
In the integrated analysis, 21.2% vs 13.5% of subjects in the 440- vs 44-µg groups achieved VH=0 at M5 (p=0.038). 68 (32.7%) subjects in the 440-µg group and 65 (31.3%) in the 44-µg group had ME at baseline (mean CRT 501.65 µm and 507.89 µm, respectively). Of these, 19.1% and 12.3% in the 440- and 44-µg groups, respectively, achieved VH=0 at M5 (p=0.282). M5 CRT data were available for 47 and 51 subjects not rescued before M5 in the 440- and 44-µg groups, respectively, with corresponding median % CRT changes from baseline of -20.6% and -15.5%. Median % CRT changes at M5 were greatest in subjects in the 440-µg group without epiretinal membrane: -55.6% vs -2.3% in the 440- vs 44-µg groups (p=0.029). Serious ocular adverse events were reported in 14.9% and 14.3% of subjects with baseline ME in the 440- and 44-µg groups, respectively.
Conclusions
An integrated analysis of the SAKURA program demonstrated that the mTOR inhibitor IVT sirolimus 440 µg can result in statistically significant improvements in VH in subjects with active NIU-PS and can improve CRT in subjects with ME.
Conflict of interest
Any consultancy arrangements or agreements?:
AbbVie, Santen, Allargan
Any research or educational support conditional or unconditional provided to you or your department in the past or present?:
Santen, Bayer, Novartis

• 2341

uveal melanoma biopsy or not (pro)

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Summary
There will be a debate on fine needle aspiration for uveal melanoma cytogenetic testing. Dr. Carol Shields will argue for biopsy. There are several reasons that biospy is important in identifing tumor cell type, genetic profile and understading risks for metastasis. If high risk, systemic therapies can be effective for reducing risk. If low risk, the patient is comfortable with piece of mind. To not do needle biopsy for melanoma is like living in the Dark Ages and never knowing what the future holds. Fine needle aspiration biopsy for uveal melanoma cytogenetic profile is smart medicine.

• 2342

Uveal melanoma biopsy or not (against)

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Summary
Biopsy for diagnostic or prognostic purposes are still controversial issues. The arguments depend on the biopsy technic used and the reason why?
Concerning the biopsy, different complications could occur such as intravitreal or tumoral hemorrhages, retinal detachment, cataract, endophthalmitis and the last one tumoral cells spreading. All these complications must be taken into account concerning the possible benefits of a biopsy.
In ocular oncology units, the diagnosis accuracy reported with noninvasive technics is over 98% with big tumors requiring enucleation. This rate could probably be similar with medium tumors. However in routine, difficult diagnosis concern small uveal tumors less than 3 mm in thickness. In a few countries physicians perform biopsy for such tumors but not in France. Our management is periodical follow up until a proof of growth. That is why, we do not really need a biopsy to diagnose an uveal melanoma!!!
On one hand, we are not able to make a prognosis in 12 to 24% of cases of cytogenetic analysis. On the other hand, nowadays, we do not have a successful proven adjuvant therapy to propose to our high risk patients. How many patients depending on their origins would like to know whether they will die or not?

• 2343

Endoresectiopn of uveal melanoma without radiotherapy

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Summary
Endoresection of choroidal melanoma without neoadjuvant radiotherapy is controversial because of concerns about iatrogenic local tumor seeding and systemic metastases. However, several authors have reported that local tumor recurrence and seeding are rare. Further, there is no evidence that metastatic disease is increased following endoresection. Recent insights into uveal melanomas indicates that metastasis depends on the genetic tumor profile and not on surgical interventions. It would seem, therefore, that the large majority of patients experiencing ocular morbidity from neoadjuvant radiotherapy are doing so unnecessarily. This problem persists because those favoring neoadjuvant radiotherapy are skeptical of the results published by authors who hold a different view from their own. There is scope for randomized clinical trials of endoresection with and without neoadjuvant radiotherapy. If the required equipoise for such trials is lacking, an ethical way should be found to allow independent inspectors to review original patient case notes and verify all the scientific claims that neoadjuvant radiotherapy is unnecessary.

• 2344

Endoresection after proton beam

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Abstract not provided

• 2345
Surgery of iris melanoma

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Summary
The most effective treatment for iris nevus and melanoma remains debatable. Typically, a melanocytic iris nevus is monitored until growth is identified. With documented growth, radiotherapy or surgical resection is usually performed. Surgical resection consists of iridectomy, which is characterized by removal of part of the iris with the tumor
Rates of cataract and glaucoma development after treatment are generally higher following proton beam and plaque radiotherapy relative to surgical resection. Moreover, radiotherapy carries the risk of limbal stem cell deficiency. Finallly, surgical resection does carry the rapidity of tumor removal
Thus, localized, circumscribed, or discrete lesions that demonstrate growth are excellent candidates for conservative surgical resection,

• 2346
Radiotherapy of iris melanoma

LUMBROSO L
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Summary
Iris melanomas represent 2 to 3% of uveal melanomas. Conservative management is often possible, with either excision of the tumor or irradiation. Proton beam irradiation for iris melanoma is used since several years, for selected small circumscribed iris melanomas. The results are excellent in terms of local control and eye preservation. The main side effect is cataract formation (45%). Progressively larger tumors have been treated with whole anterior segment irradiation (large tumors or lesions associated with extensive pigment dispersion or iridocorneal angle invasion). Local control is also excellent in this setting. For these larger lesions side effects consisting in corneal alterations and glaucoma are frequent than for localized lesions, especially if there was high ocular pressure anterior to the treatment. Glaucoma, can be challenging to treat leading to vision loss. For all patients the survival is excellent. Proton beam irradiation allows the treatment and avoids surgery of small circumscribed iris melanomas with very little side effects and excellent local tumor control. For larger, not resectable lesions, it allows ocular preservation with good local control, corneal alterations and glaucoma are frequent.

• 2347
Suspicious naevi: treat

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Summary
Small melanocytic tumors
Treat
Laurence Desjardins
According to the study performed by Shields the risk factors for growth of small melanocytic lesions are the presence of symptoms, subretinal fluid,proximity of ON , orange pigment , thickness of more than 2mm and diameter of more than 7 mm. Performing genetic test on small melanocytic lesions is not always useful , as it has been shown that a good prognosis lesion can grow and change in a bad prognosis. In a recent European study , metastasis have been observed for lesion of 6 mm in diameter and 2,3 mm in thickness
Ophthalmologists are always trying to preserve vision as a rule. Nevertheless with possibly malignant lesions, the metastatic risk has to be considered before a therapeutic approach is decided. Factors like age of the patient, number of risk factors for growth and location of the tumor should be taken in account. Thus the practician should advise the patient and discuss and explain the decision. We usually recommend treatment if there are at least 3 risk factors and if the patient is young and the lesion away from the posterior pole. In all different situations we usually recommend close follow up for suspicious lesions and treatment in case of documented growth.

• 2348
Suspicious naevi: observe

ZOGRAFOS L
Prof. Leonidas Zografos, Ophtalmology, Lausanne, Switzerland

Summary
Differential diagnosis of large choroidal nevi and small choroidal melanomas may be challenging. The diagnostic approach is guided by various clinical criteria including tumor thickness, presence or absence of subretinal fluid, orange pigment, presence or absence of symptoms, presence or absence of drusen and pin points. In case of doubt, a periodical observation can confirm the correct diagnosis. Taking in account that an irradiation treatment of tumors located close to the macula or the optic disk can produce major irradiation induced complications and visual loss, a carefull periodic observation in selected cases appears as the best diagnostic option.

• 2351

OCT angiography in retinal disease

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Abstract not provided

• 2352

OCT angiography in ONH disease

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Summary
OCT angiography is a technique that has attracted much interest over the recent years. The main application is in retinal disease such as diabetic retinopathy or age-related macular degeneration. The technique has, however, also been applied to patients with optic nerve head disease such as glaucoma or optic neuropathies. This talk summarizes what has been achieved so far and highlight problems such as quantification of perfusion.

• 2353

AO Imaging - will it become a clinical tool?

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Abstract not provided

• 2354

Imaging endpoints in clinical trials

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Summary
Clinical drug trials usually rely on primary endpoints that are well-described direct measures of patient benefit or are closely related to clinical outcomes such as visual field testing. However, there is a lack of short-term, easy to measure, highly reproducible endpoints predictive for visual acuity outcomes that would qualify as sufficiently predictive variables for patients´ benefit in clinical trials. This of special importance for the follow up of slowly developing diseases, which requires long-term studies with large sample sizes. The rapid progression in the development of in-vivo imaging techniques offers now new and exiting possibilities to assess human anatomic or physiologic information in unprecedented high resolution. Thus, the use of these new imaging techniques such as optical coherence tomography as possible endpoints in clinical phase III trials has been widely and controversially discussed. This talk aims to summarize the potential and limitations of modern imaging techniques to serve as surrogate parameters to substitute for clinical endpoints in ocular drug development.

• 2355

Ultrawidefield OCT

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Summary
Retinal wide-field imaging plays an increasingly important role for the diagnosis of various types or pathologies, some of which start or prevalently appear in the periphery. Despite the great value of wide field fundus cameras and scanning laser ophthalmoscopes for diagnosis and documentation, these devices only acquire 2-dimensional data in form of en face projections. However, cross-sectional imaging with optical coherence tomography (OCT) can provide a wealth of additional information. To cover a wide area of the retina of 100° or more of viewing angle, 5 – 10 million OCT scans are required. Current commercially available OCT technology is not able to capture such large data sets and the acquisition time would be prohibitively long.
We recently developed retinal Megahertz OCT (MHz-OCT), an OCT system that can acquire more than 1 million depth scans per second. It can achieve the high speed by using a new type of swept laser source: the Fourier Domain Mode Locked (FDML) laser. This high speed enables us to acquire a densely sampled 3-dimensional OCT data set in the non-mydriatic eye, covering an area of up to 100° angle on the human retina. Technology development and diagnostic potential of such devices will be discussed.

• 2356

Updates on retinal imaging technology for screening and diagnosis

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Summary
There has been a revolution in retinal imaging, allowing better screening, diagnosis, risk stratification and management of diabetic retinopathy (DR), age-related macular degeneration (AMD), and retinal vascular disorders. In terms of DR screening, current imaging techniques employ fundus photography and skilled readers for DR assessment. There has been development of automated retinal image analysis software such as deep learning techniques using artificial intelligence. Current screening programs also do not effectively screen for diabetic macular edema (DME). Optical coherence tomography (OCT) can potentially provide cost-effective solutions for improving DME detection. New screening techniques to image the peripheral retina such as ultra-widefield imaging offers further potential.
For diagnosis and risk stratification, spectral domain OCT (SD-OCT) and swept source OCT (SW-OCT) are increasing used to diagnosis AMD, DME, and other conditions. Traditionally, FFA is used to evaluate AMD and DR. OCT angiography (OCT-A) technology is a major advance that offers the opportunity to non-invasively visualize different retinal capillary layers without injection of dye. OCT-A is primed to replace FFA for most clinical scenarios.
Conflict of interest
Any consultancy arrangements or agreements:
Tien Y Wong is a consultant and advisory board member of Abbott, Allergan, Bayer and Novartis and Roche

• 2361

Targeted NGS: an effective approach for molecular diagnosis of hereditary vitreoretinopathies

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Summary

Hereditary vitreoretinopathies (VRPs), traditionally divided into the groups of exudative and degenerative VRPs, encompass a number of diseases affecting the vitreous and the retina. These disorders are the commonest cause of inherited retinal detachment with high risk of vision loss during infancy. We designed a next generation sequencing (NGS) assay including ATOH7, COL2A1, COL9A1, COL9A2, COL9A3, COL11A1, COL18A1, FZD4, KCNJ13, KIF11, LOXL3, LRP5, NDP, TSPAN12, VCAN and ZNF408 allowing an exhaustive genetic screening with the most frequently mutated genes reported to be associated with all inherited VRPs. The diagnostic performance of this new design was evaluated on a cohort of 166 probands with a suspected clinical diagnosis of exudative or degenerative VRPs comprising 47% of children under 15 years old. We identified a large spectrum of causative mutations (single nucleotide changes as well as copy number variants) diagnosing molecular defects for 60% of the patients. Our NGS panel is therefore a promising screening method to be used efficiently in routine practice, able to detect a higher number of molecular defects than Sanger sequencing, improving significantly the molecular diagnosis of inherited VRPs.

• 2362

Update in low vision reeducation

ATILLA H

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Summary

In pediatric age group, diagnosis of retinal diseases require detailed clinical evaluation, mostly under general anesthesia and comprehensive diagnostic tests such as electroretinography, genetic tests, and systemic examination. With the advances in treatment modalities for premature retinopathy vision can be restored even in very low birth weight babies. Advances in chemotherapy result in higher survival rates in retinoblastoma. For hereditary dystrophies gene therapy is promising. However in spite of advances in therapies for retinal diseases, it is still one of the main reasons of low vision. In infants with low vision and normal ocular structures, retinal disorders such as hereditary dystrophies, should be considered. Neurological and developmental problems may be associated with retinal abnormalities and detailed evaluation are needed in these babies and children in order to increase vision and quality of life.

• 2363

Update in vitreoretinal diseases in children

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Abstract not provided

• 2364

New insights on the anatomy and function of the retina in sickle cell disease

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Summary

Introduction : The recent rise of OCT showed that asymptomatic atrophy of the median temporal raphe of the retina (ATR) was a frequent occurrence in sickle cell disease (SCD). However, the prevalence, mechanisms and significance of ATR is not known, especially in the paediatric field. Methods: SCD-children prospectively underwent a fundus examination and an OCT of the macula and the temporal retina. Atrophy of the MTR was quantified on thickness maps. Data from brain imaging were collected in SS-type SCD children. Results: Eighty-one children were studied; 64,2% exhibited ATR, while 29,2% had peripheral SCD retinopathy. ATR was often limited to areas located temporally from the usual macular map OCT programs, so that it could be missed with these programs. Patients with peripheral retinopathy were more likely to also exhibit ATR (p=0,02). While peripheral retinopathy was significantly associated with the children age (p= 0,02), ATR was not. Conclusion: ATR seems to occur very early in children with SCD and to display most distinct features from the well-known peripheral SCD retinopathy.

• 2371

What makes ocular surface anatomy attractive for a scleral lens?

KNOP E

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Summary

The ocular surface consists of the moist mucosal organs at the anterior eye surface. They are a continuous anatomical unit from the lacrimal gland over conjunctiva & cornea into the lacrimal drainage system. Joined by the flow of tears and governed by regulatory systems, e.g. nerves, hormones & immune system - thus they also form a functional unit as a constant moist chamber (for details please see: WWW.OSCB-BERLIN.ORG). The main function is to provide the environment for vision by the entrance of light and its refraction.

"MOISTURE is KEY" because it keeps the cornea transparent and establishes the pre-ocular tear film as main refraction unit. At the same time the moist chamber is highly endangered in our humid environment.

SCLERAL CONTACT LENSES are large contact lenses that rest on the sclera and vault over the cornea by providing a pool underneath, with the patient´s own tears including all factors for nutrition & regulation. Sclerals are thus a unique medical tool to restore both essential functions when the ocular surface and particularly the cornea is altered: constant moisture and a homogeneous refraction interface. In addition they shield the cornea against the chronic mechanical forces in eye movements and blinking.

• 2372

Scleral lens as lifeline for dissatisfied patients after refractive reshaping corneal surgery

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Summary

We present our experience of scleral lens fitting after refractive failure of corneal reshaping surgery. 100 eyes of 90 patients unsatisfied after corneal reshaping surgery: Lasik (55), PKR (15), Radial keratotomy (10) and intra corneal ring segment implantation (20) are enrolled in this retrospective study. Visual acuity outcomes, quality of life using the contact lens impact quality of life (CLIQ) questionnaire and complications of scleral lens wear are discussed.

Conflict of interest

Any Stocks or shares held by you or an immediate relative:

I'm local representative of scleral lens manufacturers.

• 2373

Sclerals contact lenses in daily practise – When is it bowl and when knife?

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Abstract not provided

• 2374

Scleral lenses - What we don't (but should) know

NAU A

Korb & Associates, 400 Commonwealth Ave #2, Boston, United States

Summary

Advances in scleral lens technology have resulted in a surge of practitioners wanting to offer this modality for patients with ocular surface diseases and, increasingly, normal refractive issues. The current literature consists primarily of case reports and case series, with few prospective clinical trials. This leaves significant gaps in our understanding of how these devices interact with the tissues of the ocular surface, and offers significant opportunity for further study. Areas of research interest which could deepen our knowledge of how and when to fit (or avoid) scleral lenses will be reviewed in this lecture.

• 2375

SURGERY: When do I still prefer surgery instead of Sclerals ?

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Abstract not provided

• 2381

Rostock Cornea Module 2.0 - a versatile extension for anterior segment imaging

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Purpose
In vivo corneal confocal laser scanning microscopy became a valuable tool for studying corneal morphology in health and disease. Enabling the optical dissection of the corneal architecture, this technique offers non-invasive in vivo imaging at a cellular level being important for current research. Presently there is only one device available without undergoing technological changes in the last years. We are presenting new Rostock Cornea Module developments for anterior segment imaging using up to date confocal scanning laser technology.
Methods
We redesigned the RCM in a modular way. It is possible to use different microscope objectives for user defined requirements as well as to choose between contact and non-contact application. Since the focal adjustment inside the cornea is often fiddly, we incorporated a fast piezo stage for closed-loop focus control and adjustment. Further topics addressed: modular setup, extended field of view, reduction of eye movement and compression artifacts as well as software based noise reduction technologies.
Results
We tested the new RCM in combination with a Spectralis platform, offering a resolution of 1536 by 1536 pixel. Performing contact measurements, we get similar results compared to the well-known RCM-HRT combination, but with a higher resolution and wider field of view. In non-contact measurements, the reflection on the cornea surface is very prominent and limits imaging of epithelial structures. We could achieve high resolution stromal imaging of e.g. keratocytes nuclei and stromal nerves.
Conclusions
The RCM 2.0 concept is a versatile extension for visualization corneal structures at a cellular level enabling instant focal plane shifts. Further improvements, wavelength adaption and dedicated customizations are subject of current research.

• 2382

Comparison of four technics of surface roughness assessment of corneal lamellar cuts

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(4) University Jean Monnet, Laboratory Hubert Curien UMR CNRS 5516, Saint-Etienne, France
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(6) French Blood Centre, Eye bank, Saint-Etienne, France

Purpose
Surface roughness of corneal lamellar cuts is a crucial quality criterion, because smother is the cutting plan, better will be the visual recovery. Nevertheless, despite several studies published in the last years, it remains difficult to reliably quantify the differences between a microkeratome (MKT) and a femtosecond laser (FSL). A possible reason could be that the different studies employed different technics to assess surface roughness. Aim: To directly compare 4 microscopy technics of surface roughness assessment of corneal lamellar cuts.
Methods
Stromal lamellae were cut in organ cultured human corneas with a Moria MKT or a FSL. Environmental scanning electron microscopy (eSEM), standard SEM and chromatic confocal microscopy (CCM) were first used to verify that dehydration and metallization of samples did not artefactually alter the surface state. Three 3 quantitative methods (Atomic Force Microscopy (AFM), CCM and Focus-Variation Microscopy (FVM)) were then compared using the same stromal lamellae. Lamellae with low or high surface roughness were selected with sSEM. The Bowman membrane was used as a smooth control. Roughness quantification was done with Mountains, a validated software.
Results
Compared to eSEM, sSEM provided better image contrast allowing better visualization of the surface roughness. Dehydration and metallization did not change the surface appearance with eSEM and sSEM, and did not modify the roughnesses measured by CCM. Only CCM and FVM were able to reveal significant differences between lamellae of different roughness. CCM allowed acquisition of larger areas, allowing a better characterization of heterogeneous surfaces.
Conclusions
CCM seems to be particularly suitable for quantifying the roughness of cutting plans obtained in the cornea.

• 2383

Revisiting corneal collagen crossliniking (CXL) safety: Evaluation of the effect of ultraviolet-A (UVA) radiation on the retina with multifocal electroretinogram (mf-ERG) and optical coherence tomography (OCT)

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Purpose
The evaluation of the effect of UVA radiation on the photoreceptors after CXL
Methods
Seventeen eyes of 17 patients with keratoconus (n=15), pellucid marginal degeneration (n=1) and post-LASIK ectasia (n=1), underwent CXL (Dresden protocol). The patients were examined preoperatively, at 2 and 6 weeks postoperatively with mf-ERG and OCT. The P1 amplitude of the photoreceptor response was documented in 4 concentric rings, with ring 1 (R1) representing the foveal response and rings 2–4 (R2-R4) corresponding to the successive annuli of stimulation. Uncorrected (UDVA) and corrected distance visual acuity (CDVA), corneal densitometry and central retinal thickness were also recorded.
Results
The preoperative mean values of P1 amplitudes for the 4 rings were R1=109.96±28.96 nV/deg2, R2=49.8±14.46, R3=29.85±8.9 and R4=19.33±6.3. At 2 weeks after CXL these values were R1=77.54±24.47, R2=36.55±12.53, R3=21.53±7.71 and R4=15.3±6.13, showing a statistically significant reduction for all rings (P<.05). At 6 weeks postoperatively P1 amplitudes were R1=99.8±31.23, R2=40.67±16.39, R3=24.98±7.13 and R4=16.35±4.84, showing for each ring no significant differences compared to preoperative values (P>.05). Corneal densitometry increased to statistically significant level at 2 (P<.001) and 6 weeks (P<.001), demonstrating a weak negative correlation with the postoperative P1 amplitudes. UDVA and fovea thickness showed no significant changes at 2 and 6 weeks.
Conclusions
This is to our knowledge the first study assessing the photoreceptor response after CXL with the Dresden protocol. Although a temporary dysfunction of the photoreceptors the first postoperative weeks cannot be excluded, the increase of 6-weeks-P1 amplitudes at preoperative (physiologic) values confirms the safety standards of the duration and intensity of UVA radiation as proposed by the Dresden protocol.

• 2384

Long term outcome of Intrastromal corneal ring segment in keratoconus

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Purpose
The Intrastromal corneal ring segment (ICRS) has been widely used to correct the astigmatism and to halt the progression in keratoconus. Although short term outcomes are well known to be effective, long term outcomes have been rarely reported and showed no consensus. Therefore, we planned to evaluate the effectiveness of ICRS in keratoconus for five years.
Methods
The retrospective chart review was done. In total, 23 eyes of keratoconus which received ICRS were included. Visual acuity, refraction, keratometer, thinnest corneal thickness and higher order aberration were evaluated at preoperative, 2 months, 1 year, 3 years and 5 years of postoperative day.
Results
Both uncorrected (UCVA) and best corrected visual acuity (BCVA) was improved at 1 year and maintained until 3 years (p<0.05). UCVA worsened at 5 years but similar to preoperative measurement. On the other hand, BCVA maintained until 5 years (p<0.05). Spherical equivalent and anterior corneal keratometer were improved at 2 months and maintained until 3 years, but it was worsened similar to preoperative level (p<0.05). Vertical coma was improved consistently for 5 years (p<0.05).
Conclusions
Both Refractive and topographic findings were improved at 2 months and the effect was maintained until 3 years. Although both of it have worsened at 5th year, the level of the measurements was not worsen than that of the preoperative day. The ICRS in keratoconus is effective in correcting astigmatism and visual acuity for 3 years and also helpful in halting the progression for 5 years.

• 2385

Two photon microscopic findings of sonoporation-assisted enhancement of corneal penetration of fluoroquinolone antibiotics

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(3) POSTECH, Biomedical Optics Laboratory, Pohang, South-Korea

Purpose
To investigate the sonoporation-assisted enhancement of corneal penetration of fluoroquinolone antibiotics.
Methods
Enucleated mouse corneas were imaged by two-photon microscopy to observe normal corneal structure ex vivo. For estimation of the threshold of corneal epithelial damage, sonoporation was applied with different intensities (1.5, 2.0 and 3.0 W/cm2) for 5 minutes on each cornea. Gatifloxacin and besifloxacin were applied on each cornea and the depth of drug penetration was observed with two-photon microscopy. After sonoporation (1.5 and 1.7 W/cm2, respectively) was applied with fluoroquinolone eyedrops, we compared the aspects of drug penetration in sonoporated cornea with those in normal cornea. In vivo two photon microscopy imaging was conducted with gatifloxacin application.
Results
Normal cornea observed with two-photon microscopy showed regular arrangement of epithelial cells without any damaged cells. Threshold intensity of sonoporation that can damage some epithelial cells without significant structural destruction was determined as 1.5~2.0 W/cm2. When gatifloxacin was applied on normal cornea, gatifloxacin fluorescence was observed only on surface of corneal epithelium. After sonoporation, whole epithelium showed increased gatifloxacin and besifloxacin fluorescence. But the penetration depth and the extent of Besifloxacin were less than those of gatifloxacin, due to its own molecular structure. The threshold intensity was revealed as 1.3 W/cm2 in vivo. In vivo corneal penetration of gatifloxacin enhanced after sonoporation, and this result was comparable with that of ex vivo.
Conclusions
We observed the enhancement of corneal penetration of fluoroquinolone antibiotics after sonoporation was done on mouse cornea ex vivo as well as in vivo. Besifloxacin showed poor penetration compared with gatifloxacin even after sonoporation.

• 2386

Hydrops: Not that bad!

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Purpose
To demonstrate that hydrops is not a disaster and often evolves favorably especially under surgical treatment.
Methods
Prospective study of 30 eyes of 30 patients with corneal hydrops who underwent clinical examination with anterior segment photography, corneal topography, ultrasound corneal pachymetry and corneal OCT. All of them underwent in an outpatient setting and under topical anesthesia, anterior chamber air injection, peripheral iridotomy and deep corneal sutures perpendicular to Descemet membrane tear then kept under observation for 1 hour. Patients were asked to stay laying on their backs for 3 days. All patients were able to wear scleral lens after 1 week post surgery.
Results
Corneal edema decreased dramatically since the first day concomitantly with corneal thickness and average SimK reading. Mean LogMAR with scleral lens was 0.4.
Conclusions
Proper surgical approach of hydrops can provide a spectacular quick healing with visual improvement avoiding corneal graft.

• 2611

Topical delivery for retinal angiogenesis - an overview of clinical developments

*BATES, David(1)**
University of Nottingham, Cancer Biology, Division of Cancer and Stem Cells

Abstract not provided

• 2612

Optimisation of novel small molecule inhibitors of SRPK1-mediated VEGF-A splicing through modelling of permeability properties required for trans-scleral eye drop delivery

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(2) Exonate Ltd, University of New South Wales, Sydney, Australia
(3) University of Nottingham, School of Life Sciences, Nottingham, United Kingdom

Summary

Purpose: Development of non-invasive therapies for wAMD and DME has not yet been successful due to poor PK/PD properties. SRPK1 is a novel target that controls VEGF-A splicing. Delivery of potent small molecules to the retina as eye drops is an unmet need due to lack of insight into drug required properties. We used rational medicinal chemistry and permeability models to identify physicochemical properties for retinal delivery.

Methods: Porcine eyes were dissected, and full thickness tissue clamped into a scaffold with drug formulations facing the sclera. Tissue sections were dissected after 24 h and compound extracted and analysed by mass spectrometry. Efficacy, toxicity and PK were evaluated in C57/Bl6 mice. PK was assessed in pigmented and albino rabbits.

Results: Highly potent and selective SRPK1 inhibitors with improved permeability (x10-6 cm/s) ex vivo (Compound A 1.47, Compound B 4.07) had improved PK in in vivo models. SRPK1 inhibitors did not inhibit retinal function yet inhibited laser-CNV following eye drops given to mice (EC50s<0.5μM, n=6-8, P<0.05, One-way ANOVA).

Conclusions: Ex vivo screening enabled modelling and design of novel compounds with improved permeability and optimisation for in vivo retinal delivery.

Conflict of interest

Any research or educational support conditional or unconditional provided to you or your department in the past or present:

These small molecule inhibitors are protected by patents from the University of New South Wales, University of Bristol, University of Nottingham and Exonate.

• 2613

Nanoparticle delivery for diabetic macular edema

STEFANSSON E
University of Iceland, Ophthalmology, Reykjavik, Iceland

Summary

Nanotechnology solves the main obstacles in topical drug delivery and delivers drugs by eye drop to posterior segment of the eye.

Cyclodextrin nanoparticles containing dexamethasone increase solubility of dexamethasone in tear fluid 30 fold and the drug stays in tear film for 6 hours compared with minutes for conventional eye drops. The high concentration gradient from tear film into eye wall creates a flux which is active for many hours following eye drop application . This delivers approximately 10 times more drug into the eye and reaches the posterior segment in significant concentration. At the same time relatively less drug is absorbed systemically.

Several clinical trials have demonstrated the efficacy of the cyclodextrin nanoparticle platform both for posterior and anterior segment use. Two clinical trials in 41 patients have shown significant improvement in visual acuity and retinal structure in diabetic macular edema. The clinical effect of the eye drops is similar to that of intravitreal anti-VEGF injections and steroid implants. Two reports show compelling effect on intermediate/posterior uveitis with cystoid macular edema.

Nanotechnology has broken the age old dogma that eye drops cannot reach the retina.

Conflict of interest

Any Stocks or shares held by you or an immediate relative:

ES is founder and share holder in Oculis ehf which develops nanoparticle eye drops.

• 2621

Simulation in flight safety - what can we learn from the airline industry?

DOW I
CAE, Flight Ops, London, United Kingdom

Summary
In this presentation I will look at the evolution of aircraft simulators since 1910, how they are currently used to deliver type and recurrent pilot training and, finally, give consideration to their impact on the safety of commercial flight since 1946.

• 2622

SOS - Simulated Ocular Surgery website and applications

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

Summary
There is growing interest in simulation training for learning surgery: there are huge benefits to patient safety if trainees can gain essential skills before they attempt surgery on real patients. In ophthalmology, traditional simulation attempts have included practicing simple surgical techniques on animal eyes, or perhaps cadaveric human tissue. These approaches, whilst undoubtedly useful, have some disadvantages e.g inability to practice in a completely realistic surgical environment, which would ideally be the trainee surgeon's own operating theatre, also, cadaveric human tissue, whilst excellent, is expensive to obtain, and store.
In the last few years, advances in virtual reality, and plastics technology have stimulated widespread interest in more realistic, and less expensive surgical simulation systems, many of which, especially plastic eyes, allow the surgeon to practice in their own operating theatre, in the office using table-top binocular microscopes, or even practice at home using loupes.
I present our experiences with the 'Simulated ocular surgery' (SOS) system, across the full range of ocular surgery, with supporting videos of trainees using this system. For further information: simulatedocularsurgery.com.

• 2623

Real-life Experience with glaucoma surgical training using SOS eyes

MERCIECA K
Central Manchester University Hospitals, Manchester Royal Eye Hospital, Manchester, United Kingdom

Summary
Surgical training in Europe is very different according to each region. National regulations, different settings and allocated resources allow for a great heterogeneity in surgical opportunities.
The equation of providing adequate training and performance levels to the surgeon while upholding the best possible practices of maximizing patient safety is a difficult task. Throughout Europe, surgeons are increasingly resorting to solutions that allow them to train in simulated scenarios before being confronted with a real life scenario. From wet-labs to electronic simulations, there is a wide range of solutions that could be adapted to each reality.
In this section of the symposium we look at real life experiences using specifically designed advanced 'dry lab eye' models (Simulated Ocular Surgery, or SOS, eyes) from the perspective of residents, glaucoma fellows and consultant trainers/supervisors. Videos and first hand experiences will be shared with the audience with useful tips, practical advice and potential drawbacks presented and described by a young qualified consultant trainer from one of the largest and oldest ophthalmic teaching hospitals in the U.K.

• 2624

The Royal College of Ophthalmologists and Surgical Training Evolution in the UK

SPENCER F
Manchester, United Kingdom,

Summary
The Royal College of Ophthalmologists (RCOphth) sets the curriculum and standards for surgical training in the UK; this receives approval from the General Medical Council. The evolution of surgical training will be presented.
A microsurgical skills course, in simulation, prior to commencing live surgery has been mandatory for more than 7 years. A new strategy to increase simulation in all surgical subspecialties was initiated in 2014. This included the development of a curriculum for simulation with recommendations and resources published since 2015.
Increasing availability of inexpensive options for simulation has allowed this to be available in all UK regions and to be considered mandatory in the required surgical competencies in the curriculum.
Recent developments have included the introduction of Entrustable Professional Activities, or EPAs, to demonstrate the ability to manage an entire surgical list, demonstrating planning, teamwork and communication in addition to surgical technique. This also highlights the importance of considering simulation in communication skills or immersive simulation techniques.

• 2625

Simulation in Mainland Europe - the present and future

ABEGAO PINTO L

Centro Hospitalar Lisboa Norte / Faculty of Medicine of Lisbon University, Department of Ophthalmology, Lisbon, Portugal

Summary

Surgical training in Europe is very different according to each region. National regulations, different settings and allocated resources allow for a great heterogeneity in surgical opportunities.

The equation of providing adequate training and performance levels to the surgeon while upholding the best possible practices of maximizing patient safety is a difficult task. Throughout Europe, surgeons are increasingly resorting to solutions that allow them to train in simulated scenarios before being confronted with a real life scenario. From wet-labs to electronic simulations, there is a wide range of solutions that could be adapted to each reality. We will explore these options, its applicability, its advantages and drawbacks, in order to promote a discussion on the validity of each option in each setting.

• 2631

Local steroidal treatments: what's new

LOWDER C
Cleveland, United States,

Summary

Local Steroidal Treatments

Severe vision loss occurs in 25%-33% of all uveitis cases. Repeated bouts of inflammation increase risk of severe vision loss.

Local Treatment Options

- Periocular steroids
- Intravitreal steroids
- Intravitreal drug delivery
  - Dexamethasone 700 ug implant (Ozurdex) up to 6 months – short term therapy
  - Fluocinolone acetonide 0.59 mg implant (Retisert) up to 36 months – long term therapy

Undergoing Clinical Trial

- Fluocinolone acetonice 0.19 mg implant (Psivida) up to 36 months – long term therapy

How to choose the appropriate treatment?

- If there is systemic disease that requires anti-inflammatory therapy, maximize immunomodulatory therapy (IMT) rather than treating both locally and systemically for extended periods of time
- "Breakthrough" cystoid macular edema in disease otherwise controlled with IMT may benefit from local therapy with Ozurdex, posterior subtenon Kenalog, intravitreal triesence or VEGF inhibition.
- Disease that needs short term treatment should not be treated with long lasting implant (fluocinolone acetonide).
- Disease likely to need many years of treatment should not be given repeated short lasting implant (dexamethasone) or intravitreal triamcinolone injections.

• 2632

New intraocular therapies for non-infectious uveitis

ALBINI T
Thomas Albini- MD, Miami, United States

Summary

Traditional local treatment of non-infectious uveitis was limited to steroids with side effects such as cataract and ocular hypertension. Intravitreal (IVT) sirolimus is a novel, non-steroid, locally delivered mTOR inhibitor under investigation. The SAKURA Program, which represents the largest study of non-infectious uveitis to date, was comprised of two Phase III (one pivotal, one supportive) multinational randomized double-masked studies evaluating sirolimus 440 µg vs 44 µg active control in subjects with active NIU-PS. 80% of subjects had Multiple Measures of Inflammation (MMI) at baseline, defined as vitreous haze (VH) ≥1.5+ and ≥1 of the following: systemic corticosteroids (overall prednisone-equivalent dose ≥7.5 mg/day), BCVA ≤75 ETDRS letters, and/or presence of macular edema. In the integrated ITT population, 21.2% vs 13.5% of subjects receiving 440 µg vs 44 µg achieved VH=0 at Month 5 (p=0.0381). Among subjects with MMI at baseline, 21.1% vs 8.0% in 440 µg and 44 µg, respectively, achieved VH=0 (p=0.0007). In the SAKURA Program, treatment with 440µg IVT sirolimus demonstrated statistically significant improvements in VH in subjects with active NIU-PS, including in subjects with MMI at baseline.

Conflict of interest

Any consultancy arrangements or agreements:

I am a paid consultant for Santen, Inc.

Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:

Travel and registration to this meeting was paid for by Santen

• 2633

Traditional immunesuppressive therapy: is there something we should know further?

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(2) Cleveland Clinic Abu Dhabi, Eye Institute, Abu Dhabi, United Arab Emirates

Summary

The cornerstone of management of ocular inflammatory disease historically has been corticosteroids, which are invaluable in the immediate control of inflammation; however, corticosteroids are inappropriate for long-term use as they are associated with a wide array of toxic side effects. As we continue to learn more about the various etiologies and elucidate the basic science pathways and mechanisms of action that cause intraocular inflammation, new therapeutic approaches have evolved. They include employment of immunomodulatory agents (corticosteroid-sparing therapies) that have expanded our treatment options for these vision-threatening diseases. These pharmacologics provide therapy for ocular and systemic inflammation in an individualized, patient-tailored, stepladder approach with the ultimate goal of durable, corticosteroid-free remission.

• 2634

Biologic therapy: let the Copernican revolution begin!

NERI P, Gorgoni F, Gennari G, Cesari C
Polytechnic University of Marche, Eye Department, Ancona, Italy

Summary

Non-infectious uveitis can be a potentially sight-threatening disease. The advent of biologic drugs has represented a Copernican revolution for ocular inflammatory diseases therapies: biologic treatments are a great opportunity for those patients affected by severe, non-responder, sight threatening uveitis. The availability of such drugs has significantly improved the uveitis outcome. Several publications have reported the efficacy of biologic agents in a progressively larger number of refractory uveitides, suggesting a central role for biologic drugs in selected cases. On the other hand, the medical literature has not provided yet significant numbers and most of the biologic drugs available have been reported in small case series. The anti-tumor necrosis factor (TNF)-α is the category with the most consistent medical literature in uveitis and, very recently, Adalimumab has recently obtained the indication for the treatment of non-infectious posterior, intermediate, pan-uveitis, representing the first on label biologic agent used in ophthalmology for the therapy of uveal inflammation.

Conflict of interest

Any consultancy arrangements or agreements:

Piergiorgio Neri is Consultant for Abbvie

Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:

Piergiorgio Neri had Travel support by Abbvie

• 2641
The first consultation

DE ZAEYTIJD J
Ghent University Hospital, Ophthalmology, Ghent, Belgium

Summary
Photophobia is a common yet debilitating symptom. Patients experience an abnormal intolerance or even pain in the eye from a light source that should not be painful. The anatomy and pathophysiology of this phenomenon will be discussed. The clinical characteristics and disorders associated with photophobia will be reviewed. And finally, a practical approach will be presented to allow you to differentiate patients with common treatable causes such as dry eye disease from patients who need an in-depth ophthalmic or neurologic evaluation to find the underlying disease.

• 2642
Photophobia in retinal disease

LEROY B P (1,2)
(1) Dept of Ophthalmology & Ctr for Medical Genetics, Ghent University Hospital, Ghent, Belgium
(2) Children's Hospital of Philadelphia, Div of Ophthalmology & Ctr for Molecular & Cellular Therapeutics, Philadelphia- PA, United States

Summary
Purpose: To describe the phenotypes and genotypes of photophobia due to inherited retinal disease.
Methods: A case presentation format will be used to illustrate different genetically determined conditions leading to photophobia. Both clinical and electrophysiological phenotypes as well as genotypes will be discussed.
Results: Phenotypes and genotypes of genetically determined diseases leading to photophobia are very different. An important distinction to be made is the one between stationary and progressive diseases. Indeed, such distinction is important as the visual outcome may differ considerably between different conditions.
Conclusions: Genetically determined retinal diseases leading to photophobia are very diverse. Visual electrophysiology allows an important distinction between progressive and stationary conditions.

• 2643
Photophobia in neuro-ophthalmic disorders

KAWASAKI A
Hopital Ophtalmique Jules Gonin, Neuro-ophthalmology, Lausanne, Switzerland

Summary
This course examines various neurologic conditions which are associated with excessive light sensitivity. These conditions vary from lesions compressing the chiasm to brainstem degenerative disorders. In the absence of corneal lesions or retinal photoreceptor disease, the basis of photosensitivity with intracranial disease remains yet undetermined. A hypothesis is proposed.

• 2644
The role of electrophysiology

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

Summary
Purpose: To demonstrate the role of electrophysiological assessment in the investigation and management of the patient with photophobia, or whose vision is worse under bright lighting conditions.
Methods: Standardised (ISCEV standard) techniques for electrophysiological assessment will be described, as will any necessary non-standard protocol additions.
Results: Selected cases will be used to illustrate the value of the objective data provided by electrophysiology. The electrophysiological data will be discussed in association with the results of relevant imaging modalities.
Conclusion: Electrophysiological assessment provides objective functional data important to the diagnosis and management of this group of patients.

• 2651

Tumors and pseudo-tumors of the iris: classification and imaging techniques

ZOGRAFOS L
Prof. Leonidas Zografos, Ophtalmology, Lausanne, Switzerland

Summary
Tumors and pseudo-tumors of the iris are classified as:
- Iris cysts
- Pigmented tumors
- Vascular tumors
- Myogenic tumors
- Tu. of the non pigm. cil. epithelium
- Neurogenic tumors
- Juvenile xanthogranuloma
- Metastatic tumors
- Pseudotumors

Split lamp examination, split lamp photography, gonioscopy and photography of anterior chamber angle as well as high frequency ultrasound are the main examination techniques.

• 2652

Nevus, melanocytoma and melanoma: differential diagnosis

SHIELDS C
Wills Eye Hospital, Ocular Oncology Service, Philadelphia, United States

Summary
A major analysis on 3680 cases of iris tumors revealed two main types of tumors including solid (79%) and cystic (21%). The most common solid mass was the melanocytic tumor, which included nevus (60%), melanocytoma (3%), and melanoma (26%).
Iris nevus is benign. This tumor tends to occur in the inferior portion of the iris. In an analysis of 1611 consecutive eyes with iris nevus, growth into melanoma was documented in 4% at 10 year followup. Statistical analysis for nevus at greatest risk for growth can be remembered by the lettering ABCDEF representing Age (< 40 years), Blood (hyphema), Clock hour inferior, Diffuse configuration, Ectropion, Feathery margins.
Iris melanocytoma is benign and appears as a dark brown mass, occasionally with iris and angle seeding. This tumor carries 1% risk for transformation into melanoma.
Iris melanoma is malignant and represents 4% of all uveal melanomas. This tumor exhibits slow growth. An analysis of 317 eyes with iris melanoma documented risk for metastasis at 10 years in 9%. Factors predictive of metastasis included extraocular extension and secondary glaucoma.
Differentiation and understanding the behavior of these three similar-appearing tumors is important in their management.

• 2653

Circumscribed irido-ciliary melanoma: surgery versus irradiation

DESJARDINS L , *Cassoux N , LumbrosoLeRouic L , Dendale R*
Institut Curie, ophtalmic oncology, Paris, France

Summary
Iris tumors include congenital benign cyst, naevi, melanocytomas malignant melanomas, benign adenoma,leiomyomas, metastatic tumors, iris location of leukemia or lymphomas and histiocytic proliferations like iris xanthogranuloma.
Patients with metastatic disease rarely develop a bilateral diffuse melanocytic uveal proliferation (BDUMP) which can cause retinal detachment and blindness.
The diagnosis of an iris tumor is made by careful medical history, slit lamp examination, UBM ultrasonography and OCT of the iris.
In rare instances fine needle aspiration biopsy can be useful but follow up is often the more important test to differentiate stable naevus versus malignant melanoma of the iris.
Treatment can be a simple observation for naevi or melanocytoma..Surgery is still the best option for adenomas and leiomyomas. Metastatic disease can be treated by chemotherapy and external beam radiation. Xanthogranulomas of the iris usually respond well to steroids. For melanoma of the iris a lot of centers do not use surgery and prefer radiotherapy most often proton beam radiotherapy. Results of proton beam therapy of iris melanoma will be presented

• 2654

Diffuse iris melanoma: proton beam irradiation

SCHALENBOURG, Ann(1)
Jules-Gonin University Eye Hospital, Lausanne, Switzerland

Abstract not provided

• 2655

Pediatric tumors of the iris

HADJISTILIANOU T

Dipartimento di scienze oftalmolgiche, Centro Regionale di Riferimento per il Retinoblastoma, Sienna, Italy

Summary

The Author in this report provides an overview of the clinical features and frequency of iris tumors in children . Iris tumors are broadly classified into cystic or solid lesions. Cystic lesions are generally benign. Solid lesions are most often melanocytic. Iris nevus is the most common solid iris tumor in all age groups .

The most common diagnoses in the pediatric group include iris nevus ,IPE cyst, iris stromal cyst ,juvenile xanthogranuloma ,and melanoma . The author report the personal experience and presents rare tumors like melanocytoma ,medulloepithelioma and choristoma of the iris.

• 2661
Update in genetics of corneal dystrophies

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Summary
Hereditary corneal dystrophies are a group of diverse bilateral disorders usually classified anatomically according to the layer of the cornea affected. They include many types, which differ by their clinical manifestations, their histological characteristics, and their pathophysiology. The molecular basis of these corneal inherited disorders have expanded greatly, and mutations in several genes have been identified. We develop a genotype-based approach by using a targeted Next-Generation Sequencing panel including 15 known genes, and a cohort of 90 French index patients were recruited after detailed ophthalmic examination. All exons of the 15 genes were amplified using the kit TrueSeq Custom Amplicon (TSCA, Illumina). The subsequent amplified libraries were sequenced using a MiSeq (Illumina, Inc, San Diego, CA, USA) sequencer. All pathogenic variants were confirmed by Sanger sequencing, and familial analyses were performed. A large spectrum of molecular defects were identified with numerous novel variants. This NGS approach is an efficient tool to improve molecular diagnosis, and provides insight into the genotype-phenotype correlation of all these corneal disorders in a cost-effective way.

• 2662
Update in CHED

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Summary
Corneal dystrophies refer to a group of corneal diseases and that are genetically determined. Our understanding of corneal phenotype has improved with improving anterior segment imaging and early genotype-phenotype correlations. Primary corneal disease includes endothelial dystrophies, corneal dermoids, cornea plana, and kerato-irido-lenticular dysgenesis (also known as Peters anomaly, types 1 and 2). Other secondary developmental corneal diseases may include Axenfeld-Rieger syndrome, Aniridia, and primary congenital glaucoma, with specific genotype. The new molecular information is challenging the traditional thinking that was usually guided by the histopathological findings. Other secondary causes are acquired and include infection, trauma, and metabolic disorders. The new molecular information is challenging the traditional thinking that was usually guided by the histopathological findings. An overview of the innovating diagnosis and treatment are summarized.

• 2663
Peters anomaly new insights

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Summary
Developmental anomalies are one of the the main pathologies seen in infancy and childhood. Embryological development of the anterior segment structures are closely related to each other and the clinical manifestations can be complex with associated glaucoma and lens opacities. Also in infancy and childhood amblyopia is needed to addressed in order to support visual system development. The spectrum of developmental anomalies known as anterior segment dysgenesis can be mild as posterior embryotoxon or can affect iris, cornea and even crystalline lens in severe cases of Peters anomaly. Peters anomaly can be seen as a genetic syndrome (Axenfeld-Rieger syndrome) or after congenital rubella. As the clinical manifestation vary, the treatment modalities vary accordingly.

• 2664
Aqueous humor cytokines report in congenital cataract

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Summary
Congenital cataract and glaucoma are an important cause of lifelong visual impairment. The management of these diseases is specific because of physiological and anatomical features of the children eye and changes related to growth.
Compared to the management in adults, the strong inflammatory tissue reactivity following surgery is particularly noteworthy and challenging in post-operative care. The presence of postoperative fibrinous uveitis is thus not uncommon in children, notably after cataract surgery. Many intraoperative and post- operativetherapeutic options have been considered to minimize post-operative inflammation, but none of these is formally recommended. The occurrence of post-operative complications should be analysed in regard to intraocular inflammation.
The aim of the presentation is to describe cohorts of congenital cataracts and glaucomas, to measure cytokines levels in operated eyes and to compare these levels to control groups (senile cataract). These datas will be discussed taking into account clinical determinants and previously published studies. These analyses may open new axes for the understanding of the pathogenesis of congenital cataract and glaucoma, based on inflammatory processes.

• 2671

LHON: A look into nuclear and environmental factors; What is "sufficient"?

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Purpose
In Leber's Hereditary Optic Neuropathy (LHON) mutations of the mtDNA, are necessary but not sufficient for visual loss. We studied nuclear/environmental interactions in patients and in the Wallace LHON mouse model, to consider what is "sufficient". The LHON mutation causes a modest decrease in ATP production, but a large increase in ROS production. Nuclear genetic and environmental factors may play upon these factors
Methods
We noted in the data of Kirkman et al (Brain 2009) that heavy smoking mitigated visual loss by delaying disease onset. We reproduced these peculiar results (Carelli et al, Brain 2013). We also studied the ND6 mutant Wallace mouse model of LHON. 30 mice of 12 groups were sacrificed at 23 months including ND6 mutant vs ND6 wildtype and nicotinamide nucleotide transhydrogenase-NNT +/+ vs -/- (NNT deletion), under different environments of air and smoke. 10 experiments compared the axonal nerve fiber spectrums.
Results
In our patient pedigrees, heavy smoking also mitigated visual loss, but we saw in this, the existence of two subtypes of LHON. Type I, with an abrupt and severe loss of vision in the teens, was characterized by severe losses of both structure and function. Type II occured decades later with a more insidious onset, with less structural than functional loss. Type II patients were more likely to smoke. In the mice, we found the predominant loss of small fibers in NNT -/- mice carrying the ND6 mutation which were exposed to smoke.
Conclusions
Both nuclear modifiers and environmental factors in combination with LHON mutations can lead to vision loss. NNT is a transhydrogenase that couples hydride transfer from NAD(H) to NADP(+) and proton translocation across the inner mitochondrial membrane. NNT is potentially an important nuclear modifying gene for LHON.

• 2673

In vitro modeling of aniridia-related PAX6 haploinsufficiency by the use of CRISPR/Cas9 on limbal epithelial cells

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Purpose
Haploinsufficiency of PAX6 in humans is the main cause of congenital aniridia, a rare eye disease characterized by iris hypoplasia and reduced visual acuity. Patients have also progressive disorders including cataract, glaucoma and corneal abnormalities making their condition very challenging to manage. Aniridia-related keratopathy (ARK), caused by a combination of factors including limbal stem-cell deficiency, impaired healing response, abnormal differentiation, and infiltration of conjunctival cells onto the corneal surface, affects up to 95% of patients. It usually begins in the first decade of life resulting in recurrent corneal erosions, sub-epithelial fibrosis with corneal decompensation and opacification. Unfortunately, current treatment options for aniridia patients are currently limited. Although animal models partially recapitulate this disease, there is no in vitro cellular model of AKT needed for drug/therapeutic tools screening and validation.
Methods
We used genome editing (CRISPR/Cas9 technology) to introduce a nonsense mutation into one allele of the PAX6 gene in TERT-immortalized limbal cells, which remain identical to primary limbal cells able to differentiate into corneal cells upon calcium raise at confluency.
Results
A resulting mutated clone, expressing half of the amount of PAX6 protein and thus representative of haploinsufficiency, was further characterized. Sequencing analysis showed that no off-target mutations were induced. The mutated cells displayed reduced cell proliferation and cell migration but enhanced cell adhesion. Known PAX6 targets expression was also reduced. Remarkably, addition of recombinant PAX6 protein was able to activate endogenous PAX6 gene and, as a consequence, rescue partially the phenotype.
Conclusions
Our in vitro model will be powerful to identify drugs that could rescue the corneal defect.

• 2672

Red light provides partial protection against retinal ganglion cell degeneration in a mouse model of dominant optic atrophy through the activation of NFkB

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Purpose
Mutations in OPA1 are the leading cause of dominant optic atrophy, a disease in which a progressive loss of retinal ganglion cells (RGCs) leads to blindness. In the B6;C3-Opa1Q285STOP mouse, an Opa1 mutation causes a decrease in ATP production and a progressive loss in visual acuity, which coincides with pruning of the predominantly ON-centre RGC dendrites. Explanting the retina, initiates further dendritic pruning. Red light has been shown to increase ATP production and provide neuroprotection. We hypothesised that 670 nm light can delay ex vivo dendritic pruning in the B6;C3-Opa1Q285STOP mouse.
Methods
We therefore monitored the effects of 670 nm light (radiant exposure of 26.4 J/cm2) on RGC dendritic pruning in retinal explants from B6;C3-Opa1Q285STOP mice, after 16 hours ex vivo.
Results
The area under the Sholl curves, the peak of the Sholl curves and the total dendritic length of ON-center RGCs showed statistically significant reductions by 28% ($p<0.05$), 27% ($p<0.05$) and 29% ($p<0.05$), respectively, from 0 to 16 hours ex vivo, with sham treatment but no statistically significant reductions were seen with 670 nm light treatment. An increase in the nuclear-cytoplasmic ratio of transcription factor, NfkB, but not Nrf2, was found in the ganglion cell layer with 670 nm light treatment.
Conclusions
The results demonstrate the ability of 670 nm light to partially prevent ex vivo dendropathy in the B6;C3-Opa1Q285STOP mouse retina, and that the transcription factor NfkB, but not Nrf2, plays a role. The findings suggests that 670 nm light may also delay the RGC dendritic pruning that occurs in vivo in the B6;C3-Opa1Q285STOP mouse and ultimately provide neuroprotection against RGC degeneration in patients with dominant optic atrophy.

• 2674

Optical coherence tomography in the differential diagnosis of true edema versus pseudoedema of the optic disc

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Purpose
To assess the predictive value of Spectral Domain OCT (SD-OCT) to discriminate between pathological true optic disc edema (ODE) and mimickers responsible for pseudoedema (PODE).
Methods
We carried out an observational cross-sectional study of subjects consecutively referred from 2011 to 2017 to the Neuro-Ophthalmology service of 4 different hospitals for presumed acute ODE. Among a total of 155 eyes, 95 were identified as ODE and 60 as PODE. Patients underwent the optic nerve OCT evaluation using Zeiss Cirrus Optic Disc Cube 200x200 analysis. Average and four principal quadrants RNFL values were compared between ODE and PODE groups and then with age-matched controls. ROC curve and AUC were calculated to determine optimal cut-off values. Mann-Whitney and chi-square tests were used to compare groups. Statistical correlation was tested by Spearman's rho test. All tests were two sided with $p<.05$ being considered statistically significant. Statistical analysis was performed with IBM SPSS Statistics 24.
Results
Average and RNFL thickness of each optic nerve quadrants resulted significantly higher in ODE compared to control and PODE; among quadrants, the highest correlation was reported for the inferior one. Combining the appropriate cut-off value for average and inferior quadrant, we found a negative predictive value of 91% for ODE when compared to PODE. No statistically significant differences were seen between control and PODE.
Conclusions
Our data show the usefulness of SD-OCT in the management of acute optic disc elevation of uncertain causes. In particular, the results herein reported provide high negative predictive value in differentiating benign mimickers from true edema of the optic disc, thus avoiding misdiagnosis and invasive procedures not necessary for such patients.

• 2675

Attitudes of parents toward eye care in children under 7 years old in the Republic of Ireland

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Purpose

Various factors have been highlighted as affecting the uptake of eye care services around the world. We surveyed the parents and guardians of children under seven years old, in the Republic of Ireland, to investigate barriers to and knowledge of eye care. A secondary objective was to determine if either varies according to parent's socioeconomic status, ethnicity or level of education.

Methods

In 2015, one thousand surveys were distributed to the parents of 4 to 6 year old school children in the Republic of Ireland.

Results

446 surveys were completed (44.6% response rate). Chi-square revealed a significant relationship between ethnicity and how to access eye care X2 (4, n=437) =27.13, p<0.001. Analysis of the raw data revealed that the majority of Asian parents, 6 out of 7 respondents (86%), did not know how to access eye care appropriate for their child's age. Thirty percent of parents/carers (n=134) reported having at least one barrier to accessing eye care. Respondents were assigned a 'barrier score'- zero barriers to a maximum of 10 reported barriers. A Mann-Whitney U test disclosed that parents from lower income families n=84 (19%) had significantly higher number of barriers to eye care (U = 12273, p = 0.002) than those from higher income households n=356 (81%). Each respondent was assigned a 'children's eye care knowledge score'. The maximum knowledge score was 5 and the minimum 0. Kruskal Wallis X2 (2, n=438) =11.34, p=0.003 revealed a significant relationship between knowledge of eye care and level of parental education. Inspection of the mean rank of groups suggest that those with higher levels of education n=314 (77%) had the highest eye care knowledge score.

Conclusions

This research has shown that there are significant barriers to eye care in the Republic of Ireland which need to be addressed when designing future eye care pathways.

• 2676

MabThera use and efficacy in patients with active moderate to severe Graves' Orbitopathy: a multicentre retrospective study of 40 cases

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Purpose

The efficacy of MabThera to treat Graves'orbitopathy (GO) is actually controversial, because of opposite results of the 2 randomized controlled trials (Stan M et al. J Clin Endocrinol Metab 2015; Salvi M et al. J Clin Endocrinol Metab 2015).

Methods

Real-life use and efficacy of Mathera in GO in a multicentre retrospective study. Patients were enrolled in case of cortico-dependant/resistant GO, with the help of endocrinologists of the French Thyroid Research Group. GO were classified according 3 components: inflammatory (CAS ≥3), muscular (constant diplopia) and neurological (visual acuity<20/40). Success was defined by the improvement of one component of the orbitopathy, without any deterioration of others.

Results

40 patients were included. 5 of the 8 patients treated simultaneously by mabthera and orbital decompression (visual threatening disease) had favourable evolution. 32 were treated because of corticoresistant disease (mean cumulative corticoid dose of 8g; mean disease duration of 19,1 months). 6 months success was achieved for 67,5% of this group. Initial CAS (3,28 ±1,57) was significantly reduced after 3 and 6 months (1,61 ±1,1; p< 0,01). Initial visual acuity improved significantly after 3 months. All diplopic patients remained diplopic. Logistic regression revealed that initial CAS ≥3 were associated with positive treatment response (OR 3.43); smoking status was a negative pronostic factor (OR 10).

Conclusions

We present the largest cohort of patients treated by Mabthera for GO. Our mean decrease of CAS after 6 months (1.68) is better than Stan's study (1.2), but not as good as Salvi (3.8). This could be explained by our delay before treatment initiation, quicker than Stan (28.9 months) but longer than Salvi (4.5 months). Mabthera could be useful second line treatments in case of recent and still active GO.

• 2681

Mutation detection of Pakistani families with autosomal recessive retinal dystrophies

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Purpose
Hereditary retinal dystrophies (RD) are a group of heterogeneous disorders caused by mutations in over 200 genes. RDs can be subdivided into different groups based on the primary degeneration of rod or cone photoreceptor cells. This study was conducted to investigate the underlying RD genes and mutation in consanguineous families from Pakistan.
Methods
Families were recruited after informed consent. Peripheral blood was collected and genomic DNA was extracted according to standard procedures. Homozygosity mapping was performed using Affymetrix Gene Chip Human Mapping 250 K-NspI arrays. The data were analyzed using Homozygosity Mapper software. Primers for amplifying all exons and intron boundaries of all genes were designed with Primer3plus software followed by PCR and Sanger sequencing. Minigene splicing assay and DNA walking were performed on respective samples.
Results
Homozygosity mapping identified a novel locus in family A, one novel gene (C8ORF37) in family B and a large novel genomic deletion of the (LCA5) gene in family C.
Conclusions
Our study indicates the heterogeneous nature of retinal dystrophies in Pakistan. Although earlier studies have explored a number of RD families, but underlying genes are still unknown for significant proportion of Pakistani families. Theoretically the traditional screening
Methods
(homozygosity mapping based candidate gene sequencing) were successful, however SNP based genome wide scan were further implemented to improve the detection of underlying variations responsible for Retinal Dystrophies. Therefore the amalgamation of traditional and modern molecular techniques is required for accurate identification of mutations. It is anticipated that these findings will contribute to future genetic testing in Pakistani families to minimize the risk of recessive disorders.

• 2682

A novel NR2E3 gene mutation in autosomal recessive retinitis pigmentosa with cystic maculopathy

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Purpose
With the context of the Ophthalmic Genetic Clinics, this presentation aims to explore the level of understanding of photoreceptor degeneration, the leading cause of inherited blindness, which presents with extreme genetic heterogeneity ,making the molecular diagnosis a challenge.The promising future for inherited retinal dystrophies with the advent of clinical trials has been described, emphasizing the increasing need to identify the causative gene.
Methods
Case: This patient was seen as a part of an EVER foundation fellowship (School of Optometry and Vision Sciences, Cardiff University, UK) in the Ophthalmic Genetics Clinics. A 44-year-old male patient was diagnosed with autosomal recessive retinitis pigmentosa with cystic maculopathy and a novel compound heterozygous mutation, c.119-2A>C and c.571+2T>C in the NR2E3 gene was discovered . The patient was treated with oral carbonic anhydrase inhibitors, which lead to the partial resolution of foveal cysts with a marked improvement in visual acuity.
Results
NR2E3 mutations lead to a defective development or abnormal maintenance of rod photoreceptors, which manifests as macular schisis.Although, the splice site mutation 119-2A>C in NR2E3 (15q23) has been previously reported , the mutation c 571 + 2 T > C in NR2E3 is novel and has not been previously reported with retinal disease.
Conclusions
Molecular identification helps to diagnose the RP subtype, improve patient follow up and helps to predict the course of the disease. The importance of identifying the genes and understanding the pathogenesis of retinal dystrophies has been highlighted with this case , in order to facilitate the development of new therapeutic interventions, hoping for a future where we can combat inherited blindness.

• 2683

Gene therapy targeting of choroidal disease and AAV transcytosis through the outer blood retina barrier epithelium

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Purpose
The retinal pigment epithelium (RPE) forms the relatively impermeable outer blood-retinal barrier, which, when intact, prevents intraocular gene therapy vectors from effectively targeting choroidal diseases such as choroidal melanoma or choroiditis. This study hypotheses that AAV vector optimisation may effectively penetrate this ocular barrier.
Methods
Monolayers of aRPE-19 and primary human RPE were established on 24 well plate transwell inserts and integrity confirmed with stable transepithelial resistance (TEER) of 35±5 Ω/cm2 and resistance to passage of FITC-Dextran (400kDa) at 4 weeks. 10^8±1 vgs of AAV serotypes 1, 2, 3, 4, 5, 6, and 8 were added to the apical surface and media collected from the basal surface at various time points. Viral concentrations were measured by qPCR.
Results
AAV serotype 6 moved through the intact monolayer of both aRPE-19 and primary human RPE. 41.5%. 47.4% and 60.4% of AAV-6 viral particles moved through the monolayer at 30 minutes, 3 hours and 5 hours respectively. Blocking RPE exocytosis with tannic acid prevented movement of AAV6 through the monolayer. All other serotypes were unable to penetrate the RPE monolayer, with less than 10% penetrance at 24 hours.
Conclusions
These results indicate that AAV6 passes through a model of the outer blood retina barrier by active intracellular transport. Additionally, this is the first report of AAV-6 transcytosis across any barrier epithelium. AAV6 may be a promising tool to deliver therapeutic genes for ocular diseases which lay beneath the retinal epithelium.

• 2684

Characteristics, socioeconomic status and ethnic variations of primary idiopathic macular hole repair in vitreoretinal centers in the United Kingdom

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Purpose
The purpose of this multicentre retrospective study was to investigate the characteristics and role of ethnicity and socioeconomic status amongst patients with idiopathic macular holes (IMH) and the surgical outcome.
Methods
Consecutive patients undergoing primary IMH surgery at three vitreoretinal units in the UK (King's College Hospital, London, UK, Western Eye Hospital, London, UK, Sunderland Eye Infirmary, Sunderland, UK) between January 2007 and May 2017 were included. The main outcome measure was anatomical closure of IMH.
Results
Two hundred and thirty three primary IMH surgeries were included. All patients underwent pars plana vitrectomy, internal limiting membrane peeling, and gas tamponade. 69.10% of patients were European Caucasian, 6.44% were Asian, and 24.46% were Afro-Caribbean. The mean base macular hole diameter (BD) was 475.5 mcm. Mean BD was 432.2 mcm in European Caucasian patients, 481.3 mcm in Asians (P=0.005), and 505.61 mcm in Afro-Caribbeans (P=0.006). Regression analysis demonstrated that BD and Afro-Caribbean ethnicity were independent significant risk factors for surgical failure. Those who have longer duration of symptoms (Afro-Caribbeans) and leave in more deprived places (Afro-Caribbeans) in England where found to have lower success rate on macular hole closure.
Conclusions
Asian and Afro-Caribbean patients present with larger IMH than European Caucasians. In addition to IMH base diameter, black origin and lower socioeconomic status are independent risk factors for surgical failure. This study presents a large population-based data analysis on ethnic variation in macular holes and may assist in the management and predicting the surgical outcome.

• 2685

Association between the retinal vascular network, cardiovascular history and risk factors in the elderly

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Purpose
To identify patterns summarizing the retinal vascular network in the elderly and to investigate the relationship of these vascular patterns with cardiovascular history.
Methods
We conducted a population-based study, the Montrachet study (Maculopathy Optic Nerve nuTRition neurovAsCular and HEarT diseases), in participants older than 75 years. History of cardiovascular disease and a score-based estimation of their 10-year risk of cardiovascular mortality (Heart SCORE) were collected. Retinal vascular network analysis was performed by means of Singapore "I" Vessel Assessment (SIVA) software. Principal component analysis was used to condense the information contained in the high number of variables provided and to identify independent retinal vascular patterns.
Results
Overall, 1069 photographs (1069 participants) were reviewed with SIVA software. The mean age was 80.0 ± 3.8 years. We extracted three vascular patterns summarizing 41.3% of the vascular information. The most clinically relevant pattern, Sparse vascular network, accounted for 17.4% of the total variance. It corresponded to a lower density in the vascular network and higher variability in vessel width. Diabetic participants with hypoglycemic treatment had a sparser vascular network pattern than subjects without such treatment (Odds ratio, [OR], 1.68; 95% CI, 1.04-2.72; P = 0.04). Participants without history of cardiovascular disease who had a sparser vascular network were associated with a higher Heart SCORE (OR, 1.76; 95% CI, 1.08-2.25; P = 0.02).
Conclusions
Three vascular patterns were identified. The Sparse vascular network pattern was associated with being a higher risk profile for cardiovascular mortality risk at 10 years.

• 2686

X-linked juvenile retinoschisis: different mutations – same phenotype

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Purpose
To describe the phenotype-genotype correlation of three X-linked retinoschisis (XLRS) cases in juveniles with different novel mutations from Lithuanian population.
Methods
Based on clinical symptoms and family history, a preliminary diagnosis of XLRS was established in three adolescent male patients. Comprehensive ophthalmological examinations, including best-corrected visual acuity (BCVA), slit-lamp, fundus examination, spectral domain optical coherent tomography (SD-OCT) and full-field electroretinography, were performed. RS1 (NM_000330.3) gene coding exons Sanger sequencing was performed.
Results
At the time of ophtalmic and genetic counselling the patients were 9, 12 and 17 years old. The patients demonstrated macular retinoschisis and typical cyst-like cavities on SD-OCT images with logMAR BCVA ranging from 0.5 to 0.2. The mean central foveal thickness was 569.7 µm. Two of the three patients presented with peripheral retinoschisis. Flash-ERG demonstrated a reduced b/a ratio (<1.0) in all patients. RS1 c.599G>T (p.R200L) mutation was detected in one case, in silico analysis showing to be pathogenic. HGMD involves three other different mutations at the same position supporting the pathogenicity of the identified variant. c.(92_97)insC (p.W33fs) mutation was identified for another proband, in silico analysis indicating the variant is possibly damaging. The third case was identified with a pathogenic mutation c.422C>G (p.R141H), HGMD CM981753.
Conclusions
These are the first cases of XLRS in the Lithuanian population confirmed by molecular genotyping. Although clinical expression of XLRS is highly variable presented patients had a different genotype but similar phenotypic traits. Functional analysis would be of benefit to characterise the identified variants on the effect of retinoschisin expression.

• 2687

Adaptive optics retinal imaging in patients with GNAT2 mutations

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Purpose
To investigate the retinal structure in three subjects, from two pedigrees, with molecularly confirmed GNAT2 gene mutations with heterogeneous phenotype.
Methods
Spectral Domain OCT (SD-OCT) scans and custom-built Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) sequences were acquired after full ophthalmological examination, ERG and colour vision testing twice, 1-2 years apart. The foveal outer nuclear layer (ONL) retinal thickness was measured using Bioptigen SD-OCT; 120 B-scans were acquired with a 7mm nominal scan width, aligned, registered and averaged in ImageJ. A 5-pixel wide longitudinal reflectivity profile provided the distance between the internal and external limiting membrane. Peak cone density and inter-cone spacing were measured at 0.5 degree from the fovea using confocal AOSLO images. Voronoi analysis was also performed.
Results
Hardy-Rittler-Rand plates suggested normal colour vision in one of our subjects. Conversely, the colour vision test for the other two subjects (from the other pedigree) suggested colour blindness. All three subjects had non-detectable cone ERG. The peak para-foveal density varied from 30 543 to 50 943 cones/mm2 and was significantly lower than previously reported values for unaffected subjects at 168 162 ± 23 529 cones/mm2 (mean ± SD). Voronoi diagrams revealed the heterogeneity of the cone mosaic with only 44% - 53% of photoreceptors having six neighbouring cells. The ONL thickness was variable and due to the small sample size no conclusion could be drawn.
Conclusions
Microscopic retinal imaging allowed photoreceptor visualisation and quantification. It can play a significant role in a multimodal investigation, including functional and structural measurements for an in depth phenotyping of GNAT2 gene, implicated in achromatopsia and other inherited retinal diseases.

• 2711
ERM management

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Summary
Epiretinal membranes are disorders which involve the vitreoretinal interface inducing tangential tractional forces on the retina. Although they may be associated with underlying ocular conditions, the majority of epiretinal membranes are idiopathic. Deformation of the inner retinal surface is a common consequence resulting in symptoms which range from symptomatic to severe metamorrphopsia and visual reduction. Epiretinal membranes are commonly classified according to their density and contractile characteristics. Optical coherence tomography (OCT) is the gold standard diagnostic tool and certain OCT features have been associated with ERM natural course and its postoperative visual prognosis. Pars plana vitrectomy and removal of ERM is indicated for symptomatic vision debilitating membranes. Surgical controversies including the extent of ERM removal, the use of vital dyes and the necessity of inner limiting membrane peel are still under investigation.

• 2712
Partial thickness Macular holes and pharmaceutical treatment of FTMH

POURNARAS J A
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Summary
The pathophysiology of full thickness macular hole and lamellar macular hole aredifferent and will be discussed. Oct characteristics will be repeated according to newclassification. Taking in account the natural history, indication of treatment will bedetailled according to each stage of those diseases. Recently, ocriplasmin has beenintroduced as an alternative treatment to vitrectomy. Favorable Prognostic factorshave been recognized as age inferior to 65 years old, full thickness macular hole < 400microns, the absence of epiretinal membrane, vitreous adhesion < 1500 microns andphakic status. While management of full thickness macular hole shows good visualprognosis for the patients, the visual result of lamelar macular hole is not so obvious.

• 2713
Surgical techniques for failed/difficult macular holes

OZDEK S O
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Summary
Free ILM flap technique for difficult macular hole cases: Failed macular holes, macular holes associated with pathologic myopia and retinal detachment and chronic atrophic macular holes are usually difficult to handle with standard techniques. Here we describe the PFCL-assisted free ILM flap technique as a good surgical option for failed MH closures. The technique is very promising in retaining the flap during the crucial FAE, which results in favorable outcomes, both morphological and functional.
Conflict of interest
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
bayer
Any Lecture fee paid or payable to you or your department:
Novartis, Bayer

• 2714
Retinal re-modelling following ILM flap technique for FTMH

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Summary
Introduction
Surgical challenges remain for large macular holes, long standing holes as well as repeat surgery for non-closed macular holes. For these indications the success rate drops dramatically. The role of ILM flaps in anatomical and visual rehabilitation remains controversial.
Method
OCT-based longitudinal cohort study of ILM flaps mapping OCT changes over time. Inclusion criteria were macular holes larger than 500 m. Primary outcome measure: anatomical macular hole closure. Further outcome measures: OCT-based longitudinal assessment of ELM as well as ellipsoid layer.
Results
We present a case series of (n=33) patients who underwent ILM flap surgery between June 2015-Jun 2016. All holes 33/33 have been anatomically closed. OCT's were recorded and anatomical and functional changes mapped. 23/33 regained a distinguishable ELM by 3/12 (70%) and 22/33 regained the ellipsoid layer by 3/12 (67%). Follow up was between 4-6/12.
Discussion
The ILM flap technique for FTMH clearly helps hole 'closure' since all holes showed anatomical closure. The regeneration of outer retinal layers seems to help visual outcome. Yet the significance of the amorphous flap tissue remains undetermined and the study cannot yet predict postoperative vision.

• 2715

Pathophysiology of macular interface

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Summary

PURPOSE: To study the pathophysiology of the vitreomacular interface disorders (epiretinal membrane, macular hole, vitreomacular traction syndrome).
METHODS: Retrospective review of published articles concerning the above entities.
RESULTS: Posterior Vitrous Detachement (PVD) variations have been considered to be the initial event leading to vitreomacular interface abnormalities. Depending on the level of PVD (eg schisis, partial or complete), different pathophysiological cataracts may occur involving a number of cells and growth factors at the vitreomacular interface.
CONCLUSIONS: The pathophysiology of the vitreomacular interface includes a sequence of events such as cellular migration, proliferation and modulation of the extracellular matrix. The quality and quantity of the involved cells and growth factors vary between different vitromacular interface disorders.

• 2716

New technologies in the investigation of macular interface disorders

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(2) Venizeleio Hospital, Heraklion, Greece

Summary

The aim of this presentation is to show the use of the new technologies in the investigation of Macular Interface Disorders Methods: I will present various cases with the most common vitreomacular interface pathologyResults : I will demonstrate tips in order
to make the new technology more useful in the investigation of Macular interfaceDiscussion: in the era of new technology Macular interface become an easier to investigate subject in order to choose the best treatment for the patient.

• 2717

Non-surgical treatment of idiopathic macular hole (IMH)

XIROU T
Red Cross Hospital, Ophthalmic, Glyfada, Greece

Summary

Ocriplasmin and Pneumatic vitreolysis are the two non surgical treatment options for the management of IMHs. While closure of IMH after vitrectomy has a success rate very high, it is challenging the option of managing IMHs without the necessity of a surgical procedure.Cost-effectiveness and safety profile are the main parameters to be considered in these relative new non surgical treatment options, mainly proposed for IMHs less than 400μm in diameter with vitreomacular traction.

• 2721
Schlemm canal stenting

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(2) Centre for Eye Research Australia, Glaucoma Research Group, Melbourne, Australia

Summary
In primary open-angle glaucoma, the juxtacanalicular trabecular meshwork and inner wall of Schlemm canal are believed to be the site of greatest resistance to aqueous outflow. Recently several new minimally invasive devices have been developed to bypass this tissue and provide direct access to low resistance collector channels in the outer wall of Schlemm canal. These devices are inserted via an ab interno approach, usually at the time of cataract surgery, and are designed to lower intraocular pressure and reduce or eliminate the need for glaucoma medications. This Special Interest Symposium reviews the growing evidence base and covers techniques and pearls for the insertion of both the iStent and iStent Inject (Glaukos Corporation, Laguna Hills, CA, USA) as well as the Hydrus intracanalicular scaffold (Ivantis Inc., Irvine, CA, USA).
Conflict of interest
Any research or educational support conditional or unconditional provided to you or your department in the past or present:
Alcon, Allergan, Bayer
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
Alcon, Allergan, Santen

• 2722
Supra-choroidal outflow

SHAARAWY, Tarek(1)*
Dr Tarek SHAARAWY, Lausanne, Switzerland

Abstract not provided

• 2723
Newer goniotomy devices

VARMA D
Oakville, Canada,

Summary
Newer goniotomy devices will discuss the role of Kahook dual blade and GATT in the spectrum of glaucoma surgical management. Patient selection, expected clinical results, surgical technique and common complications will be presented. Video and cases will be used to supplement learning.

• 2724
Sub-conjunctival drainage

RATNARAJAN G
Eye unit and Eye bank, Ophthalmology, East Grinstead, United Kingdom

Summary
Minimally invasive glaucoma surgery (MIGS) has a favourable safety profile compared to traditional filtering glaucoma surgery. The term MIGS was originally coined to utilize the eyes natural outflow pathways.
Newer subconjunctival surgeries have shown much promise in the published literature thus far whilst still maintaining excellent safety, and therefore the remit of MIGS has expanded.
Xen surgery is an ab-interno implant that has internal lumen of 45 microns and total length of 6mm. It is inserted via both gonioscopic and external visualisation penetrating sclera 3mm from the limbus usually in the superior nasal quadrant. I will discuss strategies to try and achieve reproducible sub-conjunctival placement of the Xen implant to achieve and maintain target IOP and reduce the risk of encapsulation and further post-op manipulations.
Innfocus micro-shunt is an ab-externo implant. Its internal lumen is 70microns and total length is 8mm. Its placement involves a periotomy and dissection of tenon's to create a potential space for drainage. It is inserted 3mm from the limbus and can be placed in any quadrant of the eye. Pearls on intra-operative and post-operative management will be discussed in the symposium.

• 2725

Non-penetrating glaucoma surgery

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Abstract not provided

• 2731

Why the eye? Current understanding on the pathogenesis of ocular toxicities

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Summary
The increased use of several different pharmaceutical agents has provided a positive impact to patients benefits. On the other hand, the ophthalmologist is seeing more patients with ocular side effects secondary to such agents. In particular, ocular toxicity induced by cancer chemotherapy, biologic agents and immunesuppressive drugs includes a broad spectrum of disorders, which reflect the peculiar physiological, anatomical and biochemical characteristics of the eye. The progresses achieved by the science in understanding ocular biostructure has allowed a better knowledge on ocular side effects. This achievement assists the ophthalmologist and other specialists to recognize them early and intervene before severe visual impairment occurs. A prompt intervention for the treatment-related toxicities may also provide the opportunity for a minimization or resolution of an expected side effect. Therefore, ophthalmologist should examine patients for any therapy that can present potential ocular side effects, according to the type of used drug. The biostructure and pathophysiology of potential toxicity of different drugs will be reviewed.

• 2732

What to look for? Monitoring guidelines

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Summary
Molecularly targeted agents are commonly used in oncology practice, and many new targeted agents are currently being tested in clinical trials. As many of the molecules targeted by anticancer agents are also expressed in ocular tissues, a wide spectrum of ophthalmologic toxicities has been reported, ranging from conjunctivitis and keratitis to sight-threatening conditions such as retinal vein occlusion and optic neuritis. It is important for the Ophthalmologist to be aware of the adverse ocular events that have been reported for different drug types, in particular tyrosine kinase inhibitors and anti-cytotoxic T-cell lymphocyte antigen-4 antibodies, as they may require dose reduction or interruption. A full ophthalmologic examination is recommended, including visual acuity, tonometry, and fundoscopy. For agents with the potential to cause retinal adverse effects, optical coherence tomography, retinography and visual field examination should also be considered. For agents with the potential to induce anterior segment pathology, a slit lamp examination with fluorescein staining and Schirmer test should be routinely performed.

• 2733

What to do? Management recommendations

DAMATO E M
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Summary
Patients on targeted oncology treatments, such as MEK inhibitors, may develop visual symptoms and can present to either their oncologist, general ophthalmologist or retinal specialist. This talk aims to describe the ophthalmic findings and main differential diagnoses, and to provide an approach to the general investigation of such patients. The significance of ocular findings is highlighted and a stepwise management strategy suggested. Close collaboration between the oncologist and ophthalmologist is recommended in these cases, which are likely to become more common in the face of ongoing advancements in the field of oncology.

• 2734

MEKi-related retinopathy

JAGER M J (1), Van Dijk E H C (1), Van Herpen C M L (2), Marinkovic M (1), Luyten G P (1), Kapiteijn E H (3), Boon C J (1)
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(3) LUMC, Oncology, Leiden, Netherlands- The

Summary
Patients that are being treated for different types of malignancies may develop eye problems, which may be due to their treatment. We studied patients that received treatment with the MEK inhibitor binimetinib prospectively: 23% of 30 patients with metastatic cutaneous melanoma and 5 patients with metastatic uveal melanoma reported visual complaints during treatment. These complaints were time-dependent, mild, and reversible. OCT revealed serous subretinal fluid in 74% of patients. Moreover, a persistent profoundly abnormal electro-oculogram was found, indicating a panretinal dysfunction of the retinal pigment epithelium. Since no other abnormalities could be detected on multimodal imaging, this clinical entity is referred to as MEK-associated serous retinopathy.
Ophthalmological monitoring is warranted in patients using MEK inhibitors; however, discontinuation of administration generally does not seem necessary because of the relatively low visual impact and transient nature of the associated serous retinopathy. Possible pathogenetic mechanisms of this retinopathy include anti-RPE and anti-retinal autoantibodies and/or direct RPE toxicity of MEK inhibitors.
Ophthalmology. 2015 Sep;122(9):1907-16. doi: 10.1016/j.ophtha.2015.05.027

• 2741
The epidemiology of refraction

OHLENDORF A
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Summary
Both, ophthalmologist and vision researcher are aware that refractive errors are a major risk factor for the development of ocular diseases and therefore, their epidemiology is not only of interest for academia. The refractive state of an eye is determined by the distance between the position of the focal plane and the photoreceptor plane, when accommodation is relaxed. When focal plane and photoreceptor plane coincide, the refractive state is zero, a condition called emmetropia. If refractive errors develop, typical visual functions such as visual acuity or contrast sensitivity are affected, which results in blurry distance vision in the case of myopia. As myopia has become a major concern worldwide due to its increasing prevalence especially in Asian countries and with its known major implications on ocular health that also considerably affect the economy, epidemiological studies are especially focused on the elongation of the eye. This talk will summarize epidemiological findings regarding the development of all the ocular components that influence the refractive state (cornea, crystalline lens, axial length) and geographic (environmental) influences.
Conflict of interest
Any post or position you hold or held paid or unpaid:
Employee of Carl Zeiss Vision International GmbH.

• 2742
What do we really mean by emmetropisation

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Summary
One of the distinctive features of refractive development is the establishment of a tight distribution of refraction by the age of 2. This can be explained by work on animal models showing that hyperopic defocus promotes, while myopic defocus slows, axial elongation, with precise compensation for the imposed refractive error. It has therefore been assumed that the end-point of human refractive development is tightly defined emmetropia, with an active mechanism for maintaining emmetropia. But in fact, human refractions generally stabilize in the mildly hyperopic range – a state which can be maintained until adult life. With educational pressures, many children become transiently emmetropic, but then progress to myopia, consistent with evidence that early emmetropia is a major risk factor for myopia. Recent work has demonstrated another control over axial elongation, based on increased release of dopamine by bright light which slows axial elongation. Refractive development in humans can be better explained if myopic defocus signals weaken after the age of 2, and once loss of lens power has slowed, the only process able to counter axial elongation associated with education is provided by the light-dopamine pathway.

• 2743
Changes in normal ocular biometry and optics with age

ROZEMA J
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Summary
Ocular biometry can vary widely between subjects of similar gender and age. The intraocular interaction to achieve a particular refraction is almost unique for each individual eye. For this reason, a single eye model cannot adequately represent the range of keratometry and axial length data (e.g. about 0.5% of the general population is represented by the Gullstrand eye). This can have practical repercussions, e.g. for IOL power calculations. Moreover, ocular biometry is known to undergo many changes with age. Such modifications are very rapid and extensive in infants, towards a more stable situation in young adults, where changes are more gradual and almost uniquely lenticular in nature. While the changes themselves have been extensively described in literature, many underlying factors remain insufficiently understood. This makes any attempt beyond descriptive modelling (e.g. forecasting refractive evolution) a very challenging proposition for now. This talk highlights observed wide variations in biometry in the general population, introduces three main types of changes with age (emmetropization, myopization and lenticular changes), and discusses how changes in biometry contribute to the known evolution of refraction.

• 2744
Age related changes of the crystalline lens

NAVARRO R
Consejo Superior de Investigaciones Científicas & Universidad de Zaragoza, Zaragoza, Spain

Summary
The crystalline lens has a double function to aid the cornea in focusing light rays on the retina and to accommodate to focus near objects. The refractive power of the lens is about half of that of the cornea, but a young lens can increase its power by more than 50%. Its gradient refractive index (GRIN) provides additional refractive power and amplitude of accommodation (AA). The optical properties of the lens change dramatically with age. The lens continues to grow throughout life (lens thickness increases about 0.024 mm/year) which has a strong impact on its optical properties. With ageing most of the GRIN tends to concentrate near the surface, which causes a decrease of both power and AA. The lens also gets stiffer with age. The maximum AA is reached early (ages 8-12 years) and then declines at a mean rate of 0.25 D/year; accommodation becomes residual after 50 years. The optical quality of the lens suffers a strong age-related deterioration: progressive lens yellowing tends to filter short wavelengths, stray light increases with age, which strongly increases the probability of cataracts. Spherical and other higher order aberrations of the lens increase so that they can duplicate their RMS value from 35 years to 75 years.

• 2745

Myopia - biological mechanisms and unresolved questions

SCHAEFFEL F

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Summary

Research in animal models has consistently demonstrated that the retina extracts magnitude and sign of defocus in the projected image. Focussing errors trigger changes in axial eye growth, initiated by the retina, to reduce these error signals. Growth control occurs at each position in the retina, but the fovea, although very important in sharp vision, covers only a small fraction of the visual field and has therefore little input. Instead, the fovea controls accommodation, shifting the image plane similarly in the center and periphery. At the end, only a complete description of the focus error signals all over the visual field and over time will finally explain the development of myopia. Myopia is tightly linked to education, with 0.5 D more myopia per year of studies. Since extensive education is mandatory in our societies, its development can only be delayed and slowed down. Three evidence-based approaches are promising at present to slow myopia progression: (1) increasing exposure to outdoor lighting, preferentially before myopia starts later at school, (2) "fooling" the retina about the true plane of focus (i.e. by multifocal contact lenses) and (3) low dose (0.01% or less) atropine eye drops.

• 2751

Corneal bacterial infections: A practical approach

GICQUEL J J
Centre Hospitalier Saint Louis / Faculté de Médecine de Poitiers, Ophthalmology, Saint Jean d'Angély, France

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

• 2752

Herpes and Zoster infections update

LABETOULLE M
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Summary
Herpes Simplex Virus (HSV) and Varicella-zoster Virus (VZV) are two leading causes of sight-threatening keratitis. Following a period of latent infection in the trigeminal ganglia, the virus can reactivate, and new viral particles finally reach the ocular tissues.
Episodes of HSV keratitis may occur spontaneously or following a triggering factor like immunosuppression (including topical steroids), topical inflammation and nerve injuries. Ocular surgery, which combines several of these factors, is a strong risk factor of HSV keratitis recurrence. In case of exposure to one of these triggering factors, prevention with oral antiviral drugs reduces the risk of relapse of HSV keratitis. To date, there is no vaccine against HSV that has proved its clinical relevance.
For VZV, the main risk factor of keratitis is the occurrence of chickenpox or herpes zoster ophthalmicus (HZO) some days to weeks before. The prescription of oral antiviral drugs at the time of cutaneous rash is efficient for reducing the risk of ocular complications of HZO. However, the most efficient way to prevent VZV-keratitis is probably to reduce the risk of chickenpox and eventually herpes zoster, by the mean of the existing vaccines dedicated to these both diseases.

• 2753

The particularities of corneal infectious diseases in children

BREMOND-GIGNAC D
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Summary
Corneal infections in children can affect subjects of all ages with a high frequency in newborns and infants. In infant, children and teenagers the most common ocular pathogens, that differ from the adult, are Haemophilus Influenzae, Staphylococcus aureus, Streptococcus pneumonia and also Moraxella species. These infections could lead to ulcers and sight-threatening complications. Infectious keratitis in children is not common but can cause a severe visual impairment if late diagnosed with delayed treatment established or with weak efficacy. In children corneal infections can be difficult to diagnose because the pathology can develop without pain. In addition, the examination may be difficult to perform. Identification of the pathogen must be performed as far as possible. The treatment should be provided earlier and aims to eliminate the bacteria, virus or fungus pathogens. Specific epidemiology of pathogens will be detailed according to age. Risks of visual impairment and amblyopia must be integrated. An update on topical antibiotics and current options will be reviewed with practical aspects, diverse clinical cases and considering quality of life of children and parents.

• 2754

New emerging treatments in severe corneal infectious diseases

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Abstract not provided

• 2761

Principles of wound healing - knowledge transfer to cornea

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Summary
The closure of both corneal and skin wounds occurs when epithelial cells migrate from the edge of the wound and re-epithelialize the injured area. Syndecan-4 (SDC4) is a heparin sulfate proteoglycan (HSPG). A natural cell migration-pathway triggered by SDC4 has been identified and proven to contribute to skin wound closure (Bass et al., Dev. Cell 2011). We have previously identified a wound-homing peptide (CARSKNKDC; dubbed CAR; Järvinen & Ruoslahti, Am. J. Pathol. 2007) that requires HSPGs for its cell-binding and penetrating activity. CAR peptide stimulates wound re-epithelialization and its cell binding and internalization are both dependent on SDC4. Its wound healing-promoting activity (stimulation of re-epithelialization) is dependent on SDC4. Thus, CAR peptide subverts normal SDC4 function to promote wound healing by enhanced re-epithelialization. CAR peptide may provide a new way of enhancing skin wound healing, and perhaps tissue regeneration in general. This therapeutic approach is dependent on the naturally occurring SDC4 dependent cell migratory pathway, which is up-regulated in skin wounds. Whether the SDC4 -cell migratory pathway is available in corneal wound healing remains to be studied and could be therapeutic.

• 2762

Inflammatory biomarkers of the tear proteome in anterior segment disease

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Summary
Ocular surface inflammation is linked to a number of adverse outcomes which vary depending on adjunct factors such as recent surgery or presence of disease. Usually the level of inflammation is thought to be important in the evaluation. However, from a clinical point of view there are limited methods of evaluating inflammation. Proteomics allows the simultaneous accurate quantification of a large number of proteins associated with inflammation using just a few microliters of tears so that individual patients can be evaluated. For example, studies have shown several members of the S100 family of proteins which are contain 2 EF hand calcium binding motifs to be upregulated in dry eye and pterygium. The S100 proteins can bind to RAGE receptors on immune cells to stimulate further inflammation. Other proteins associated with inflammation include various heat shock proteins such as HSPA8, 70 kDa protein. YWHAZ is found which is associated with cell injury and may be directly related to the type of pathology. Thus, using proteomics a more complete picture of the ocular surface inflammation can be developed and used to predict clinical outcomes.

• 2763

Cornea and lacrimal gland synergy, a corner stone for a healthy vision

MICHON F
Helsinki, Finland,

Summary
A disturbed tear film secretion results in an ocular dryness, which can induce a corneal opacification. Interestingly, few studies have correlated the cornea renewal to the LG secretion. Nonetheless, our preliminary data suggested that LG secretion changes from birth to the eyelid opening, happening two weeks after birth in mouse. We have investigated the transcriptomic signature of the LG and cornea in embryonic, postnatal (eyelid closed) and adult animals. This analysis confirmed that the LG secretes morphogenetic factors (IGF2, HGF, EGF, KGF), while not expressing the receptors. Interestingly, the cornea epithelium expresses the corresponding receptors, but not the ligands. Moreover, the secretion of these factors is peaking prior the eyelid opening, correlating to an intense proliferation in the cornea epithelium. Moreover, the changes of secreted factors shortly after cornea wounding demonstrates a direct regulatory loop between the two organs modulating the tear composition. Our data provide a new research avenue for the development of tear film biomimetic enhancing the corneal healing.

• 2764

Proteomics as a tool for stem cell research in the anterior segment of eye

MIKHAILOVA A
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Summary
Limbal epithelial stem cells (LESCs) are essential for corneal transparency and normal vision, as they are responsible for renewing the corneal epithelium. Damage or loss of LESCs may cause the ocular surface to become opaque and vascularized. Patients suffering from such severe ocular surface disorders do not benefit from corneal transplantation alone, because it does not replace the damaged stem cells.
LESCs derived from human pluripotent stem cells (hPSCs) offer a novel cell-based approach for ocular surface reconstruction. However, critical evaluation of these cells is crucial before considering clinical applications. Proteomics can help verify the authenticity of hPSC-derived cells on a large scale.
This talk will discuss proteomics as a tool for stem cell research, focusing on the ocular surface. As an example, a study using proteomics to compare native corneal cells at different maturity levels and LESCs derived from hPSCs in feeder-free and serum-free conditions will be presented.

• 2771

Show me the money - funding opportunities for fellowships

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(2) University Hospitals Leuven, Ophthalmology, Leuven, Belgium

Summary
In a time when a fellowship can make a difference in a young ophthalmologist's curriculum, it is vital to know where to look for funding and plan ahead to be eligible for the opportunities.
This talk will focus on potential sources for fellowship funding, providing links and information to attendees. It will cover both national and international funding sources, as well as an overview of specific funding for certain fields of Ophthalmology. Both research and clinical fellowships will be included in this overview.
In the end, attendees are supposed to know where and when to look for funding opportunities.

• 2772

Choosing your fellowship and getting the most out of it - advice from Fellows

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Summary
Choosing a place for fellowship can be challenging. Every young ophthalmologist looks for a rewarding experience, trying to improve his/her knowledge in a specific area. Achieving this might be dependent on multiple factors. First, it's important to do some research about places where our area of interest can be mastered. After this, comes the "geographic" decision. Time away from family and friends is important for most people, and so is being able to visit them. Besides this, it's crucial to have at least a basic knowledge of the main language that will be spoken. English is widely spoken in most fellowship opportunities, but in my case it was of master importance to be fluent in the local language. Another factor to consider is the size of the hospital/clinic. Is it better to choose a big center with a lot of other residents or is it worth to choose a one-on-one experience, where you can sit side by side in an everyday basis with your tutor? For me, this second option worked perfectly and I will explain why. According to my expectations and personality, all the objectives were achieved. I'll try to explain this experience in every important detail and will also discuss some pros and cons of different types of opportunities.

• 2773

Choosing your fellowship and getting the most out of it - advice from Fellows

LUKIC M
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Summary
The aim of this lecture is to present young ophthalmologists the process of getting fellowship at Moorfields Eye Hospital in London, UK. The presentation will contain important facts and advice for application process, interview and opportunities when someone become a fellow. Likewise, it will be mentioned the procedure and requirements to get GMC registration and licence to practice which is mandatory to be able to apply for any fellowship in the UK and eventually to work in the UK as a medical doctor. Then, I will show the recent audit results about fellows' opinion on MR fellowship at Moorfields Eye Hospital and show a few testimonials from my colleagues fellows. Lastly, I would like to give some additional information about finding out the accommodation and general costs of living in London which is important before someone decides to move in to London.

• 2781

Novel genes associated with isolated optic nerve hypoplasia in 6 family trios - a clinical and exome study

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(5) APHP Banque d'ADN - Hôpital Robert Debre, Banque d'ADN, PARIS, France
(6) CEPH- Hôpital Saint Louis, Bioinformatique, Paris, France
(7) Banque de Cellules Hôpital Cochin, Banque de Cellules, Paris, France

Purpose
Optic nerve hypoplasia (ONH) is a rare blinding malformation,ONH is often syndromic with MRI pituitary anomalies. We explore genetic causes of isolated ONH
Methods
Probands (2F/4M) 0.5-6 yrs with normal pituitary MRI were enrolled after consent with Pediatric, dysmorphologic and ophthalmologic endocrine examinations SNP aCGH, WES & Sanger validation sequencing. Ophth. exam: VEP,ERG,fundoscopy, color & acuity testing. Male patients tested for HESX. DNA extracted from lymphoblastoid lines or blood. DNA sequenced 30X in > 92% on Illumina platform; QC used Sam, Picard, Bed tools, variant call GATK, annotation snpEff/snpSift; filter using Autosomal Dominant hypothesis, absence in 1k, 65k 19 genomes,Exac databases. Variants present in subjects but not parents were selected and tested using polyphen2, Sift and mutation taster. 2nd approach for variant filtering using ANOVAR yielded 197 variants with strong deleterious effect; variants present in at least 2 pedigrees were then prioritized
Results
Patients followed 2-15 yrs had normal intelligence, eye examination showed normal ERG with abnormal VEP, dyschromatopsia VA ~20/200. 3 had learning difficulties, One F severe dyspraxia, and one M GH, Cortisol testosterone deficit and micropenis. 3 had sleeping disorders treated with melatonin. No HESX mutations were identified. All parents were healthy but 3 fathers were unavailable for blood sampling.SNP array CGH revealed a paternally inherited single 410,4 kb deletion of the 2p26.1 VRK2 gene described in complex intellectual disability. 5 genes showed deleterious missense mutations identified and being confirmed by Sanger sequencing
Conclusions
A 2p16.1 inherited deletion variant of unknown significance was identified on array CGH. WES analysis identified 5 candidate genes confirmed by Sanger sequencing which will need confirmation in a different dataset

• 2782

The RaDiCo AC-OEIL : a French rare disease cohort dedicated to ocular developmental anomalies in children

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(5) French rare diseases networks, Genetics and ophthalmology, Strasbourg & Dijon, France

Purpose
Ocular development may be disrupted at various stages, leading to a wide range of congenital ocular dysgenesis. Incidence of such defects is estimated to 1-2 in 10.000. They may be isolated or associated with extra-ocular malformations. In addition, psychomotor delay may be present, secondary to the sensory involvement or linked to a cerebral developmental anomaly leading to intellectual disability. Visual outcome, frequency of extra-ocular features and psychomotor delay are still poorly known. Given the rarity of these malformations, available data concern very heterogeneous groups of patients, which make their utility limited in clinical practice. It is thus difficult to anticipate visual and neurologic outcomes when a congenital ocular developmental anomaly is diagnosed.
Methods
RaDiCo-AC-CEIL is an observational study launched in May 2017 sponsored by Inserm, relying on the French Rare Diseases healthcare networks SENSGENE and ANDDI-Rare for patients' enrolment, and supported by patients 'associations. Patients will have a maximum of three clinical examinations (at time of diagnosis, at 5-7-year-old, and at 9-11-year-old) during which visual, neuro-developmental and quality-of-life data will be collected in addition to the usual clinical data, using REDCap EDC system. It will extend to other EU countries once regulatory requirements will be fulfilled.
Results
About 800 patients are expected to be enrolled during a recruitment period of 10 years.
Conclusions
RaDiCo-AC-CEIL will improve i) our knowledge on the natural history of ocular developmental defects in children ii) the identification of prognostic factors for ocular and neurodevelopmental outcome iii) genetics counselling and iv) the design of optimised management protocols. This project will also pave the way to clinical and basic research in a homogeneous cohort.

• 2783

Mutation in the Crybb1 gene encoding beta-B1-crystallin leads to recessive cataracts in the mouse

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Purpose
Congenital cataracts are caused by mutations in various genes, and CRYBB1 is one of them. Aim of the study was to create a corresponding mouse model for a cataract-causing mutation in Crybb1.
Methods
The ENU-sperm archive of F1 mouse mutants (https://www.helmholtz-muenchen.de/ieg/services/scientific-resources/index.html) was searched for mutations in Crybb1. After selection of an appropriate mutation the corresponding mouse mutant was recovered after in-vitro fertilization.
Results
We recently identified a mutation in exon 6 of CRYBB1 (c.613delC; p.Q205Sfs4*) as causative for congenital dominant cataracts in an Indian family. Correspondingly, we established a mouse mutant line, which affects the exon 5 of the Crybb1 gene (c.500A->T; p.D167V). The mouse mutation affects the 3rd Greek Key motif; correspondingly, the size of the alpha-helical region and the size of several beta-sheets might be modified in the mutant protein. PolyPhen-2 predicted this mutation as "possibly damaging" with a score of 0.731. This mutation leads to a recessive form of cataracts with clear lenses in heterozygotes, although Crybb1 is expressed in mouse lenses from E12.5 onwards. Similar to other beta-crystallins, Crybb1 is also expressed in the brain, which might lead to additional neuronal changes and might explain the involvement of Crybb1 in association with schizophrenia and stress (Spadaro PA et al., Biol. Psychiatr. 2015;78: 848-859).
Conclusions
In humans, several cataract-causing mutations have been identified - most of them leading to dominant cataracts, and only a few of these mutations have been shown to cause a recessive way of inheritance. Here we present the first Crybb1 mouse mutant line suffering from a recessive congenital cataract.

• 2784

Segregation of novel p.(Ser270Tyr) MAF mutation and p.(Tyr56*) CRYGD variant in a family with dominantly inherited congenital cataracts

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Purpose
To identify the molecular genetic cause in a three generation family with the occurrence of congenital cataracts, variably associated with iris colobomata and microcornea.
Methods
Whole-exome sequencing was performed in three affected family members, one unaffected first degree relative, and one spouse. Sequence variants previously reported as disease-causing, and novel sequence variants within genes listed in CatMap (http://cat-map.wustl.edu/) were given a priority for further evaluation. Verification of possibly pathogenic sequence variants was performed by conventional Sanger sequencing.
Results
Sequence variant c.168C>G; p.(Tyr56*) in CRYGD, previously reported as pathogenic, and a novel mutation c.809C>A; p.(Ser270Tyr) in MAF, were identified in two affected family members; the grandmother, and half-brother of the proband. The proband inherited only the MAF mutation, whereas her clinically unaffected sister had the CRYGD change. In silico analysis supported a pathogenic role of p.(Ser270Tyr) in MAF, which was absent from publicly available whole-exome datasets, and 1,161 Czech individuals. The frequency of CRYGD p.(Tyr56*) in the ExAC dataset was higher than the estimated incidence of congenital cataract in the general population.
Conclusions
Our study highlights that patients with genetically heterogeneous conditions may exhibit rare variants in more than one disease-associated gene, warranting caution with data interpretation, and supporting parallel screening of all genes known to harbour pathogenic mutations for a given phenotype. The pathogenicity of sequence variants previously reported as cataract-causing may require re-assessment in light of recently released datasets of human genomic variation.
Supported by AZV 17-30500A.

• 2785

Ocular traumas in the Finnish elderly- Helsinki Ocular Trauma (HOT) Study

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Purpose
To describe epidemiology, causes, treatments, and outcomes of all ocular injuries in southern Finland among people aged 61 and older.
Methods
All new ocular trauma patients, admitted to the Helsinki University Eye Hospital, during one year in 2011-2012. The data was from hospital records and prospectively from patient questionnaires. The follow-up time was three months.
Results
The incidence for ocular injuries among the elderly was 38/100,000/year. From 118 patients 69% were men. The mean age was 70.9 years old (median 67). Hospitalization rate was 14%. Injury types were minor traumas (48%), contusions (22%), chemical injuries (10%), eyelid wounds (8%), open globe injuries (OGI) (7%), and orbital fractures (5%). The injuries occurred at home (58%), in institutions (12%), and in other public places (12%). The main causes of ocular injury were falls (22%), sticks (19%), superficial foreign bodies (18%), and chemicals (12%). All OGI and 88% of contusions needed a life-long follow-up. A permanent visual or functional impairment occurred in 15 (13%) patients. Of these 53% were OGI, 40% contusions, and 7% chemical injuries. The causes of permanent injuries were falls (7 cases, 47%), work tools, sports equipment, sticks, chemicals, and eyeglasses.
Conclusions
Minor trauma was the most frequent type, and home was the most common place of eye injuries. Falls were the most frequent and serious cause, but behavioral causes (alcohol consumption and assaults) were not significant. Preventive measures should be directed towards the main identified causes and risk factors of the eye injuries in the elderly.

• 2786

Directed migration of retinal astrocytes by PDGF signaling

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Purpose
Proper patterning of astrocytes is crucial for retinal angiogenesis in both rodents and human. Platelet-derived growth factor (PDGF) is one of the key regulators of cell migration, but distinctive downstream pathways have been implicated in a variety of cell types. Herein we investigated the detailed mechanism of PDGFA-directed astrocyte migration in early postnatal mouse retina.
Methods
Transgenic mice with glia-specific deletion of PDGFRα and multiple potential downstream effectors of PDGF signaling pathway are generated. Perinatal astrocytes and retinal vasculature are evaluated by whole mount IHC.
Results
Astrocyte migration and retinal angiogenesis are severely impaired in knockout mice of PDGFRα. This is phenocopied by mutations in PI3K catalytic subunits p110αβ, as well as in mutations of PI3K binding site in PDGFRα. Rac/Rap mediated cytoskeleton rearrangement is also imperative for the patterning of astrocytic network. On the other hand, disruption of mTOR signaling by knocking out binding partner Raptor or Rictor had no effect on astrocyte motility. PLCγ pathway, which is essential for PDGF chemotaxis in mesenchymal cells, is also dispensable for astrocyte migration.
Conclusions
This study demonstrated that PDGFA-directed astrocyte migration is mediated through PI3K and Rac/Rap signaling, but not PLCγ or Akt/mTOR pathway. These findings add mechanistic insight into cell type-specific regulation of migration by PDGF.

• 2787

Genetic evidence for the role of ultraviolet radiation in the pathogenesis of uveal melanoma

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Purpose
Recent advances in the understanding and treatments of metastatic cutaneous melanoma (CM) have not led to parallel improvements in the care of metastatic uveal melanoma (UM), and consequently, the two conditions are now often viewed as separate entities. One possible difference is the aetiological role of ultraviolet (UV) radiation, which although well-established in CM, remains uncertain in UM. This study hypothesised that UV radiation is a pathogenic factor in UM development, evidenced by genetic changes consistent with UV-related damage in UM.
Methods
We analysed data from 993 UM patient samples and 11803 CM patient samples available from the Catalogue of Somatic Mutations in Cancer (COSMIC) as well as 80 UM patient samples and 343 CM patient samples from the Broad Institute GDAC FireBrowse. UM samples were probed to identify the most frequently mutated genes, mutation types and specific nucleotide substitutions. Somatic mutation data was then cross-correlated with CM samples from COSMIC and Broad Institute GDAC FireBrowse.
Results
The most common overlapping mutated genes were BRAF, PTEN, CDKN2A, TERT, NRAS, TP53 and ARID2, with four shared point mutations in BRAF (V600E (1799T>A)), NRAS (Q61R (182A>G)) and TP53 (R273C (817C>T)), R248Q (743G>A)). These gene mutations were found to be strongly associated with UV-related damage in previous scientific reports. The proportion of samples with C>T substitutions (a marker of UV-related damage) were similar between UM and CM on both DNA strands (20.35% vs 20.05%) and coding strand (11.3% vs 15.7%).
Conclusions
These findings support the hypothesis that the pathogenesis of UM is more dependent on UV radiation than previously thought.

• 2788

Recurrent corneal erosions dystrophy (ERED) in a Finnish family is caused by a COL17A1 splice-altering mutation

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Purpose
The epithelial recurrent erosion dystrophy (ERED) is a rare autosomal dominant corneal disease. Recently, mutations in collagen type XVII, alpha 1 (COL17A1) gene have been identified as the cause of ERED. Here we report a Finnish family with recurrent erosions with dominant inheritance pattern. We performed COL17A1 candidate gene sequencing.
Methods
Five affected and five unaffected family members underwent standard ophthalmological examination, corneal topography, anterior segment optical coherence tomography and in vivo confocal microscopy. Next-generation exome sequencing of peripheral blood was made in two of the affected individuals to identify mutations in the large COL17A1 gene. Sanger sequencing was used to verify the presence of the identified variant in the other family members.
Results
Affected patients reported recurrent corneal erosions beginning at the age of 4-6 years. The frequency of erosions decreased in adult age. Corneal scarring and anterior stromal opacities were observed. The visual acuity slowly deteriorated. Exome-sequencing revealed a synonymous splice-altering variant c.3156C>T in COL17A1 in two affected patients. Sanger sequencing confirmed the presence of the same variant in four affected family members and its absence from two unaffected ones. The variant was not present in the Sequencing Initiative Suomi (SISu) database consisting of 10,490 Finns.
Conclusions
The variant c.3156C>T in COL17A1 is reported recently in five English, American, New Zealand, and Tasmanian families with ERED. Our finding of the same synonymous variant in yet another population strengthens the evidence this variant is a frequent cause of ERED.

• 2831

Objective assessment of the superficial ocular surface and tear film in dry eye

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Abstract not provided

• 2832

Bioprotection in dry eye: pre-clinical evidences

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Abstract not provided

• 2833

The effects of Treahalose/sodium hyaluronate eyedrops on biomarkers

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Abstract not provided

EVER 2017
FRIDAY
SEPT 29

• 3111

Tips and tricks in open globe injuries (management of intraocular foreign bodies)

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Summary
Traumatic open globe injuries with intraocular foreign bodies (IOFBs) may result in severe visual loss depending on a number of factors including elevated risk for endophthalmitis, toxicity to the IOFB material, and postoperative proliferative vitreoretinopathy. Surgical removal of an IOFB is perhaps the most unpredictable surgery, especially in the presence of media haze, requiring intense preoperative workup and patient counseling. There is still significant controversy in the management of IOFBs, particularly the timing and method of surgery. The purpose of this topic is to familiarize clinicians with the recent advances in diagnosis and management of such injuries.

• 3112

Tips and tricks in pediatric retina surgery

OZDEK S O
Gazi University- School of Medicine, Ophthalmology Department, Ankara, Turkey

Summary
Pediatric vitreoretinal surgery has a different philosophy from adult surgery. It has its own rules, own complications, does not forgive faults, does not accept apologies. The eye is very small, there is a narrow space for maneuvers (15-19mm). Lens is relatively large, vitreous-retina relation is different, pars plana has not developed, sclera is thin and elastic. Posterior hyaloid is tightly attached. PFCL and Silicon oil is rarely used. They do not obey the head positioning! Retinal breaks usually ends up with surgical failure. PVR is frequent and severe! There is an additional amblyopia problem. We will talk about the details of these problems and the solution of them in ROP, PFV, Coats and FEVR cases.
Conflict of interest
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
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Novartis, Bayer

• 3113

Tips and tricks in macula surgery

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Summary
The presentation will focus on the following macula diseases: epiretinal membranes, lamellar macular hole, full thickness macular hole, haemmorhagic AMD, diabetic macular oedema.
All presented cases will be illustrated with spectral domain or swept source OCT or swept source OCT angiography.
In epiretinal membranes and lamellar macular holes a guide to select proper cases for surgery will be presented. In full thickness macular holes the inverted ILM flap techniqe will be discussed. In this technique the ILM is not completely peeled, but a small fragement is left in order to cover the macular hole. Repeated surgery with autologous ILM flap transplants will follow.
In heammorhagic AMD subretinal rTPA injections will be presented with results of following long- term anti- VEGF treatment.
In diabetic macular oedema the surgical tip would be ILM peeling followed by subretinal fluid injection.
Conflict of interest
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• 3114

Retinectomy and silicone oil in PVR surgery-pearls and tricks

ACAR N
ISTANBUL, Turkey,

Summary
TITLE: " Retinectomy and Silicone oil in PVR Surgery-Pearls and Tricks"
Appropriate surgical technique is the most important factor for the anatomical success in the management of retinal detachment (RD) with PVR. Retinectomies are frequently required in detached eyes complicated by severe PVR. Knowing when and how to perform a retinectomy is necessary for a vitreoretinal surgeon and this talk will cover important steps in this surgical maneuver.
Silicone oil endotamponade is also frequently preferred in PVR surgery. How to handle silicone oil during injection and its removal is important to avoid its major complications. Pearls related to these steps as well as some important properties of silicone oils will be discussed in this talk.

• 3115

Advanced vitreoretinal surgery

KOCH P

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Summary

Title: Tips and tricks to manage complications in retinal detachment surgery

Introduction: Retinal detachment surgery can remain a tricky surgery that associates with different kind of complications. It is interesting to observe that our success rate did not increase so much in the literature since the 1940's, remaining between 80 and 90% as a whole.

Methods: We will therefore try to understand why complications arises in retinal detachment to figure out how to reduce it and thus increase our success rate. Since glaucomatous problems are a relevant complication of retinal detachment treated by silicon oil, we will identify how to reduce intra-ocular pressure problems related to silicon oil use. In the same way, with the advent of heavy liquids like PFCL to stabilize the retina during surgery, we will try to understand how to work properly with PFCL or fix related complications. In a final step, we will examine the causes of macular pucker and recurrences of retinal detachment to enhance our success rate through different methods.

Conclusion:

This session will be organized around theories commonly accepted in the literature and multiple videos to demonstrate tips and tricks to manage complications in retinal detachment surgery.

• 3121

Automatic tool for quantification of nerve fibres in corneal confocal microscopy images

MALIK R
Doha, Qatar,

Summary

Failure after failure of phase 3 clinical trials in diabetic neuropathy has led to the realisation that potentially effective treatments have failed because of inadequate end-points in clinical trials. Our pioneering studies showed that corneal confocal microscopy (CCM) had excellent diagnostic potential in diabetic somatic and autonomic neuropathy. We and others subsequently used CCM to diagnose peripheral neuropathies in obesity, impaired glucose tolerance, hereditary neuropathy (CMT1A, Friedreich's ataxia), Fabry's disease, amyloid neuropathy, CIDP, HIV etc. Of significant potential as a surrogate end-point, we have shown that CCM detects nerve fibre regeneration within 6 months of pancreas transplantation in diabetic patients and after 24 months of an improvement in glycaemic control, blood pressure and lipids, continuous subcutaneous insulin infusion and after bariatric surgery. We have shown nerve repair in several phase 2b trials of ARA290, a peptide derivative of erythropoietin, in patients with sarcoid neuropathy and diabetic neuropathy. We have also shown that CCM detects axonal pathology which relates to the severity of neurological deficits in patients with Parkinson's disease, multiple sclerosis and dementia.

• 3122

Mosaicking the subbasal nerve plexus

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(2) *University of Rostock, Department of Ophthalmology, Rostock, Germany*

Summary

Corneal confocal microscopy (CCM) has been established as a noninvasive, in vivo imaging technology that provides high-resolution images of the corneal tissue layers at a cellular level. In particular, several research groups focus on the nerve fiber bundles constituting the subbasal nerve plexus (SNP). The ability to visualize - and quantify - morphological alterations of the SNP provides a new and potentially sensitive diagnostic approach for peripheral neuropathies, e.g. associated with diabetes. However, because of the small field of view of current CCM systems (approx. 0.16 mm^2) and the locally inhomogeneous distribution of the subbasal nerve structures, a single image does not reliably reflect the condition of the SNP. To address this issue, we present a highly automated and integrated system that facilitates the imaging of an extended contiguous SNP area in a short recording time by guiding the gaze direction of the patient with a computer-controlled moving fixation target. The system achieves growth rates of the scanned area of approximately 0.16 mm^2 per second. Following the image acquisition process, a high-quality mosaic image of the scanned area is computed using specialized image processing software.

• 3123

Corneal nerves as a biomarker of peripheral neuropathy : the example of transthyretin amyloidosis

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Summary

Transthyretin amyloidosis (TTR-A) is a rare autosomic disease associated with severe sensorimotor and autonomic neuropathy. A practical and objective method for the clinical evaluation of TTR-A neuropathy is needed to improve the management of this disease.

We conducted a study on 15 patients and 15 controls to determine the correlations of sensorimotor and autonomic neuropathy with corneal nerve parameters in TTR-A patients. We found that corneal nerve fiber length (CNFL) measured using IVCM was inversely correlated with the severity of autonomic and sensorimotor neuropathy, assessed both with clinical and paraclinical tests, including intra-epidermal nerve length in skin biopsy.

In these 15 subjects, IVCM measurement permitted rapid, non-invasive evaluation of small-fiber alterations in TTR-A patients and could be used to assess neuropathy. CNFL could be measured in all patients, thus avoiding the floor effect seen with other neuropathy measures. Through the example of this rare disease, our study illustrates the emerging idea that corneal nerve parameters assessed with IVCM could become a potent surrogate biomarker for peripheral neuropathy.

• 3124

The corneal nerves in glaucoma and ocular surface diseases

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Summary

In addition to their important sensory function, corneal nerves provide protective and trophic functions and also regulate corneal epithelial integrity, proliferation and wound healing. The well-defined in vivo confocal microscopy (IVCM) appearance of the subbasal corneal nerves has facilitated their quantitative in vivo analysis in ocular surface diseases. Although patients with dry eyes and patients treated for glaucoma experience similar ocular surface signs and symptoms, different correlations between corneal sensation and nerve morphology were observed in these two groups of patients. The relationship between corneal nerve function and structure remains complex, and nerve alteration and/or dysfunction could be different among different ocular surface diseases. Improvements in IVCM image acquisition and analysis will be an important step to further evaluate the role of corneal nerves in physiological and pathological ocular surface conditions.

Conflict of interest
Any Lecture fee paid or payable to you or your department:
Alcon, Allergan, Théa, Santen.

• 3131

OCT and OCTA: new technology, new terminology

AMBRESIN A
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Summary
This topic will introduce the course « current contribution of OCT angiography in clinical practice ». OCT angiography is a recent device that has already reached a wide acceptance among ophthalmologists in real life practice. Nevertheless, the images interpretation often remains a challenge for practioners. A overview about the OCT angiography technology will be given and the new terminology to interpret an OCTA will be exposed. Clinical examples will be presented using the suitable terminology.

• 3132

The role of OCT algorithms and OCT A in glaucoma care

MANSOURI K
Lausanne, Switzerland,

Summary
Background: The role of blood flow in the pathogenesis of glaucoma is not well understood.
Objective: To discuss applications of OCTA in glaucoma diagnosis and management.
Methods: Review of literature and presentation of ongoing clinical trials.
Results: More than 50 peer-reviewed publications on OCTA in glaucoma are available. Data demonstrate good reproducibility and repeatability of OCTA measurements in glaucoma patients. Good correlation to structural and functional measures of glaucoma have also been found. Preliminary data have not found a demonstrated effect of IOP-reduction of OCTA-derived vessel density measurements. At present, studies on the long-term role of OCTA in glaucoma evaluation are ongoing.
Conclusions: OCTA measurements of vessel density in glaucoma are reliable. Good correlation to structure-function has been demonstrated. Available data suggest a role of OCTA for better understanding of the pathophysiological processes in glaucoma. It is unclear, at present, how this technology can be integrated into the long-term management of glaucoma patients.
Conflict of interest
Any consultancy arrangements or agreements:
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• 3133

OCT and vitreomacular interface

POURNARAS J A
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Summary
Nowdays, OCT examination is currently available and offers many insights for the management of vitreomacular interface disorders. We will review carefully the natural history of these disorders nicely described by OCT images. Furthermore, mainly after surgery, this examination play an important role in the followup of those patients and will be presented.
At the first visit, correct recognition of the alterations of vitreomacular disorders helps clinicians to predict the visual prognosis of the patients.

• 3134

OCT and retinal ganglion cell layer

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

Summary
Vision is highly dependent on both retinal ganglion cells (RGC) and their axons. Vision salvation depends on the prevention of RGC loss, and the time window to initiate a neuroprotective therapy after injury is not well defined in humans.
Recent developments in both OCT technology and software have allowed a precise and reproducible assessment of the RGC layer to be possible in vivo in humans. The goals of this presentation are two-fold : first, to review the mechanisms of both axonal and RGC degeneration; second, to discuss the time-course of RGC loss after either antechiasmal or retrogeniculate lesions.
At the end of the talk, participants should understand the mechanisms and time-course of RGC and axonal loss.

• 3135

OCT in age related macular degeneration

MANTEL I
Jules-Gonin Eye Hospital, Lausanne, Switzerland

Summary
This part of the special interest symposium gives an overview about the features on OCT that can be seen in the context of age-related macular degeneration (AMD). The role of OCT in diagnosis, treatment guidance, and the functional relevance are the topics approached. In addition, the signs that need to be distinguished in order to avoid misleading interpretation are presented. The overview focuses on topics with clinical relevance, using numerous imaging examples.

• 3136

OCT in retinal and choroidal inflammatory disease

VAUDAUX J
RétinElysée, Lausanne, Switzerland

Summary
OCT angiography (OCT-A) is a novel method of retinal imaging enhancing visualization of retinal and choroidal vascular components. OCT-A clinical applications are increasingly described in various retinal and choroidal diseases such as diabetes, AMD and vascular occlusive conditions. Its use in retinal and choroidal inflammatory diseases begins to be acknowledged, but clinical descriptions remain few in the literature. OCT-A allows for more detailed analysis of normal retinal vascular networks and pathological conditions of the retina and choroids, particularly when neovascularization is suspected. It may contribute to a better understanding of the pathogenesis of certain retinal and choroidal inflammatory conditions, and may turn out to be a very useful tool in the follow up and monitoring of therapy. However, additional studies and experience will be required to further describe the fundamental semiology of OCT-A in retinal and choroidal inflammatoy diseases.

• 3141

Activity in eye surface sensory neurons is disturbed by inflammation, and vice versa

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Instituto de Neurociencias- UMH-CSIC, Ocular Neurobiology, San Juan de Alicante, Spain

Summary
Ocular pain results from noxious stimulation of peripheral axons of functionally heterogeneous (Mechanonociceptors, polymodal nociceptors, and cold thermoreceptors) trigeminal ganglion neurons whose sensitivity to different stimulating agents depends on the expression of specific classes of membrane channels, evoking also different pain sensations.
Inflammatory mediators increase the excitability (sensitization) of ocular polymodal nociceptors, enhancing pain sensations. In turn, excited polymodal nociceptors release locally neuropeptides, contributing to local inflammatory reaction (neurogenic inflammation). However, inflammatory mediators reduce the excitability of cold thermoreceptors.
Regenerating nerve terminals damaged by ocular surgery, trauma, infections or systemic metabolic diseases, develop spontaneous activity and abnormal responses to natural stimulation, inducing changes in the experienced sensations (dysesthesia, neuropathic pain), and disturbances in tearing, blinking and ocular surface trophism. Besides, ocular tissues provide molecular signals that increase nerve regeneration.
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• 3142

Ocular surface inflammation, nerves and brain: dangerous interactions?

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Summary
Sensory nerves have been typically studied for their sensory functions. It is now clear, however, that in the cornea they are relevant inflammatory modulators. Specifically, functional activation, or, on the other hand, disruption of corneal nerves is associated with highly prevalent ocular disorders, including infectious keratitis, and dry eye disease. Although the modulatory activity of nerves on inflammation has been demonstrated in peripheral tissues, it is not clear whether peripheral disruption of nerves in the cornea could induce modifications also in the central nervous system. In order to test this hypothesis, we have used a well-known animal model of ocular surface injury. Then, we have quantified the inflammatory response, with in vivo magnetic resonance imaging and ex vivo, in the cornea and in the trigeminal ganglion. As a result, we observed increased leukocyte infiltration following ocular surface injury. Pro-inflammatory cytokines IL1-beta, TNF-alpha and VEGF were also increased. Interestingly, inflammatory cytokine expression were also augmented in the trigeminal ganglion contralateral to the damaged cornea. Our findings support involvement of central nervous system following acute injury to the ocular surface.

• 3143

Novel concepts in corneal reconstruction

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(2) *Friedrich-Alexander-University Erlangen-Nürnberg, Department of Polymer Physics and Processing, Erlangen, Germany*

Summary
This presentation will present new approaches regarding biomaterials for ocular surface reconstruction.

• 3144

Nanoparticle eye drops: A new generation of corticosteroid eye drops

STEFANSSON E
University of Iceland, Ophthalmology, Reykjavik, Iceland

Summary
Nanotechnology solves the main obstacles in topical drug delivery. Nanotechnology provides increased solubility of lipophilic molecules in tear fluid and sustained release for several hours.
Cyclodextrin nanoparticles containing dexamethasone increase solubility of dexamethasone in tear fluid 30 fold and the drug stays in tear film for 6 hours compared with minutes for conventional eye drops. The high concentration gradient from tear film into eye wall creates a flux which is active for many hours following eye drop application . This delivers approximately 10 times more drug into the eye and reaches the posterior segment in significant concentration. At the same time relatively less drug is absorbed systemically.
Several clinical trials have demonstrated the efficacy of the cyclodextrin nanoparticle platform both for posterior and anterior segment use.
Two clinical trials in 41 patients have shown significant improvement in visual acuity and retinal structure in diabetic macular edema. Two reports show compelling effect on intermediate/posterior uveitis with cystoid macular edema. Once a day treatment following cataract surgery is effective and the dexamethasone nanoparticle eye drops can replace mitomycin C in trabeculectomy.
Conflict of interest
Any Stocks or shares held by you or an immediate relative:
ES is co-founder and share holder in Oculis ehf, which developes nanotechnology eye drops.

• 3145

The role of IL-6 and IL-6-blockade in the pathogenesis and treatment of uveitic macular edema

MESQUIDA M

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Summary

Macular edema (ME) is a leading cause of visual loss in uveitis patients. The pathogenesis of uveitic ME includes disruption of tight junction proteins and subsequent breakdown of the blood-retinal barrier (BRB) that leads to accumulation of fluid within the macular retina. IL-6 is a pro-inflammatory cytokine that has been implicated in uveitic ME. Such a notion is supported by clinical cohort studies showing that IL-6R blockade is beneficial in the treatment of uveitic ME. After studying the clinical efficacy of IL-6 inhibition in uveitis patients, our group aimed to interrogate the effect of IL-6 and its blockade with tocilizumab (TCZ) on the barrier properties of an in vitro model of the inner and outer BRB. Our preliminary in vitro data support the hypothesis that IL-6 disrupts the BRB and contributes to the pathogenesis of ME. Indeed, IL-6-induced disrupted ZO-1 expression was accompanied by an increase in paracellular permeability, and decreased transepitelial electrical resistance (TEER) of ARPE-19 and human retinal microvascular endotelial cell (HRMEC) monolayers, whereas TCZ-treated cells could restore IL-6-induced barrier disruption.

Course: EOVS/MBGE - Structure and function in retinal disease; the role of ISCEV standard electrophysiology (ISCEV, the international society for clinical electrophysiology of vision)

• 3151

An introduction to the tests and clinical interpretation

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

Summary
This lecture will introduce the standard tests used in routine electrophysiological practice, namely full-field, pattern and multifocal electroretinography, and electro-oculography. Although the Course will concentrate on disorders of retinal function, the cortical visual evoked potential will also be briefly addressed. The origins of the signals will be discussed and common disorders used to illustrate the principles of clinical interpretation ie the separation of rod and cone system function; localisation of disease either to photoreceptors or inner retina; and the distinction between localised macular disease and generalised retinal dysfunction, always relating the nature of the electrophysiological abnormalities to the underlying pathophysiology.

• 3152

Inherited retinal disease

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Abstract not provided

• 3153

Acquired retinal disease

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Summary
This lecture will address the role of electrophysiological testing in the diagnosis and management of acquired retinal disease. Topics will include toxic, vascular, inflammatory and autoimmune disorders. The functional data provided by electrophysiology will be combined with the structural data from various imaging modalities to show that the optimal management of the patient requires knowledge both of structure and function.

• 3154

Paediatric applications

THOMPSON D
Great Ormond Street Hospital for Children, Clinical and Academic Department of Ophthalmology, London, United Kingdom

Summary
The International Society for Clinical Visual Electrophysiology of Vision, [ISCEV], publishes standards for performing five clinical visual electrophysiology tests; ffERG, mfERG, PERG, VEP and EOG, (www.ISCEV.org/standards). Older and co-operative children tolerate these adult standard protocols well. Less compliant, younger infants, children with systemic as well as ocular disease or those with learning difficulties can benefit from adaptations that account of visual system maturation, make the test time shorter and the test experience less stressful. This talk will describe the key maturational changes and their impact on ERGs and VEP waveforms.
Ways of combining and modifying tests for alert infants will be described that account for visual pathway development and limited tolerance. These will include the effects of anaesthesia, choice of electrodes and stimulation techniques. Case examples will be presented to show how visual electrophysiology maybe used to diagnose retinal dysfunction and to monitor visual pathway dysfunction in children.

• 3161

How to handle the posterior lens capsule in children

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Summary

One of the multiple challenges posed by pediatric cataract surgery relates to the special management of the posterior capsule (PC).

The risk of PC opacification is much higher in children, nearing 100% in the course of a few months with the standard techniques and intraocular lenses (IOL), even with a thorough capsular bag polishing. As the performance of a Nd:YAG laser capsulotomy can be impractical in children, an intraoperative solution is advisable. This normally involves a posterior capsulorhexis, with or without anterior vitrectomy, and either with a standard IOL or a special design such as the bag-in-the-lens concept or using techniques as posterior capture of the optic.

Pediatric cataracts frequently include special features as in opacities a the PC level, which can range from cellular to fibrotic, with different degrees in the maturity of fibrous membranes. In some cases as with posterior polar cataracts there may be an extreme weakness or absence of the central PC. Other situations may involve additional materials as in persistence of anterior hyperplastic primary vitreous.

This presentation reviews the decision process, surgical options, and possible risks involved in dealing with the PC in pediatric cataract surgery.

• 3162

Anterior vitreo-lenticular interface in children

TASSIGNON M J
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Summary

To demonstrate that developmental cataract involves more than opacification of the lens: the anterior vitreo-lenticular interface plays an important role in the surgical approach

All babies and children operated for congenital cataract since 2004 using the bag-in-the-lens technique, which requires both anterior and posterior capsulorhexis, independently of the presence of persistant hyperplastic primary vitreous or fetal vasculature

By reviewing the surgical video's the relationship between anterior hyaloid and posterior capsule, defining Berger's space, shows a large variety of anatomical particularities. It is possible to carefully dissect these structures in an attempt to reduce anterior vitrectomy to a minimum. Bridges between anterior hyaloid and posterior capsule can easily be ruptured by ocular viscoelastic dissection

Better knowledge of the anterior vitreo-lenticular interface would largely increase the surgical outcome of developmental cataract. Currently medical devices allowing to visualize this interface prior to surgery are lacking. Dissection of primary vitreous from posterior capsule is time-consuming but feasible. Chemicals, like microplasmin, may be of some benefit for the cataract surgeon to optimize the separation

Conflict of interest

Any consultancy arrangements or agreements:

Bag-in-the-lens is licensed to Morcher GmbH

• 3163

Genetic anomalies in congenital cataract

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Summary

Developmental anomalies of the anterior segment of the eye encompasse a spectrum of disorders affecting the cornea, iris, lens, ciliary body, and/or the trabecular meshwork. Besides, nonsyndromic congenital cataract (CC) is a common cause of visual disability in children. All these genetic disorders are highly clinically and genetically heterogeneous, making challenging a proper diagnosis based solely on a phenotype-based approach. We develop a genotype-based approach by using a targeted Next-Generation Sequencing panel including 50 known genes. A cohort of 150 French index patients were recruited after detailed ophthalmic examination. All exons of the 50 genes were amplified using the kit TrueSeq Custom Amplicon (TSCA, Illumina). The subsequent amplified libraries were sequenced using a MiSeq (Illumina, Inc, San Diego, CA, USA) sequencer. All pathogenic variants were confirmed by Sanger sequencing, and familial analyses were performed. A large spectrum of molecular defects were identified with numerous novel variants. This NGS approach is an efficient tool to improve molecular diagnosis, and provides insight into the genotype-phenotype correlation of all these ocular disorders in a cost-effective way.

• 3164

Protein analysis of the plaques in congenital cataracts

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(2) University of Antwerp, Centre for Proteomics, Wilrijk, Belgium

Summary

Purpose: to identify the protein composition of posterior capsular plaques (PCP) in congenital idiopathic unilateral cataract with anterior vitreolenticular interface dysgenesis (AVLID).

Methods: samples of PCP's were collected during cataract surgery in children with congenital unilateral cataract presenting with a PCP and with vitreolenticular adherences observed during posterior capsulorhexis procedure. Proteome analysis was performed on the collected PCPs.

Results: PCP collection and proteome analysis was feasible from four children. A large portion of the proteins found in the PCPs were similar to the proteins known to be present in lens epithelial cells and fibers. Proteins like vimentin, fibronectin, actin, collagen type I, collagen type VI, lumican and keratin were also found which typically are present in mesenchymal tissue but not in lens tissue or capsule.

Conclusions: cases of unilateral idiopathic congenital cataract with AVLID typically present with a PCP. The protein composition in these PCPs, measured by means of proteome analysis, includes atypical proteins for lens and lens capsule and may be suggestive for an epitheliomesenchymal transformation (EMT).

• 3165

Contact lens service in pseudophakic and aphakic children

ROSENSVARD A
Stockholm, Sweden,

Summary

In Sweden cataract surgery is performed at two specialized centers during the first 2 years of life. Intraocular lenses (IOL) are implanted if possible. Amblyopia treatment and contact lens (CL) service is also provided for at these centers for the youngest.

At the clinic the patient meets a team; an orthoptist, an optician and a pediatric ophthalmologist.

Newborn aphakic children first get a standard CL +37 D. Children with IOL are made hyperopic with the ambition to obtain emmetropia in adult life. CL are prescribed after retinoscopy finding. Infants are corrected to a slight myopia. From 2 years of age the correction is for emmetropia and near addition of 2,5 diopters are prescribed in bifocal glasses. Aphakic children combine CL with bifocals and the children with IOL have only bifocals.

The CL are inserted every morning and removed and cleaned every evening. Some children learn to handle their CL themselves (video).

There are advantages with CL in comparison to glasses such as visual fields, aberration, flexibility and cosmetic.

PECARE (PEdiatric CAtaract REgistry) is a web-based national register in Sweden for children operated for cataract. Many of the congenital bilateral cases develop vision enough for driving licence.

• 3171

Cracking the nuclear-mitochondrial code in Leber hereditary optic neuropathy

CARELLI V

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Summary

Leber hereditary optic neuropathy (LHON) is primarily determined by mtDNA pathogenic mutations affecting complex I that are necessary but not sufficient to express the disease. In fact, there remain incomplete penetrance and male prevalence for which it is assumed that further complex genetic, anatomical and environmental interactions are necessary to trigger the neurodegenerative process. On the genetic ground, besides the primary mtDNA mutations there are further determinants, like the mtDNA copy number and the mtDNA background variability (haplotype) that are certainly relevant. However, variability of the nuclear genome is also assumed to play a relevant modifying role. Currently, multi-layered strategies are employed to crack this nuclear-mitochondrial code to finally reach a complete understanding of the genetic basis of LHON. The combination of next generation sequencing approaches, expression and metabolic profiles, and functional studies of neuronal tissue generated from patient-derived reprogrammed stem cells casts hope to shed light on the genetic basis and pathogenic mechanisms in LHON, ultimately leading to the development of targeted therapeutic strategies.

Conflict of interest

Any consultancy arrangements or agreements:

Consultancy agreements and clinical trials with GenSight, Stealth Peptides, Santhera and Edison Pharmaceuticals

Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:

Reimbursement of travel expenses

Any Lecture fee paid or payable to you or your department:

Honoraria for talk from Santhera

• 3172

Novel pathophysiological mechanisms in dominant optic atrophy beyond the mitochondrial dynamics equilibrium

LENAERS G , Charif M , Amati-Bonneau P , Chao de la Barca J , Procaccio V , Chevrollier A , Leruez S , Bonneau D , Reynier P

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Summary

Inherited Optic Neuropathies are blinding diseases related to mitochondrial dysfunctions in retinal ganglion cell (RGC). There are two main forms: the Leber Hereditary Optic Neuropathy (LHON) related to mutations in the mitochondrial genome, and the Kjer dominant optic atrophy (DOA) related to mutations in nuclear genes. Since the initial discovery of the OPA1 gene in 2000 as the major gene causing DOA, the use of WES and re-sequencing chips disclosed many novel genes responsible for DOA. Beyond genes recently identified involved in mitochondrial dynamics, we identified novel candidate genes crucial for RGC physiology. Using patient fibroblasts, we analyzed the consequences of their mutation on mitochondrial physiology and metabolism. Altogether, these data are shedding novel lights on DOA pathophysiology, beyond mitochondrial dynamics, as novel culprit mechanisms responsible for RGC degeneration, which should condition the design of future therapeutic approaches.

• 3173

Antisense oligonucleotide therapy for splicing defects in OPA1-related dominant optic atrophy

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

Summary

Mutations in OPA1 are the main cause of dominant optic atrophy (DOA) and have also been implicated in a variety of syndromic neuropathies such as DOAplus or Behr-like syndrome. We have recently discovered a disease-causing deep intronic mutation (DIM) in OPA1 that induces a constitutive inclusion of a cryptic exon into OPA1 transcripts. As a potential therapeutic strategy we sought to correct mis-splicing of the mutant pre-mRNA by using antisense oligonucleotides targeting the cryptic acceptor splice site and the novel branch point created by the DIM, respectively. Transfection of patient-derived primary dermal fibroblasts with AONs resulted in splice correction of the mutant pre-mRNA in a time and concentration dependent manner. Maximal rescue efficacy of up ~55% was obtained with the cryptic acceptor splice site targeting AON. Peak efficacy of splice correction was observed at 4 days after treatment. However, significant effects were still seen 14 days post-transfection in the proliferating cell culture. Western blot analysis revealed increased amounts of OPA1 protein with maximum amounts at ~3 days post-treatment. In summary, we provide the first mutation-specific rescue strategy for OPA1 deficiency using synthetic AONs.

• 3174

Advances in gene therapy for Wolfram syndrome

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(2) *Institute for Neurosciences of Montpellier- Hôpital Saint Eloi, INSERM U1051, Montpellier, France*

(3) *University of Tartu, Department of pathophysiology, Tartu, Estonia*

Summary

The Wolfram Syndrome (WS) is an early onset genetic disease (1/200 000) featuring diabetes mellitus and progressive optic neuropathy ensuing mutations in the WFS1 gene. To date, there is no treatment to stop the progression of the disease. We have characterized the visual impairment of 2 mutants animal models for WFS1 (Wfs1exon8-/- and Wfs1E864K) and shown that these 2 models developed an optic atrophy. We started for 1 year intravitreous micro injections of therapeutic vector AAV2-CMV-WFS1 on 1 month-old Wfs1exon8-/- . Our results showed that mice injected exhibited a stabilization of their visual acuity at 3 and 6 months post-injection, and a decrease of optic disc pallor and optic nerve damage. These promising results demonstrate the validity of the pre-clinical approach to treat Wolfram Syndrome by gene therapy and encourage further studies under a treatment for the Wolfram Syndrome patients.

• 3175

Clinical trials for inherited optic neuropathies

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(3) David Geffen School of Medicine at UCLA, Department of Ophthalmology and Doheny Eye Institue, Los Angeles, United States

Summary

The best scientific evidence for use of a clinical intervention is based upon data obtained from Phase III clinical trials.

The robustness of a clinical trial is dependent on the quality of the metrics collected which in turn is dependent on the design of the study.

Clinical trials involving inherited optic neuropathies such as Leber's Hereditary Optic Neuropathy (LHON) encounter some unique challenges which can be divided into two broad groups: patient-centric factors and test-centric factors. Patient-centric factors include the heterogeneous phenotypic presentations in LHON with variable rates of spontaneous recovery and time to nadir and plateau. Test-centric factors include the subjective nature of most visual metrics; intertest and intratest variability, which is compounded by patient adaptation to visual loss.

Collectively these issues must be addressed when designing a clinical trial, especially in rare diseases where patient recruitment can be a challenge

Conflict of interest

Any consultancy arrangements or agreements:

GeneSight Biologics

Sealth Biotechnology

• 3181
Ocular inflammatory diseases in ebola survivors

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(1) HOPITAL CLAUDE HURIEZ, OPHTHALMOLOGY, LILLE, France
(2) Brien Holden Vision Institute, Ophthalmology, Sydney, Australia
(3) Pitié Salpétrière Hospital, Ophthalmology, Paris, France
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(5) Nzérékoré regional Hospital, Ophthalmology, Nzerekore, Guinea
(6) IRD, IRD UMI 233 INSERM U 1175, Montpellier, France
(7) CADESSO, Ophthalmology, Conakry, France

Purpose
The last Ebola outbreak severely affected West Africa and led to 2543 deaths and 1268 survivors in Guinea, where it began. The survivors faced various symptoms and disorders including ocular pain and erythema, itching, tearing, photophobia and blurry vision. The purpose of our study was to describe uderluing ocular diseases.
Methods
This is a prospective observational multicenter cohort study initiated in March 2015 which included survivors followed up in the infectious disease ward of Conakry and Nzérekoré. The patients received multidisciplinary medical follow-up that included an eye examination.
Results
Systematic examination of 341 survivors highlighted 46 cases of uveitis (13.5%), six episcleritis (1.8%), and three interstitial keratitis (0.9%). Uveitis were more unilateral (78.3%) and anterior (47.8%) and occurred within the 2 months following discharge from the Ebola treatment center. Moreover, relapses were found up to 13 months after healing. Eleven eyes with anterior chamber inflammation presented with cataracts and visual acuity ≤ 5/10. Ten eyes with chorioretinal scars presented decreased visual acuity ≤ 5/10. Among 46 survivors with uveitis, 13 (28 %) suffered from visual alteration on at least one eye.
Conclusions
Nearly 17 % of Ebola survivors presented ocular disorders that may be very delayed in some patients. Moreover our study brought out relapses. We were not authorized to take intra-ocular samples to identify the virus. The mechanism behind these uveitis is probably is an association between a direct cytopathic impact of the virus and an immune reaction to it. The corticosteroid therapy that is actually recommended by WHO can't be used safely during the acute infection but seems to be efficient in survivors. The current issue is to perform safely cataract surgery in survivors.

• 3182
Endophthalmitis: what role does vitrectomy play?

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Purpose
To evaluate predictors of visual outcome in a series of patients treated for postoperative endophthalmitis (PE) and analyze the role of therapeutic vitrectomy (TV).
Methods
All patients who were clinically diagnosed with endophthalmitis and underwent eye procedure less than six weeks before presentation were included. Visual acuity (VA) was assessed and intravitreal antibiotics administered at the time of diagnosis for all patients. Some of them underwent TV. Main outcomes were best VA after treatment and variation of VA.
Results
Sixty-one patients were included. Group of patients who underwent TV have a statistically significant greater proportion of patients with comorbidities (42.4% vs 17.9%) and median of VA after treatment was worse (2.1 LogMAR vs 0.5 LogMAR). Good VA, defined as ≤ 0.3 LogMAR, were reached only by 13 of 49 patients (26.5%). Presenting VA and performance of TV presented statistically significant differences in this analysis. On simple linear regression, we found that age, worse VA at diagnosis and the performance of TV were significantly associated to worse VA after treatment, and that longer time to the onset of symptoms and until TV are significantly associated with sorter variation of VA. Performing TV in the first 24h after diagnosis presents a greater variation of VA than performing it after this time. After first 24h, there seems to be increasingly worse outcomes with longer periods.
Conclusions
Our findings are consistent with previous ones. TV should be done considering the overall clinical course and each patient's characteristics, but if it was the option, shouldn't be delayed

• 3183
Surgical management of Acute Retinal Necrosis (ARN): Timing and outcomes

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Purpose
To evaluate the demographics, etiology, clinical and surgical management, and functional outcomes of an Acute Retinal Necrosis (ARN) series from a referral Italian Centre. Both clinical characteristics and treatment strategies of ARN are valid and debated issues. Several dedicated articles appear every year in highly impacted medical journals.
Methods
Observational series of biopsy-proven ARN cases between January 2010 and March 2017. All the considered patients had the last visit in 2017. Soon after diagnosis patients had received systemic antiviral therapy according to the specific guidelines. No intravitreal injections or "early" (i.e. in the absence of retinal detachment, RD) pars plana vitrectomy (PPV) were adopted.
Results
Seven patients (5 men) were included with a mean age of 52±18 years (range 31-78 years). HZV was detected in 4 cases, HSV in 2 cases, CMV in 1 case (the sole with positive serology for HIV). PPV was performed in 6/7 subjects, with a mean delay of 43±33 days since diagnosis. Only in 1 case silicone tamponade removal was successfully reached. A second PPV was required in 4/6 patients, because of RD recurrence or posterior bleeding. In one HSV case a complete healing was achieved with medical treatment. Visual acuity (VA) averagely improved in the whole cohort either between diagnosis (0.91±0.25 logMAR) and the end of follow up (0.77±0.51 logMAR); or between preoperatively (1.15±0.03 logMAR) and the end of follow up. In both cases, however, statistic was not significant (P> 0.05).
Conclusions
The efficacy of prophylactic laser in our series, as in the literature, remains unclear. VA improvement was achieved even without early PPV. This evidence, along with the possible adjuvant effect of intravitreal antivirals, warrant comparative discussion with literature data.

• 3184
Case series and literature review: Is there a role for antiviral prophylaxis in patients who have had herpetic encephalitis?

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Purpose
To report a case series involving two cases of acute retinal necrosis (ARN) presenting after treatment and resolution of herpes simplex virus (HSV) encephalitis. In neither case was antiviral prophylaxis after initial episode of encephalitis used. Literature review is presented to evaluate the benefit of prophylaxis in such cases.
Methods
Two case reports are described and fundus photos presented of patients presenting to the Ophthalmology Department of Queen Alexandra Hospital, Portsmouth, UK within the last 3 years. PubMed was used to conduct the literature review.
Results
A 67-year-old female presented with rapid painful unilateral visual loss. She had had a history of HSV encephalitis 6 years before, treated successfully with no recurrences. Clinical assessment was in keeping with ARN. She was admitted for intravenous acyclovir for 8 days followed by long-term oral antiviral treatment. Her vision remained poor with a best-corrected visual acuity (BCVA) of 6/60 in the affected eye.

A 66 year-old male presented with a 10-day history of painful unilateral visual loss. He had had a history of HSV encephalitis 6 months before and a relapse 2 months later treated successfully with acyclovir. Clinical assessment demonstrated a panuveitis and retinitis in keeping with ARN. He was admitted for intravenous acyclovir then kept on long-term oral treatment of 400mg twice-daily. The BCVA in his affected eye has remained at 5/60.
Conclusions
HSV encephalitis has been widely documented as a risk factor for ARN and has been reported to occur up to 20 years after initial illness. The virus may reach the eye via a trans-axonal route and reside in a reservoir awaiting re-activation within retinal neurons. We propose that prophylaxis with long-term low-dose antivirals is necessary after all cases of HSV encephalitis to reduce the risk of ARN.

• 3185

Inflammatory markers but not symptoms are a strong predictor of temporal artery biopsy outcome – the Portsmouth experience

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Purpose
To investigate the correlation of biopsy proven temporal arteritis with clinical symptoms and inflammatory markers.
Methods
Retrospective study of all patients (n=89) referred for temporal artery biopsy (TAB) over a 30-month period. Ten patients were excluded due to inconclusive biopsy or insufficient data. Correlation of presenting symptom (localised headache LH, jaw claudication JC, pain over temporal artery PTA, constitutional symptoms CS) and inflammatory marker level (ESR, CRP) with histological outcome (presence of giant cells) were assessed using a two-tailed unpaired t-test.
Results
50 cases had a negative (-ve) biopsy result and 29 positive (+ve). Mean age (SD) for each group was 71yrs (10) and 77yrs (6) respectively. No significant correlation was found between presenting symptom and biopsy result (-ve:+ve LH 88%:79%, PTA 46%:62%, CS 40%:59%) except for jaw claudication (36%:62%, $p<0.05$). Inflammatory marker result was found to significantly correlate with biopsy outcome. Mean ESR (SD) was 23 (21) in the –ve and 34 (24) in the +ve ($p<0.05$) and mean CRP (SD) was 33 (40) in the -ve and 98 (81) in the +ve group, ($p<0.001$). Mean ESR+CRP (SD) was 55 (52) in the –ve and 132 (87) in the +ve ($p<0.0001$). There were no significant differences in duration of steroid treatment prior to TAB or time to TAB between the two groups. One patient had normal ESR and CRP with a positive biopsy result.Treatment with steroids was continued for 48% of patients with –ve biopsy on clinical grounds.
Conclusions
Elevated ESR and CRP are strongly predictive of positive TAB outcome. Combining ESR+CRP increases the significance of the correlation. Further studies with larger patient numbers may identify an appropriate cut-off level which, combined with age and clinical features, may provide a clinical score to aid decision making regarding which patients require TAB.

• 3186

Portuguese prescription patterns of topical antibiotics in Ophthalmology: a yearlong analysis

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(2) Vision Sciences Study Center, Universidade de Lisboa, Lisboa, Portugal
(3) Serviços Partilhados do Ministério da Saúde - SPMS, EPE, Lisboa, Portugal

Purpose
Scarce data is available regarding topical antibiotics prescribing patterns in Ophthalmology. We aimed to describe and analyze the nationwide prescription of these antimicrobials during the year of 2016.
Methods
Cross-sectional study. A common electronic drug prescription system is used by all public or private hospitals and clinics in Portugal. We used this national database and included all the 2016 prescriptions of topical antibiotics used prophylactically or therapeutically in ophthalmology. Patients' demographic data and medications prescribed were provided in an encrypted form and anonymously extracted. Results were stratified by region, physician specialty (ophthalmology vs. general practitioner) and public/private sector. Statistical analysis was performed using STATA v14.1.
Results
During 2016 in Portugal, a total of 458,638 topical antibiotic medications were prescribed to 324,683 different patients (47% male), corresponding to approximately 3.2% of the country population. Mean age was 46.4 ± 29.9 years. Of all prescriptions, 46.6% were from ophthalmologists, 31.9% from general practitioners and 11.3% from pediatricians. The most prescribed drugs were chloramphenicol (24.2%), ofloxacin (14.0%) and fusidic acid (9.0%). A similar rank was found in the public sector, but in private practice moxifloxacin was the third most prescribed. The prescription pattern was markedly different among the different country regions. Lastly, a seasonal effect is suggested, since more than 35% of the prescriptions were made from October to December.
Conclusions
This nationwide study revealed prescription's trends of topical antibiotic drugs in Portugal. These results might contribute for the development of a wiser use of antimicrobial drugs, thus promoting the best patient care and the whole system sustainability.

• 3311

27 Gauge vitrectomy (pros & cons)

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Summary
The introduction of 23- and 25-gauge systems was a game changer for vitreoretinal surgery. Recently, 27-gauge systems have been commercialized. Only non-complex cases would be suitable for surgery with the first generation 27-gauge instrumentation. Recent enhacements however would allow the use of such systems even in very complex cases. In this special interest symposium we will discuss in depth the advantages and the limitations of 27-gauge vitrectomy systems and ways to improve our outcomes.

• 3312

3D visualization systems

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Summary
Panoramic visualization systems offers new possibilities for all surgeons in the peroperative management of patients affected by vitreoretinal disorders.
Ultradigital 3D heads up surgery offers enhanced 3D visualization with high-definition resolution, image depth, clarity and color contrast while helping to minimize light exposure to the patient's eye. All surgical or patients advantages and inconvenients will be discussed.

• 3313

Intra-operative OCT

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Abstract not provided

• 3314

Combined procedures

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Summary
Aim: the purpose of this presentation is to provide evidence for the necessity of combined vitrectomy and cataract removal in many cases
Methods: We reviewed the data of 850 phacovitrectomies performed under the same settings.
Results:
We evaluated and present the acceptance from the patients , the final outcome and the complications following the procedure. We will also present tips on how to achieve the best results.
Conclusion:
We will present the evidence to why we believe that phacovitrectomy is a easy , safe and necessary procedure

• 3315

Submacular hemorrhage management

POURNARAS C

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Summary

Submacular haemorrhage (SMH) is a sight threatening complication that can occur in exudative age related macular degeneration (AMD). Left untreated, SMH carries a grave visual prognosis. Diagnosis and effective management of this complication are important.

The treatment strategies for SMH include displacement of blood from the fovea, usually by injection of an expansile gas, pharmacologic clot lysis such as with recombinant tissue plasminogen activator (rtPA) and treatment of the underlying choroidal neovascularization (CNV), such as with antivascular endothelial growth factor (anti-VEGF) agents. These three strategies have been employed in isolation or in combination, some concurrently and others in stages.

In cases presenting early, pneumatic displacement alone with anti-VEGF may be sufficient. rtPA has demonstrable effect on the liquefaction of submacular clots but there are remaining uncertainties with regards to the dose, safety and the timing of initial treatment. Potential side effects of rtPA include pigment epithelial toxicity, increased risk of vitreous haemorrhage and systemic toxicity. Anti-VEGF monotherapy is a treatment option particularly in patients with thinner SMH and those who are unable to posture.

• 3321
Normal and abnormal corneal innervation

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Summary
The objective of this talk is to provide an understanding of the latest view on corneal innervation and the changes that occur during disease processes and their possible role in corneal pathology. The cornea is innervated essentially by the 5th cranial nerve. The nerves enter the limbus equally all around the circumference, travel as stromal nerves and undergo dichotomous branching to form sub Bowman's nerves that penetrate the Bowman's zone and end in terminal bulbs. From these, the neuritis of the subasal plexus arise. There is also a signifiant sympathetic innervation of the cornea. There is very little knowledge on the histological changes in corneal nerves during disease process to IVCM studies are many. Recent studies have shown remarkable changes that occur in the stroma, and epithelila nerves in conditions such as bullous keratopahty, corneal grafts, keratoconus, and following refractive surgery. This indicates that corneal nerves are not passive bystanders but contribute actively to corneal pathology.
Conflict of interest
Any consultancy arrangements or agreements:
HS Dua is consultant to Dompe, Croma, Thea, Allergan

• 3322
Neurotrophic Keratitis: Definition, clinical presentation and diagnosis

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Summary
Neurotropic Keratitis is a non-healing or repeated break down of corneal epithelium associated with degenerative changes resulting from impaired corneal innervation. Later complications such as infection scarring and perforation can follow. A reduced or absent corneal sensation is the hallmark of the disease
Patients present with dryness, photophobia and inability to read for prolonged duration which is worse by computer work or air draft
Signs are divided into 2 parts: Signs related to the disease process such as corneal epithelial irregularity and clouding, reduced tear break up time and superficial punctate keratitis mostly inferior, Later persistent epithelial defect, corneal ulcers with rolled edges and loose epithelium surrounding the edges which can later develop infection, melting , scarring or perforation. Signs related to the underlying cause such as lagophthalmous and reduced blink reflex, signs of previous herpetic keratitis with scarring, vascularization and or patches of iris atrophy. Stromal dystrophy or beaded corneal nerves, advanced diabetic retinopathy or retinal laser marks
Diagnosis includes clinical presentation, duration of non-healing epithelial defect and measuring corneal sensation with Coche-Bonnet test

• 3323
Medical management of neurotrophic keratitis

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Summary
Considerations for the medical management of neurotrophic keratopathy (NK) depend upon the stage/ severity and pathology of the underlying disease process. Therapeutic approaches are broadly divided into strategic areas that encompass categories of treating the underlying disease process, treating any concurrent infections, preventing disease progression, promoting epithelialisation, providing tear replacement, reducing inflammation, preventing stromal tissue loss or perforation and avoiding complications.
Conflict of interest
Any consultancy arrangements or agreements:
Consultant fees

• 3324
Surgical management of Neurotrophic keratitis

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Summary
Surgical treatment of neurotrophic keratitis (NK), is indicated in advanced disease (stages 2 and 3) refractory to medical management. The objective is to prevent stromal involvement and to prevent corneal perforation. The cornerstone of surgical therapy is tarsorrhaphy which narrows the palpebral fissure and decreases the area of exposed cornea. It can be temporary or permanent and partial or complete. An alternative to surgical tarsorrhaphy is botulium A toxin injection into the upper lid. Other surgical options are amniotic membrane transplantation to cover the epithelial defect (stage 2) or corneal ulcer (stage 3) and punctal occlusion to increase the amount of tears and improve lubrication. Corneal perforation, the ultimate sight threatening complication of NK, can be managed using cyanoacrylate glue or in larger defects a tectonic keratoplasty. Conjunctival flap may also be indicated in impending perforation. Outcomes of penetrating or lamellar corneal transplants in neurotrophic keratitis are very poor. Direct neurotization of the cornea using branches of the contralateral ophthalmic division of the trigeminal nerve is difficult to perform but preserves cosmesis and can restore function.

• 3331

Measurement of oculomotor parameters and visual processing times without eye-tracking

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Purpose
Oculomotor parameters and visual processing times affect visual performance. In addition, mental health disorders and common drugs can also affect task completion times and the efficiency of visual search. Eye-trackers are useful in such studies, but expensive equipment and careful calibration is needed. A new, simple method that does not require eye-tracking is proposed. The EMAIL (Eye Movement and Intrinsic Latency) test captures parameters that describe both the time course of eye-movement generation as well as the time needed to detect and process specific stimulus attributes at the end of each saccade.
Methods
The test relies on measuring the time needed to detect peripheral targets, carry out an appropriate eye-movement and process some feature of the stimulus (such as colour, coherent motion, rapid flicker, spatial orientation or acuity). In this round of experiments, the stimulus was a Landolt ring flanked by distractors and presented at a randomly selected location on either side of fixation, 8o in the periphery. The measurement variable is the target presentation time, δT, needed to achieve ~ 71% correct response. The subject's task is to saccade to the peripheral target, to register the stimulus attribute of interest and to press one of four response buttons to indicate the correct orientation of the gap.
Results
The results obtained so far show a significant effect of stimulus contrast, age and fatigue. The measured times vary systematically with age in the range 160 to 300 ms. Longer times are observed in schizophrenia and other mental health disorders.
Conclusions
The new EMAIL test provides a simple method to assess changes in oculomotor parameters and decision response times with potential applications in the study of fatigue and the evaluation of drug efficiency in the treatment of mental health disorders.

• 3332

Normal upper age-limits for photopic and mesopic visual acuity and functional contrast sensitivity

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Purpose
Normal, healthy aging causes a gradual worsening of vision with more pronounced effects at lower light levels (mesopic range). Normal spatial vision enables us to resolve fine spatial detail and to detect faint edges and boundaries that make up objects. Age-related changes in the optics of the eye and diseases of the retina and / or systemic diseases that affect vision can also cause a loss of spatial vision. In order to separate the latter from the effects of normal aging, reliable, upper, normal limits of spatial vision are needed for both photopic and mesopic light levels. The purpose of this investigation was to measure visual acuity (VA) and functional contrast sensitivity (FCS) as a function of age in a large sample of normal subjects and to establish reliable, statistical limits to describe normal vision.
Methods
206 subjects (age range: 10-77 years) have been investigated. A detailed medical and ocular history and eye examination were carried out. We measured photopic and mesopic VA and FCS in each subject under binocular and monocular viewing conditions with both positive and negative contrast using the Acuity-Plus test (http://www.city.ac.uk/avot).
Results
The best visual performance corresponds to ~ 15 to 35 years. The gradual increase in thresholds with increasing age was surprisingly small under all stimulus conditions below the fifth decade with significant differences between photopic and mesopic conditions.
Conclusions
Thresholds of VA and FCS increase gradually in normal aging. These preliminary results reveal a more pronounced effect between the fifth and sixth decade of life. On completion of this study, statistically-reliable, upper, normal limits for VA and FCS will be determined as a function of age. These data will make it possible to detect reliable significant loss of spatial vision that cannot be attributed to normal aging.

• 3333

Changes in axial length in adult eyes

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Purpose
It is generally assumed that axial length remains constant in adults, although there have been reports of gradual axial length decreases with age. These findings are often considered with scepticism by the authors themselves, however. This work investigates the cause for this apparent decrease and looks into any other factors that may influence axial length measurements.
Methods
The analysis reviews the literature on non-myopic axial length changes with age in adults and correlates these changes against year of birth and average level of education obtained from United Nations reports. Furthermore a series of calculations were performed to assess how optical biometry methods respond to the thickening of the crystalline lens, while its equivalent refractive index decreases, as well as how they respond to refractive index increases due to cataract.
Results
The literature analysis shows that axial length does not significantly decrease with age (linear regression, $p = 0.071$ for the linear term). Axial length does increase with the year of birth, especially in Western countries that all saw similar economic developments during the 20th Century. In non-Western countries, where the economic development was more diverse, the changes were less pronounced. The correlation of the axial length increase with the increasing education level that occurred in all countries on the other hand was very high ($r^2 = 0.681$; $p < 0.001$).
Optical axial length measurements appear to increase by 0.07 mm between 20-80 years of age due to internal media changes, even if the actual length remains constant. Apparent increases due to cataract are of the same order of magnitude.
Conclusions
The reported axial length decrease with age is an artefact caused by the gradual myopization of the population. Optical artefacts due to changes in the optical media have very little effect.

• 3334

Retinal vascular fractal dimension and cerebral blood flow, the CRESCENDO study

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Purpose
The retinal vascular fractal dimension (FD) is a marker of retinal complexity of vascular tree. It has been associated with neurodegenerative and cerebrovascular diseases. Arterial spin labelling is a non-invasive technique to evaluate the cerebral blood flow (CBF). The purpose of this study was to explore the relationship between retinal vascular FD and CBF.
Methods
Cross sectional analysis comprising 29 individuals aged 65 years and over from the Cognitive REServe and Clinical ENDOphenotype (CRESCENDO) cohort of healthy older adults. Retinal vascular FD was measured from fundus photographs using semi-automated standardized imaging software "Singapore Eye Vessel Assessment (SIVA)" system. CBF was estimated in various gray matter regions from a 2D Pulsed arterial spin labelling sequence from MRI.
Results
A higher venular FD was associated with higher CBF in all cerebral regions of interest ($p<0.01$). No significant associations were found between CBF and other parameters derived from SIVA or the central retinal arterial or venular equivalent. This association was stronger for opposite eye to handedness ($p=0.03$). No relationship was observed between arterial FD and CBF ($p>0.07$).
Conclusions
Venular FD was the main parameter associated to cerebral perfusion whereas retinal vascular calibers were not. It may be evaluated in clinical studies for early and non-invasive detection of subclinical cerebro-vascular pathologies including dementia and stroke.

• 3335

How to explain "flat" electroretinograms when patients with Leber's congenital amaurosis aren't blind

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Purpose
To explain how a 'flat" or 'extinguished" electroretinogram (ERG) in a patient with Leber's congenital amaurosis may not necessarily be indicative of a corresponding loss of vision.
Methods
Basic principles of ocular as well as auditory electrophysiology, wave physics, phototransduction metabolic pathways and ophthalmic genetics were reviewed and organized to reveal heretofore overlooked pathways. Correlations of ocular as well as auditory electrophysiology characteristics for Leber's congenital amaurosis and congenital auditory neuropathy/dys-synchrony were made.
Results
Variably delayed individual photoreceptor cell signaling secondary to metabolic enzymatic deficiencies involved in phototransduction results in ERG a-waves produced, and subsequent b-waves, to interfere destructively with each other, rather than allow for averaging in-phase summation to permit recordable ERG signals. Despite the delayed visual cycle, intraretinal synaptic transmission may proceed uninhibited to activate retinal ganglion cells and axonal pathways to the visual cortex.
Conclusions
A 'flat" or 'extinguished" ERG need not indicate absent vision, but overall destructive interference of individual a-waves and b-waves averaged for the recorded ERG. Analogous auditory electrophysiologic findings are noted in corresponding so-called congenital auditory neuropathy/dys-synchrony. Such findings are of great diagnostic utility and may be considered pathognomonic. Theoretically, the stability or progression of a patient with Leber's congenital amaurosis, and their response to an interventional genetic or pharmacologic therapeutic regimen, could be followed in more sensitive and objective manner at the cellular level via electro-oculography, prior to visual acuity, visual evoked potentials, or ERG testing revealing any changes in overall retinal function.

• 3336

Proteinics study: Relevance and interest for screening, follow-up, etiopathogenesis of AMD

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Purpose
To evaluate Proteinics study impact on AMD diagnosis, screening, follow-up, etiopathogenesis
Methods
AMD: 40 patients,16 men,24 women,30 with AMD.4 Groups A,B,C,T. A:10 first stage AMD patients,B:10 Atrophy AMD patients(predominant atrophic areas),C:10 patients with Neovascular AMD,T:10 normal patients,control group. Ophthalmologic exam included ETDRS visual acuity(VA),complete ophthalmic examination, Fundus examination, autofluorescence imaging (FAF), (RegionFinderSoftware), optical coherence tomography (HRA Spectral Domain OCT) (OCTenFace software, M-S software), Fluorescein angiography(FA)and ICG when Neovascular complication. Proteinics Study: Blood tests and analysis, proteinics qualitative and quantitative analysis,all the same for all patients,whatever group. Blood test is done during ophthalmologic exam. Plasma congelation,then Elisa technic,3 stages(SimpleStep Elisa kits)for detection and quantification of IL1β,IL6,IL10,TNFα,tau protein. Classic Elisa technic,2stages,for Amyloid peptid Aß1-40.Each sample quadruplicate; MicroBCA analysis.
Results
Analysis will determine proteinics quantitative values in each group of patients, and proportion, characterization, singularity of each of them: group A and C:similar results, higher for C; group T and B:similar results, lower for B. So, characterization, prevalence, specifics of and for each group, therefore a proteinics profile. Proteinics study'evaluation, identification, classification in AMD patients, and especially A, B, C groups allow AMD screening, follow-up, particularly according to AMD type and stage. Proteinics study may have biomarker feature and let AMD prevention
Conclusions
Proteinics study enhance AMD characterization, allow better diagnosis, follow-up, screening. Interrelations, correlations between AMD and Proteinics lead to better etiopathogenesis understanding and therapeutics prospects

• 3341

Conjunctival melanoma: association of cyclooxygenase-2 tumour expression to prognosis

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Purpose
Conjunctival melanoma is a rare but potentially lethal tumour. Its biologic profile is still largely unknown, with recent studies aiming at establishing histopathological and genetic tumour profiles. The aim of this study was to analyse the association between clinicopathological characteristics and tumour expression of cyclooxygenase-2 (COX-2) to prognosis, assessing its usefulness as a possible prognostic marker.
Methods
Case series of 50 patients from 1991 to 2008 with pathologically proven conjunctival melanoma. Demographic, clinical and pathological characteristics were evaluated by reviewing clinical files and pathology. Expression of COX-2 was studied by immunohistochemistry of formalin-fixed paraffin-embedded tissue samples of 20 melanomas. Samples were classified in a score which included intensity of staining and percentage of cells with positive reactivity.
Results
Clinicopathological features significantly associated ($p<.05$) with a poor prognosis (death) included involvement of fornix and tarsal conjunctiva, tumour thickness exceeding 2 mm, local tumour recurrence, lymph node and systemic metastasis. In the immunohistochemistry study (n=20) all cases expressed COX-2 although with different scores. However, only cases with score 4 were associated with a poor outcome. Multivariate association analysis revealed that recurrence rate, metastasis, corneal invasion and tumour thickness were associated with score 4 cases and, therefore, with a clinical profile with a higher risk of death.
Conclusions
Results suggest that higher COX-2 expression may be a negative prognostic factor in conjunctival melanoma. Further studies can address the potential use of anti-COX-2 drugs as adjuvant therapy of this disease.

• 3342

β-catenin activation in conjunctival melanocytic proliferations

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Purpose
Conjunctival and cutaneaous melanoma partially share similar genetic alterations. β-catenin is a dual-function protein that acts not only as a structural component of adherens junctions but also as an effector molecule involved in the Wnt pathway. In skin melanoma, in vitro activation of the Wnt pathway led to nuclear localization of β-catenin and increased invasiveness. We investigated the expression and activation of β-catenin in benign and malignant conjunctival melanocytic proliferations.
Methods
β-catenin expression was assessed by immunohistochemistry in 43 conjunctival naevi, 48 PAM (including 23 PAM with atypia) and 44 conjunctival melanomas as well as in 4 conjunctival melanoma cell lines at various stages of confluence. Statistical analysis was performed with JUMP 8.0 software.
Results
In the naevi, membranous expression of β-Catenin was found in all the cases and nuclear expression in 14% of the cases.
In the PAM, membranous expression of β-catenin was identified in all the cases without nuclear expression.
Membranous expression of β-catenin in melanoma was found in 94% of the cases and nuclear expression in 15.9% of the cases. There were no significant differences in the nuclear expression of β-catenin between conjunctival nevi and melanoma. In the melanoma group, there was a significant correlation between nuclear expression of β-catenin and depth of invasion.
In the 4 conjunctival melanoma cells lines, no significant nuclear expression of β-catenin was identified at various stages of confluence.
Conclusions
β-catenin activation and nuclear localization does not appear to be a major mechanism occurring in conjunctival melanoma. It is however possible that β-catenin activation might occur at a late stage in tumor development.

• 3343

Comparing anterior segment optical coherence tomography and ultrasound biomicroscopy with histopathology in measurement of corneal and bulbar conjunctival tumors depth

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Purpose
Corneal and bulbar conjunctival tumors can be visualized and measured by Anterior Segment Optical Coherence Tomography (A-OCT) and Ultrasound Biomicroscopy (UBM). We compared tumor depth measured by histopathology (HP) with measurements by UBM and A-OCT to investigate whether the two techniques are as accurate as HP.
Methods
35 patients with 42 corneal or conjunctival bulbar tumors were imaged with A-OCT and UBM. 11 of the tumors were excised and analyzed on histopathology. The correlation of the depth measurements on HP versus A-OCT and UBM was statistically analyzed. When the tumor was not excised, depth measurements on A-OCT versus UBM were compared.
Results
Statistical analysis showed that UBM and HP measurements of tumor depth are positively correlated, as are UBM and A-OCT measurements. It was not possible to obtain statistically significant data for the correlation between HP and A-OCT measurements because of the small study population. Image quality was overall better with A-OCT than with UBM, but in 12 tumors, depth measurement on A-OCT was impossible because of tumor shadowing (thick or highly pigmented tumor).
Conclusions
UBM can measure tumor depth as accurately as HP. Tumor depth measurements on A-OCT and UBM are positively correlated. A larger study is needed to investigate whether measurement of tumor depth with A-OCT is as accurate as HP. Because of drawbacks of depth measurements on histopathology, we believe that A-OCT and UBM could become the golden standard for measuring corneal and bulbar conjunctival tumor depth. We advise to use A-OCT if the tumor is not too thick or too pigmented, and to use UBM in case of posterior tumor shadowing on OCT.

• 3344

Micro-CT study of Bomirski melanoma growing in hamster eye

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Purpose
The Bomirski Hamster Melanoma (BHM) cell line has been successfully used as an eye tumor animal model in the studies on tumor vascular network, metastasis and radiation treatment. Visualization and modeling of neoangiogenesis is crucial for further ocular tumor research. This work presents visualization and image analysis of BHM eyeballs using X-ray microtomography (micro-CT).
Methods
Micro-CT is a nondestructive preclinical imaging method with isotropic micron resolution suitable for small ex-vivo samples. This technique provides 3D distribution of linear attenuation coefficient realized as a stack of cross-sectional images. The micro-CT scanning and analysis protocol was optimized for simultaneous visualization of normal ocular tissues, and pathological vasculature of BHM. Micro-CT image contrast was enhanced using iodine (Lugol's solution) staining technique. In this investigation the Bruker SkyScan 1272 micro-CT system was used.
Results
The iodine staining method provided well contrasted images presenting a globe anatomy in fine details. Advanced malignancy, with the tumor occupying the entire anterior chamber and the pathological disorganized irregular tumor vascular network was also visualized. Image analysis and processing allowed to distinguish grey level range corresponding to the particular globe and tumor structures. Quantitative analysis of BHM vessel size distribution and complexity level was performed.
Conclusions
Micro-CT enhanced with Lugol solution staining method has a great potential in preclinical eye tumor research using small animal models.

• 3345

Application of label-free 2-photon fluorescence lifetime imaging microscopy to measure endogenous melanin profiles in human eye melanocytes, naevus and melanoma cells

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Purpose
The progression of choroidal melanoma (CM) is complex, involving genetic and immune-related factors. Melanin/pigmentation genes and forms (eumelanin/dark and pheomelanin/light) can also impact on CM progression. In this study, an optimised 2-photon fluorescence lifetime imaging microscopy (FLIM), with phasor analysis, was used to identify melanin fluorescence lifetime (FL) profiles in formalin-fixed, label-free paraffin sections of human melanoma and naevus, with surrounding heterogeneously pigmented melanocytes.
Methods
Sections of 'light CM' (n=3) with 'mixed surrounding melanocytes' and 'dark naevi' (n=3) with 'dark surrounding melanocytes' were imaged with FLIM (3 sampled regions). Fluorescence lifetimes were measured at every pixel of captured FLIM images, Fourier transformed and presented in a 'fit-free' phasor plot. These plots were segmented by 7 phasor clusters of linearly increasing fluorescence lifetimes mapped to intracellular melanin in melanocytes, naevus and melanoma cells. The mean fraction of FLIM image pixels linked to each melanin-mapped cluster was obtained for all sampled regions to form melanin FL profiles.
Results
The measured sampled regions displayed distinct intracellular melanin (eumelanin:pheomelanin) profiles with varying dominant melanin-mapped clusters. The dominant 'highest pixel fraction' cluster measured in 'light CM' mapped to long FLs, implying a low eu:pheo ratio. The 'mixed pigmented melanocytes around CM' showed a mixed eu:pheo content based on the dominant mid-valued FL cluster. The 'dark naevi and surrounding melanocytes' were mapped to mostly short FLs (high eu:pheo ratio).
Conclusions
Our FLIM-phasor method provides a fast 'model-free' way to unmix melanin fluorescence lifetimes in melanocytes, naevi and CM, and provides a basis for exploring the role of melanin forms in eye melanoma pathogenesis.

• 3346

Primary human choroidal melanocytes express functional Toll-Like Receptors (TLRs)

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Purpose
Human choroidal melanocytes (HCMs) are an abundant heterogeneous, melanin-containing population of cells within the vascular uveal tract. Toll-like receptors (TLRs) are pattern recognition receptors involved in the innate immune response against phylogenetically conserved microbial components. Immune cells are established to express TLRs and more recent studies showed TLR expression on non-immune cells including corneal and conjunctival epithelia, retinal microglia and RPE, iris pigment epithelium, and skin melanocytes. The expression of TLRs on uveal melanocytes however remains to be investigated.
Methods
HCMs were isolated and cultured from donor human eyes. TLR1-10 and MYD88 (a critical adaptor protein in the TLR signalling pathway) expression was investigated using RT-PCR and confirmed by immunocytochemistry. The production of IL-8 and CCL2 in response to TLR agonists was measured by ELISA.
Results
HCMs constitutively expressed TLR1-6, TLR9, and MYD88. Stimulation of HCMs with bacterial-derived TLR agonists [Pam3CSK4 (TLR1/2), HKLM (TLR2), LPS (TLR4), Flagellin (TLR5) and, FSL-1 (TLR6/2)] and virus-mimicking TLR agonists [Poly I:C (TLR3), Imiquimod (TLR7), ssRNA40 (TLR8) and ODN2006 (TLR9)] induced variable secretion of IL-8 and CCL2 (MCP-1). Control levels of IL8 (140pg/ml) increased in response to Pam3CSK4 (2360pg/ml), Poly I:C (3620pg/ml), LPS (4100pg/ml), Flagellin (1550pg/ml) and FSL-1 (2160pg/ml). Virus-mimicking agonists imiquimod, ssRNA40 and ODN2006, and intriguingly bacteria-derived HKML, did not significantly affect secreted IL8. Secreted CCL2 showed a similar pattern of response following stimulation with TLR agonists. HCMs were immunoreactive for TLR2, TLR3 and TLR4 protein.
Conclusions
The findings suggest that HCMs are potentially involved in innate immune responses against bacterial and viral pathogens within the human choroid.

• 3352
Tear sample collection in ocular allergy

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Summary
Purpose: To evaluate four different methods of tear collection in healthy participants.
Methods: Four methods used for tear collection were evaluated in both eyes of 20 healthy participants. Methods tested: capillary tubes (CT), capillary tubes with instillation of saline (CT saline), Schirmer's Tear Test Strips (STTS) and Polyvinyl Alcohol sponges (PVA). Volume, duration of collection, participant-reported discomfort, concentration and mass of histamine were evaluated.
Results: With CT saline the largest volume was collected in the shortest time. A significantly higher concentration of histamine was found in samples collected with STTS compared to CT saline (p=0.04) and PVA (p=0.02). CT and CT saline were associated with no or mild discomfort in 95% and 90%, STTS and PVA with moderate or severe discomfort in 70% and 85%.
Conclusion: For collection of tear fluid for the measurement of histamine the CT saline method was found to be a technically easy and quick method of obtaining sufficient volumes of tear fluid, with low discomfort for participants.

• 3353
Molecular diagnostics of ocular allergy

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Summary
Ocular allergies may severely impact on daily activities and overall quality of life. Conventional allergy testing with skin prick tests and circulating serum immunoglobulin E often falls short of identifying the culprit ocular allergens. On the other hand, targeting the ocular milieu may prove valuable for ocular allergy diagnostics. Conjunctival provocation testing and specific immunoglobulin E detection in tear fluid provide data on local ocular hypersensitivity. We focused on specific IgE testing by means of a commercial allergen microarray (ISAC® 112, Thermo Fisher Scientific). We report here the contribution of allergen microarray testing to identifying the culprit allergen in a 42-year old woman presenting with perennial allergic conjunctivitis.

• 3354
Update in topical ciclosporine in VKC

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Summary
Severe allergic conjunctivitis in children may be severe causing loss of quality of life and visual impairment. Vernal keratoconjunctivitis and atopic keratoconjunctivitis are rare diseases but must be distinguished because of their evolution. Imaging of these diseases and systemic treatment are reviewed and developed. An overview of the innovating diagnosis, new imaging techniques and treatment is summarized for a better comprehension of severe allergic ocular surface diseases.

• 3361

Vitreo-retinal pathology and multifocal IOLs

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Summary

Cataract surgery is the most common and successful surgical procedure performed today. Multifocal intraocular lenses (m-IOLs) offer good uncorrected distance and near visual acuity. However, the reduction in contrast sensitivity attributed to m-IOLs might manifest as compromised visual acuity, especially in eyes with macular disease. Because of this, not every currently available IOL is suitable for every patient. Furthermore, retinal visulization problems when performing vitrectomy with these lenses in place can be challenging. We will discuss the visual disturbances that m-IOLs produce in a patient with vitreoretinal pathology; the need for an accurate preoperative evaluation to assess macular function, including the role of OCT for identifying occult macular disease preoperatively in patients with dense cataracts; the convenience or not of m-IOLs in the presence of macular disease, which depends on the stability or the expected progression of the condition over time, and the availability of treatment. Finally, retinal surgeons need to be aware of the challenges of the impaired fundus visualization during vitrectomy following m-IOL implantation and the recommended strategies to minimize intraoperative complications.

• 3362

Indications and limits of the implantation of diffractive and refractive intraocular lenses in patients with ocular comorbidities

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Abstract not provided

• 3363

Ocular motility, do we know what is the dominant eye?

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Summary

Ocular motility, do we know which is the dominant eye?
Ocular dominance, is the tendency to prefer visual input from one eye to the other. It is somewhat analogous to the laterality of right- or left-handedness; however, the side of the dominant eye and the dominant hand do not always match.
Approximately two-thirds of the population are right-eye dominant and one-third left-eye dominant; however in a small portion of the population neither eye is dominant. Eye dominance has been categorized as "weak" or "strong" and highly profound cases are sometimes caused by amblyopia or strabismus.
This talk will discuss
-what is ocular dominance
-different techniques for measuring dominance
-what we have learnt from contact lens practice and monovision
-whether it can change and what influences that change
-surgical interventions relevant to ocular dominance
The relevance to multifocal intraocular lenses with comorbidity will be detailed
Conflict of interest
Any consultancy arrangements or agreements:
Lenstec Inc
Oculentis GMBH
Any research or educational support conditional or unconditional provided to you or your department in the past or present:
Most multifocal IOL manufacturers
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
Lenstec Inc
Oculentis GMBH
Any Lecture fee paid or payable to you or your department:
Lenstec Inc
Oculentis GMBH

• 3364

Varifocal intraocular lenses, how to play with different optical profiles for a better outcome or Trifocal IOLs: results of a randomized clinical study

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Abstract not provided

• 3365

Limits for the indication of multifocal lenses based on the contrast sensitivity function

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Summary

Multifocal IOLs are more often responsible for lower contrast sensitivity (CS) than monofocal IOLs, especially in mesopic light conditions. Thus, multifocal IOLs are contraindicated in many ocular diseases, which are characterized by decreased contrast sensitivity function. They included irregular astigmatism, Fuchs dystrophy, and many retinal diseases affecting macular function like retinitis pigmentosa, Stargardt disease, diabetic retinopathy, age-related macular degeneration, epiretinal membrane, and many optic nerve disorders. IOL decentration and tilt lead to decreased contrast sensitivity, aberrations, and ultimately decreased visual acuity, thus zonular weakness, esp. when severe, should be regarded as absolute or relative contraindication to choosing a multifocal IOL. Since contrast sensitivity is found to be most affected in eyes with aberrations and implanted multifocal IOLs, increased aberrations are relative contraindications for multifocal IOL implantation. It was proved that patients with the aspheric multifocal IOL had significantly better contrast visual acuity than patients with the spherical multifocal IOL.

• 3371

Exploring molecular mechanisms underlying Fuchs endothelial corneal dystrophy and their relevance to therapeutic interventions

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Summary
Fuchs endothelial corneal dystrophy (FECD) is an age-related degenerative condition characterised by bilateral progressive loss of corneal endothelial cell (CEC) function leading to severely impaired vision. An unstable intronic tri-nucleotide CTG repeat expansion within the transcription factor-encoding gene, TCF4, has recently been discovered to account for more than 70% of cases. An overview of our current understanding of the genetics of FECD, as well as the underlying molecular mechanisms responsible for the disease pathology will be provided. Furthermore, future potential avenues for targeted therapeutic interventions will be discussed in context of what has already been learnt from the broader field of non-coding repeat expansion disease, well-established causes of both neuromuscular and neurodegenerative disorders.

• 3372

Posterior polymorphous corneal dystrophy; novel clinical and molecular genetic insights

LISKOVA P
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Summary
Posterior polymorphous corneal dystrophy (PPCD) is a rare disorder inherited as an autosomal dominant trait. The general prevalence is unknown except for within the Czech Republic, where patients with PPCD have been systematically followed for decades. Currently there are over 125 living patients, leading to an estimated prevalence 1 affected individual per 80,000 inhabitants. Based on molecular genetic findings there are three subtypes recognized (PPCD1-PPCD3). Recently OVOL2 promoter mutations have been discovered as causing PPCD1. As there is mutual inhibition relationship between OVOL2 and epithelial-to-mesenchymal (EMT) transition inducer ZEB1, encoded by an established gene implicated in the development of PPCD3, the disease mechanism seems to lie in imbalance of transcription factors involved in EMT. Clinically, individuals with PPCD3 typically show in comparison to PPCD1 patients abnormal corneal steepening and lower incidence of secondary glaucoma and necessity for corneal grafting. Supported by GACR 17-12355S

• 3373

Novel tissue-targeted localized corneal gene therapy

MOHAN R
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Summary
This presentation will provide an overview of corneal gene therapy and stipulate novel bench-to-bedside translational strategies for human application. The talk will include information about identified potent adenoassociated virus (AAV) and nanoparticle vectors, simple and minimally invasive vector delivery techniques for delivering genes into desired corneal cells, and defined gene therapy approaches for introducing therapeutic genes selectively into corneal keratocytes or endothelium in vivo through single application of vector employing customized delivery techniques. Further, talk will discuss cornea-specific mechanisms driving pathologic process, novel molecular targets for interrupting TGFb1 signaling pathways, and therapeutic genes identified from basic-science corneal wound healing investigations performed in my lab laboratory using established small and large animal and donor human corneas. Finally, it will show potential of single- and two-gene combination therapy given locally in the cornea via optimized methods in inhibiting and eliminating corneal scarring and neovascularization in vivo in preclinical rabbit studies. The optimized gene therapy approaches could be easily applied in a clinical setting, if safety and toxicity are proven.

• 3374

Viral and non-viral vectors for cell and gene therapy of the corneal endothelium

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Summary
This presentation highlights non-viral and viral vector strategies to modify corneal endothelial cells. Functional data will be presented.

• 3381

Promoting women career through changes of societal stereotypes and academic efficiency indicators

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Abstract not provided

• 3382

Life as a junior postdoc in ophthalmology and neurobiology research: challenges and opportunities

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Summary
While equally represented in scientific courses at the age of 16-19 years, only 28% of researchers are women – according to the UNESCO report on science in 2030 (2015) – and only 3% of the Nobel Prizes for Science (6% for Medicine) have been awarded to women. Despite the progress that has been made, glass ceilings still appear to hinder the career of woman in science, female top scientists still miss out recognition for their work, and the scientific community – especially leadership positions – remains male-dominated. What struggles are women in science (woman in EVER) being faced with, and how can we use creativity and innovation to overcome these issues?

• 3383

Seeing the light: A perspective from a junior scientist on her journey from psychology to physics to ophthalmic research

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Summary
While there is no magic formula or a single path to achieving independence in an academic research setting, apart from intellect and scientific ability, persistence, drive, and flexibility certainly belong to the mix of valuable skills. In a perspective from a junior scientist on her own journey to independence, this talk discusses some of the challenges and obstacles encountered along the way, and shares personal insights, in an attempt to aid the upcoming generation of early-career scientists in their own journey.

• 3511

Swept Source OCT Angiography after retinal detachment treatment with different techniques

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Summary
Introduction: The aim of this study is to present Swept Source OCT Angiography images of eyes after retinal detachment treated with different techniques
Material and Methods: 100 eyes of 100 patients were treated with pneumatic retinopexy, segmental buckling, cerclage, primary vitrectomy or combined scleral buckling and vitrectomy. In all eyes swept source OCT angiography was performed one week, one and three and six months after surgery. ILM was peeled in all vitrectomized eyes. 3x3 and 9x9 Swept Source OCT Angiography images were obtained.
Results: Deep retinal vessels were intact only in eyes after pneumatic retinopexy and plombae. After cerclage the density of deep retina vessels was decreased. After vitrectomy deep retina vessels were irregular and had decreased density.
Conclusions: Retinal attachment might be obtained with all techniques when administered properly. Pneumatic retinopexy and segmental buckling are still the least invasive retinal detachment surgery, even in days of small gauge surgery. Vitrectomy was associated with most significant changes in retina vasculature, but it must be considered it was also chosen more often in eyes with more a severe disease.
Conflict of interest
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
Topcon
Any Lecture fee paid or payable to you or your department:
Topcon

• 3512

Endoocular OCT assisted epimacular surgery with preliminary vitreoretinal adhesions mapping

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Summary
Membranectomy is critical and one difficult stages of macular surgery. The difficulty is caused by heterogeneity of the adhesion of epiretinal tissue to the retina, and if it is large, traumas of the retina appear that are the main cause of loss of visual fields in the central area. Also, that in the overwhelming majority of cases (more than 50%), the onset of membranectomy is accompanied by a trauma of the retina, which occurs when the epiretinal tissue is first captured with forceps. Selective surgery, in which the map of adhesion of epiretinal tissue to the retina is created with the help of OCT at the preoperative stage and membranectomy is carried out only in areas of low adhesion, significantly reduces the probability of traumas of the retina.
In the process of vitrectomy and membranectomy, the redistribution of mechanical stress occurs in the epiretinal tissue. Because of this, the topology of the adhesion map changes. Dislocations of the boundaries of high adhesion zones in the process of membranectomy can reach 1.5 mm and with the probability greater than 0.7 are greater than 0.5 mm.
Uses endoOCT allows to control these changes in process of surgery, allowing it is essential to increase its efficiency.

• 3513

Surgical treatment of traumatic macular hole

RUBAN A
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Summary
Purpose: To present the results of the treatment of traumatic macular holes.
Methods: This study is a retrospective consecutive case series of 7 patients who underwent a 25G PPV with the displacement of macular retina after subretinal balanced salt solution injection to treat traumatic full thickness macular holes (TFMH). The efficiency was evaluated by the anatomical macular hole closure rate and best-corrected visual acuity (BCVA) during follow-up visits. The degree of retinal displacement was accessed by comparing the preoperative and postoperative fundus photographies.
Results: Complete closure of macular hole was achieved in 85,7% and 14,3% had partial closure. Average macular hole diameter was (825 μm). Visual acuity after surgery in the total group was significantly increased. All patients revealed a negative correlation between postoperative visual acuity and the time elapsed from the moment of the trauma, and a strong positive correlation between the macular hole size and elapsed time from the injury. There were no intraoperative or postoperative complications.
Conclusion: Vitrectomy with the «retinal displacement» technique may be an effective addition to surgical options for treating traumatic macular holes.

• 3514

Intraoperative OCT for inverted ILM flap technique

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Summary
Purpose: to evaluate the use of intraoperative spectral-domain optical coherence tomography (iSD-OCT) for large macular hole (MH) surgery using inverted internal limiting membrane (ILM) flap technique.
Methods: We analyzed 7 consecutive cases of iSD-OCT assisted pars plana vitrectomy (PPV) with inverted ILM flap technique for large and chronic MHs. iSD-OCT was performed using Rescan 700 (Zeiss, Oberkochen, Germany). iSD-OCT data were post-processed and analyzed postoperatively (study of tissue behavior).
Results: In all cases iSD-OCT imaging allowed the surgeon to carry on the procedure without significant time consumption. The iSD-OCT imaging assisted: 1) to find the safe place on the retina while starting ILM peeling; 2) to control the formation of the inverted ILM flap; 3) to conduct the inversion of the ILM flap over MH. iSD-OCT allowed to keep safe positioning of the vitreoretinal instruments.
Conclusions: iSD-OCT is a strong supporting tool during PPV, that gives prompt information about tissue behavior and surgical maneuvers. Inverted ILM flap technique for large MH can be performed in more controlled and save way without interruption of the surgical workflow.

• 3515

Nanofibrous carrier for transplantation of retinal pigment epithelial cells

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Summary

The most common retinal degenerative diseases such as age-related macular degeneration (AMD) and retinitis pigmentosa belong to serious eye diseases that cause dominant number of cases of impaired vision or even legal blindness. Because there is no treatment method to stop progression of these diseases or even treat them, it is supposable that cell therapy based on replacement of retinal pigment epithelial (RPE) cells can serve as an effective treatment for AMD and other degenerative diseases. The study was aimed at development of a new delivery technique for transplantation of RPE cells using two complementary delivery devices: a membraneous cell carrier and an injector as trans-scleral implantation instrument. The design of the suggested nanofibrous carrier with a peripheral frame was optimized to provide a minimal diffusion barrier for the flow of nutrients in the subretinal space and at the same time to resist surgical handling. An implantation instrument together with the cell carrier ensured a safe transfer of an organized RPE cell monolayer into the subretinal space. Different designs of the carrier seeded with cultured RPE cells and the implantation instrument was assessed in both ex vivo and in vivo animal experiments.

• 3521

Changing the fate of retinal ganglion cells following retinal ischemia: is autophagy the way?

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Summary
Autophagy is a highly conserved catabolic pathway for cell components to be degraded through the lysosomes and recycled under normal and stressful circumstances. The involvement of autophagy has been proven in several models of neurodenegerative diseases; however, its role in the neurodegenerative process occurring in retinal ganglion cells (RGCs) exposed to glaucoma-related stimuli is still controversial.
Here we show that retinal ischemia induced by acute elevation of intraocular pressure (IOP) is associated with a dynamic, biphasic, modulation of the autophagic pathway, characterized by an initial upregulation of the process, which is followed by a reduced efficiency. Increased RGC death was reported in mice with partial genetic autophagy impairment (AMBRA1 +/-) and subjected to retinal ischemia. Conversely, boosting basal autophagy, either by caloric restriction or pharmacological treatment, improved RGC survival suggesting that the catabolic pathway can be targeted to achieve neuroprotection.

• 3522

Neurotrophins involved in neuroprotective antibody effect

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Summary
Lower levels of different antibodies (abs) can be detected in glaucoma. Several have neuroprotective effects on retinal ganglion cells. Indicated by up-regulation of glutamine synthetase previous studies show that Müller cells (MC) participate in this effect and we aimed to analyse MC participation in more detail. Primary porcine MC incubated with different abs (0.5µg/ml γ-synuclein, 1µg/ml 14-3-3 or GFAP abs for 3h), a control ab (anti-myoglobin) or without added abs. To win conditioned medium containing secreted proteins MC were incubated with serum-reduced medium. BDNF, CTNF, IL6, glutathione, neurotrophin 3, ILG1 and bFGF levels were analysed. Organ cultures were incubated with the conditioned media, medium containing 10ng/ml CNTF or control medium. MC incubated with 14-3-3 (p=0.045) or GFAP (p=0.031) abs showed increased CNTF secretion. In comparison to control explants (740 rgc/mm2) rgc/mm2 quantification showed a significant increase in explants incubated with GFAP abs (1014 rgc/mm2, p=0.04) or 14-3-3 abs (910 rgc/mm2,p=0.07) conditioned medium. Control abs had no effect. We conclude that the neuroprotective antibodies also have an indirect effect on rgcs by increasing CNTF secretion and GS in Müller cells.

• 3523

Role of GSK3 activity in optic nerve regeneration

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Summary
Retinal ganglion cells (RGCs) do not normally regenerate axons upon optic nerve injury. However, inflammatory stimulation (IS) significantly enables axon growth in the injured optic nerve. Here, we demonstrate that optic nerve crush strongly induces inhibitory phosphorylation of GSK3α and GSK3β in RGCs. To investigate the role of GSK3 in this context we tested IS induced regeneration and neuroprotection in conditional GSK3α and GSK3β knockout mice (GSK3α-/-, GSK3β-/-) as well as GSK3αS/A and GSK3βS/A mice expressing resistant GSK3 isoforms to this inhibitory phosphorylation. In contrast to GSK3α-/-, GSK3β-/- markedly potentiated IS induced optic nerve regeneration. On the contrary, IS mediated regeneration was significantly reduced in GSK3S/A mice. These findings suggest that active GSK3 intrinsically limits the outcome of CNS axon regeneration. Thus, treatments activating the intrinsic growth state combined with GSK3β inhibition might be suitable to further improve the regenerative outcome after CNS injury.

• 3524

siRNA and regeneration

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Summary
Crushing the optic nerve induces death of retinal ganglion cells (RGC) by apoptosis, but suppression of CASP2, using a stably modified short interfering RNA CASP2, inhibits RGC apoptosis. Combined delivery of short interfering CASP2 and inhibition of CASP6 using a dominant negative CASP6 mutant activates astrocytes and Müller cells, increases CNTF levels in the retina and leads to enhanced RGC axon regeneration. In mixed rat retinal cultures, dominant negative CASP6 mutant + short interfering CASP2 treatment also significantly increases GFAP+ glial activation, increases the expression of CNTF, and increases the number and length of RGC neurites. These effects are abrogated by the addition of MAB228 (blocks the CNTF receptor) and AG490 (inhibitor of CNTF signalling). Similarly, in the optic nerve crush injury model, MAB228 and AG490 neutralizes dominant negative CASP6 mutant + short interfering CASP2-mediated RGC axon regeneration, Müller cell activation and CNTF production in the retina without affecting RGC survival. We propose that axon regeneration promoted by suppression of CASP2 and CASP6 is CNTF-dependent and mediated through the JAK/STAT signalling pathway.

• 3525

Remyelination of regenerating axons

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Summary

Remyelination depends on adult multipotent progenitor cells, called oligodendrocyte progenitor cells (OPCs) that give rise to remyelinating oligodendrocytes. With age, remyelination slows and axons remain demyelinated, rendering them vulnerable to irreversible degeneration. which eventually contributes to the accumulation of disability in patients with chronic demyelinating diseases, such as multiple sclerosis. The rate limiting step for remyelination in aged individuals is the maturation of OPCs into oligodendrocytes. Here we report that aged OPCs undergo inherent changes that prevent their differentiation. Using alternate day fasting to ameliorate the effects of ageing, we were able to restore remyelination in aged rats. Mechanistically, this involved the molecular rejuvenation of aged OPCs and amelioration of ageing hallmarks. By exposing aged OPCs to metformin we were able to phenocopy the effects of fasting in vitro and in vivo. Our results suggest that implementation of remyelination therapies will require both understanding and overcoming the effects of ageing, as well as finding ways to modulate extrinsic factors to generate a permissive environment for regeneration.

• 3531

Multiple evanescent white dot syndrome

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Abstract not provided

• 3532

Primary stromal choroiditis

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Summary
Optimal outcome measures are necessary to monitor adequately the diverse uveitis entities and follow-up modalities should be tailored according to the disease process. Stromal choroiditis entities are diseases predominantly involving the choroidal stroma, such as Vogt-Koyanagi-Harada disease (VKH) and birdshot retinochoroiditis (BRC), both considered as primary stromal choroiditis because the disease process starts within the stroma of the choroid. Sarcoidosis and tuberculous chorioretinitis are considered as secondary choroiditis, as the choroid is the innocent bystander structure where a systemic disease causes lesions Consequently a follow-up modality capable of optimally evaluating this structure should be privileged in the assessement at presentation and for monitoring disease evolution. Among imaging modalities, the ones best accounting for choroidal stromal involvement are indocyanine green angiography (ICGA) and measurement of choroidal thickness by enhanced depth imaging optical coherence tomography (EDI-OCT). ICGA is more suited for acute and subacute stages of disease, while EDI-OCT useful to follow medium and long-term evolution. The precision obtained with these modalities will be demonsrated.

• 3533

Tuberculosis

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Summary
The diagnosis of intraocular tuberculosis (TB) is often presumptive, made on the basis of suggestive ocular features, evidence of latent or manifest TB, exclusion of other causes of uveitis, and positive response to antitubercular treatment (ATT). The most typical features include serpiginous-like choroiditis and occlusive retinal vasculitis. When the posterior segment is involved, treatment relies on ATT, usually in association with systemic or periocular corticosteroids. Patients should be monitored for response of inflammation to treatment, recurrences, adherence to ATT and treatment side-effects. Clinical assessment of ocular TB at presentation and during follow-up includes grading of vitreous haze, characterization of choroidal involvement, retinal vascular involvement and optic disc changes, and evaluation of anterior chamber cells and flare. Laser flare photometry may be used to monitor anterior chamber inflammation. Ocular imaging tests including fundus autofluorescence, fluorescein angiography, indocyanine green angiography, SD and EDI optical coherence tomography (OCT), and OCT angiography may be very useful in analyzing and quantifying specific TB retinal and choroidal changes.

• 3534

Sarcoidosis

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Abstract not provided

• 3535

Idiopathic multifocal choroiditis

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Summary
Idiopathic multifocal choroiditis (IMFC) is an umbrella term used to describe a specific phenotype of uveitis, which presents multiple inflammatory foci in the retino-choroidal tissue. In the past, such disease has been described with a number of different names, such as punctate inner choroidopathy, multifocal choroiditis with panuveitis and progressive subretinal fibrosis and uveitis syndrome. This chronic, progressive, bilateral inflammatory chorioretinopathy has been recently identified as a unique entity with a variable phenotype both in terms of clinical expression and severity. The sites which are affected most are the retinal pigment epithelium (RPE), outer retinal spaces and choriocapillaris, while the choroidal stroma has a marginal involvement. During the acute stage, choroidal neovascularization (CNV) can occur, representing the most severe complication in such disease. Albeit there is not general agreement for the treatment strategy, steroids and immunesuppressive agents, with or without intravitreal anti-vascular endothelial growth factor (VEGF) drugs depending on the presence of CNV, represent effective methods for the control of IMFC.

• 3541

Optic disk melanocytoma and juxtapapillary melanoma. Diagnosis and management

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Summary
The two most important pigmented lesions of the optic disc include melanocytoma and melanoma. Melanocytoma is a benign nevus and a normal finding in some lower animals such as camels, crocodiles and snakes. It appeas as a dark brown-black mass at the disc, often with disc atrophy and invasion of retina and choroid. Transformation to melanoma is rare. On the other hand, optic disc melanoma generally arises from a juxtapapillary choroidal melanoma and secondarily invades the nerve. There is usually subretinal fluid and overlying orange pigment in the choroidal portion. Of all uveal melanomas, less than one percent invade the nerve. Enucleation is usually necessary. Understanding the differences in these two tumors is important.

• 3542

Juxtapapillary tumors and pseudo-tumors of the retinal pigmented epithelium

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Summary
The most conspicuous retinal pigment epithelium (RPE)-associated lesion, most of which typically occur in the peripapillary region, is known as the combined hamartoma of the retina and the RPE although not all of them extend to the level of the RPE. This congenital lesion, which also has a vascular and an epiretinal component, often will slowly evolve during observation, not infrequently leading to reduced vision from distortion of the macula. It appears as a greyish-brown, slightly elevated fundus lesion. It may be associated with neurofibromatosis type 2, although most seem to be isolated. None of the other RPE lesions occurs predominantly in the peripapillary region, although congenital hypertrophy of the RPE, simple hamartoma of the RPE, adenomas and adenocarcinomas of the RPE, and acquired reactive proliferations leading to RPE hyperplasia can do so. Except for the first one, these are slightly to moderately elevated lesions. Finally, rare congenital pigmentary changes such as pigmented optic disk, thought to be of RPE origin, can sometimes be observed.

• 3543

Vascular tumors and malformation of the optic disk

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Summary
Three main types of angiomatous tumors of the optic disc may be considered:
1. Capillary angiomas associated or not with retinal angiomatosis are considered as a peculiar form of von Hippel or von Hippel-Lindau disease. If they grow they may provoke extensive exudative response resulting ultimately in functional loss of the eye. However treatment is quite challenging. As long as vision is not threatened observation is advised. Direct laser photocoagulation of the tumor will result in severe nerve fiber damage and major loss of visual loss. PDT with or without intravitreal anti-VEGF injections can be considered. The use of proton beam irradiation has been advocated in selected cases. 2. Cavernous angiomas of the optic disc are very rare. They may also be associated with a cavernous angioma of the retina. As most cases are non-progressive, treatment is not advised. Neuro-imaging has to be considered as cavernous angiomas of the retina can be associated with a cerebral angioma. 3. Angioma racemosum or congenital retinal AV malformations. In such cases the optic disc involvement is only part of the fundus lesion.If associated with cerebrovascular and dermatological anomalies the disease is called Wyburn-Mason syndrome.

• 3544

Irradiation induced optic neuropathy

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Summary
Irradiation induced optic neuropathy is a major complication of conservative management of intra-ocular tumors. An irradiation dose of 20 Gy or more delivered on the optic disk is the major risk factor. The final visual acuity in case of irradiation induced optic neuropathy is 0.2 or more only in 25% of the cases. Vascular damage can be located in the retrobulbar arteriovenous network, on the choroidal peripapillary network and on the central retinal artery or vein. In case of retinal ischemia, panretinal photocoagulation and intravitreal anti-VEGF medication is currently used. The preventive use of anti-VEGF and steroids is still controversal.

• 3545

Optic nerve sheath tumors

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Summary
Various neoplasms may originate from or secondarilry involve the meninges surrounding the optic nerve. This course will examine the more common of such neoplasms and review the clinical manifestations as well as management.

• 3546

Optic disk invasion in SNC lymphoma

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Abstract not provided

• 3551

Infectious keratitis: new concepts for old enemies

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Summary
Microbial keratitis (MK) represents one of the main causes of blindness in the world due to corneal scarring, perforation and endophthalmitis. MK remains a challenging public health concern with the need for more effective treatments. Since resistance to therapies has developed over time to several pathogens, ophthalmologists should pay attention to diagnostic procedures. In order to achieve such goal, animal models and novel studies on disease signaling pathways and pathogenesis have given new therapeutic targets. The most common agents include bacteria (ie: Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus pneumoniae and Serratia species), fungi (ie: Fusarium, Aspergillus and Candida species), and protists, such as Acanthamoeba spp. Several innovative treatments have been proposed, such as lipid based therapy and microRNA based therapies. Corneal cross-linking might become an alternative to standard antibiotic therapy for treatment of bacterial and fungal corneal infections, decreasing microbial resistance to antibiotics and other drugs. Moreover, deep anterior lamellar keratoplasty (DALK) seems to be more appropriate in herpetic infections than perforating keratoplasty (PK).

• 3552

Latest in diagnosis and management of fungal keratitis

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Abstract not provided

• 3553

Acanthamoeba keratitis – pKP versus conservative treatment in a 20-year follow-up study

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Summary
This presentation reports data from conservative versus surgical treatment of acanthamoeba cases collected at Dusseldorf University Eye Hospital over the last 20 years.

• 3554

Corneal crosslinking in microbial keratitis

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Summary
The effect of crosslinking (CXL) on microorganisms and on viral, bacterial, mycotic and acanthamoeba keratitis is summarized. Experimental studies have shown that herpes simplex virus will be reduced on a LogMar scale by 4-5 lines, of Staphylococcus aureus, Pseudomonas aeruginosa or Candida albicans strains by 1-2 lines. Previous clinical studies have shown that CXL may heal bacterial, mycotic or even acanthamoeba keratitis, but leads to corneal necrosis in herpetic keratitis. Acanthamoeba cysts also survive CXL therapy. Therefore, CXL may be used as an alternative treatment option in bacterial, mycotic and acanthamoeba keratitis, if they are therapy resistant.

• 3555

Imaging of the ocular surface in corneal inflammation

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Abstract not provided

• 3561

Systematic laser suturolysis in post-operative management in trabeculectomy – early results from pilot study

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Purpose
The early stages of a filtering surgery are usually associated with a number of procedures aimed at sustaining an optimal aqueous humour drainage. One option is to decrease the resistance to outflow by laser suturolysis of the scleral flap. We aim to explore the early effects of systematic suturolysis in efficacy and safety in post-operative trabeculectomies.

Methods
Prospective interventional study enrolling patients undergoing primary trabeculectomies with mytomicinc C (0.4mg/mL) for open angle glaucoma. A protocol in which suturolysis were done routinely if intraocular pressure greater than 10mmHg starting at day 8 post-operative. Only one suturolysis was done at each visit. Intraocular pressure (IOP) - lowering efficiency of each suturolysis was assessed. Safety parameters were also analyzes.
Results
Thirty-one eyes of 27 patients (13 males) were enrolled with a mean age of 68 years. Pre-operative pressure was 25mmHg. Twenty-nine patients underwent a suturolysis on day 8, with an IOP-lowering efficacy of 36%. A second suturolysis, when performed (n=17), had an additional IOP lowering of 27%. At 1 month, 3.2%, 96,8% and 51,6 % of patients had 0, 1 or 2 suturolysis, respectively. Mean IOP at this period was 12.93mmHg. During this period, there were 2 patients with choroidal detachments, and 9 patients needed an additional bleb needling with 5-fluorouracil (5-FU).
Conclusions
Systematic suturolysis may be an effective tool to lower IOP during the early post-operative period. This pilot study suggests an acceptable safety profile, with no significant adverse effects resulting from these procedures. Longer follow-up is needed to determine the sustainability of this IOP-lowering protocol.

• 3562

High-intensity focused ultrasound cyclo-coagulation: a prospective study from a tertiary center

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Purpose
High-intensity focused ultrasound (HIFU) technology aims to achieve selective coagulation of the cilliary body, thus reducing aqueous humor production and lowering intraocular pressure (IOP). This study evaluated safety and efficacy of HIFU cyclo-coagulation using EyeOP-1® device in 44 glaucoma patients.
Methods
Glaucoma patients with uncontrolled IOP despite optimal medication were scheduled for HIFU treatment and followed for 12 months. The primary efficacy and safety outcomes were IOP reduction and major adverse events, respectively. Statistical analyses were performed using STATA v14.1.
Results
Fourty-four patients (23 male) with a mean age of 70 ± 15 years were studied. Mean preoperative IOP reduced from 26.6 ± 3.8 mmHg to 17.7 ± 4.3 mm Hg at month 6 and 17.4 ± 3.3 mm Hg after 12 months ($p<0.01$). Mean number of medications also decreased from 3.1 ± 0.8 at baseline to 2.4 ± 0.9 after 6 months and 2.3 ± 0.5 at month 12 ($p<0.01$). More than 80% of the patients achieved an IOP-reduction of more than 20% compared to baseline, being almost all cases within the target IOP range. One serious adverse event (hypotonia) was registered.
Conclusions
This innovative device seems to be effective in decreasing IOP and to contribute to decrease the number of administered glaucoma drops, with a good safety profile.

• 3563

Socioeconomic deprivation status of patients undergoing Trabeculectomy surgery. A 9-year review at Queen Alexandra Hospital, Portsmouth

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Purpose
To evaluate the socioeconomic status of patients undergoing Trabeculectomy surgery.
Methods
The study population consisted of all individuals who underwent Trabeculectomy surgery (TS) recorded on the Medisoft electronic database. Socioeconomic status was investigated by correlating each individual's postal address with the 2015 Index of Multiple Deprivation (IDM) decile from the UK national database. The IDM decile is a combination of seven indices; income, employment, education skills and training, barriers to housing services, crime, living environment, health and disability, where decile 1 is ranked as the most deprived. In order to account for the socioeconomic status of the population served by our unit, patients that underwent cataract surgery (CS) were used as controls.
Results
582 individuals that were recorded as having TS from Nov 2008 to Apr 2017; Male:Female 1.02:1, mean age 70.9 (SD 11.9) were compared to 39,805 individuals who underwent CS from Jul 2004 to Apr 2017; Male:Female 1:1.51, mean age 76.4 (SD 10.2). The percentage of the population of TS patients belonging to IDM decile 5 and below was 32.82% compared to 39.62% of CS patients. The percentage of TS patients belonging to IDM deciles 1 to 3 was lower than that of CS patients, but higher In IDM deciles 6 to 10. More specifically the percentage of TS patients belonging to decile 1(3.26%) and 2(4.64%) are significantly lower compared to CS patients of the decile 1(6.20%)*** and 2(6.85%)** (***$p<0.01$, **$p<0.05$, two-tailed z-test).
Conclusions
Our results show that more deprived patients are less likely to have a TS compared to CS. This might indicate either that the more deprived individuals present with glaucoma late and cannot be treated surgically, or that the less deprived patients are more concerned about their vision or both.

• 3564

Iatrogenic intraocular pressure elevation after repeated intravitreal injection, a prospective cohort study

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Purpose
To report the rate of intraocular pressure (IOP) elevation after repeated intravitreal injections (IVIs) of anti–vascular endothelial growth factor (anti-VEGF) agents and to assess its evolution over time.
Methods
Our study was a prospective cohort including 221 patients (253 eyes) with exudative age-related macular degeneration (AMD) or diabetic macular edema , undergoing ranibizumab (n =207) or aflibercept (n=44) or bevacizumab (n = 21) IVIs. Patients who received intravitreal or periocular corticosteroid injection were excluded. The incidence of ocular hypertension (OHT) after these injections was investigated with respect to the number of injections, pre-existing open-angle glaucoma, diabetes, YAG capsulotomy, age, and sex.
Results
1721 IVIs was performed. After a mean of 7.3-4.1 IVIs (range 3-62), 10 (4.6%) had IOP elevation more than 25 mmHg and required medical treatment, 1.4% of them spiked above 30 mmHg. 12 patients received medical treatment (10 monotherapies and 2 dual therapies), no surgical or laser treatment was required.Patients with pre-existing glaucoma experienced higher prevalence of OHT (11.9%) and greater rates than the control group (19.3-6.2 mmHg vs 15.6-5.2 mmHg, $p<0.001$). No significant difference was found in the diabetes subgroup (81(??%, $p=0.55$) or in the YAG capsulotomy subgroup (32(??%, $p= 0.44$) compared with the control group. The IOP peak was significantly correlated with the total number of IVIs ($p=0.0002$). Results are consistent with previous work on the oldest cohort.
Conclusions
Serial IVIs may lead to persistent IOP elevation that requires medical IOP-lowering therapy. The risk is correlated with the number of injections and increases in the glaucoma population, therefore should be checked during follow-up.

• 3565

Three year results of iStent + Phacoemulsification cataract surgery for glaucoma

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Purpose
To evaluate long-term safety and efficacy of iStent trabecular micro-bypass stent implantation + cataract surgery (phaco) in glaucoma: A retrospective, interventional, open label study.
Methods
Cases of glaucoma who had phacoemulsification surgery planned, were included. Preoperative and postoperative evaluations included intra-ocular pressure (IOP), topical ocular hypotensive agent use, best corrected visual acuity, perioperative complications and adverse events.
Results
A single trabecular micro-bypass iStent was implanted at the time of phacoemulsification cataract surgery. A temporal incision approach was used in all cases. The results from 35 eyes in 25 patients were analysed for 3 years postoperatively. 49% (n=17) were male. Mean age was 80 ± 7 (SD). 3 eyes had angle closure with previous peripheral iridotomies.
Mean preoperative IOP was 18.5 ± 3.2 mmHg; this was significantly reduced at 12 months (p=0.008), 24 months (p=<0.001) and 36 months (p=<0.001). Mean IOP was 15.9 ± 4.5, 15.0 ± 4.5 and 15.6 ± 3.6 respectively. The mean number of preoperative IOP lowering agents was 2.3 ± 1.0 and 2.5 ± 1.0 at 36 months. This was not significantly reduced at any follow up time period. Secondary interventions were required in three eyes. Cyclodiode laser was required in 2 patients. ALT was carried out in 2 eyes. There were no significant intraoperative complications and no post-operative hypotony. At 36 months, visual acuity was ≥6/12 in 29 eyes (83%).
Conclusions
Trabecular micro-bypass stent implantation during cataract surgery is safe and effective for patients with glaucoma. We measured a sustained reduction in IOP over 36 months in the real world clinic setting.

• 3566

Efficacy and safety of the pars plana clip in the Ahmed valve device in patients with refractory glaucoma

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Purpose
To evaluate the efficacy and safety of the pars plana clip (PPC) in the Ahmed valve tube PC7 inserted via the pars plana in patients with secondary refractory glaucoma.
Methods
Prospective and interventional case series that included 8 patients with secondary refractory glaucoma. The pars plana vitrectomy and the implant of the modified tube were performed during the same surgery. Control of intraocular pressure (IOP) and the development of intra- and postoperative complications were evaluated during the follow-up.
Results
Follow-up time was twelve months in all the patients. Control of IOP was achieved in 85% of patients, and 75% needed no antiglaucoma treatment. The complications that occurred were transient hypotony in two cases, choroidal detachment in two cases, and one case of intraocular hemorrhage and one case of hyphema. No case of tube extrusion was observed.
Conclusions
Our clinical experince suggests that implantation of the Ahmed tube modified with the PPC via the pars plana is safe and effective in patients with secondary refractory glaucomas.

• 3567

Supracilliary Micro-Stent (CyPass®) is associated with lack of disease progression and minimum usage of IOP lowering medications in patients with POAG 2-Years Post-Implantation

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Purpose
Glaucoma is a progressive disease marked by deterioration in the visual field, optic nerve cupping and nerve fiber layer thinning. Glaucoma treatment is aimed at slowing disease progression through control of intraocular pressure (IOP). Minimally invasive glaucoma surgery (MIGS) has become available as a treatment modality offering effective IOP lowering without the high rate of complications associated with traditional glaucoma surgery or the reliance on strict patient adherence required for pharmacological intervention.
Methods
One such MIGS device, a supracilliary micro-stent (MS), implanted during cataract surgery, has recently completed a large 2-year trial in the US (COMPASS trial) - 505 patients were randomized to MS (n=374) or cataract surgery control (n=131).
Results
MS showed sustained 24-month efficacy > than phacoemulsification alone. Importantly, visual fields (VF) did not progress with MS treatment over control (baseline and 2-year mean deviation [MD] -3.4, -3.2 MS; -3.7, -3.2 control) while the percent of patients requiring IOP lowering medications was 15.2% for CyPass group versus 40.9% for control. The percentage of patients with VF progression (≥2.5 dB MD decrease) was 6.7% for MS and 9.9% for control. There was a three-fold lower incidence of disc hemorrhage for MS vs. control (0.5% vs.1.6%), fewer IOP spikes (≥10 mmHg) over the 30-day post-op period (6.4% vs. 20.6%), and fewer subsequent glaucoma surgeries (0.6% vs.3.8%).
Conclusions
While these are post-hoc descriptive observations, the data suggest that the benefits of reliable, effective, sustained IOP-lowering through the use of a supracilliary micro-stent implant may include limiting disease progression in patients with mild-to moderate primary open-angle glaucoma. Additional studies aimed at monitoring progression in patients with the micro-stent are warranted.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Medical Affairs Lead Surgical Glaucoma EMEA at Alcon

• 3568

Follow-up of non-complicated filtering surgeries under ambulatory care with no control at Day 1

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Purpose
In most cases, filtering glaucoma surgery is performed as an outpatient procedure and recommendations suggest performing follow-up at least at Day 1, Day 8, Day 15 and Day 30. As many of our patients have difficulties to come to follow-up and because of the economical cost of medical transportations we decided to evaluate the results of a group of patients without clinical control at Day 1.
Methods
Retrospective monocentric study in the department of ophthalmology. All patients (naïve of surgical treatment for glaucoma) underwent of surgery of a primary open-angle glaucoma in an ambulatory care unit between May 2014 and July 2016. A nurse made a phone call to the patients at Day 1. Clinical controls were due at Day 5 and Day 21. In case of problems detected during the phone call, patients were examined earlier.
Results
One hundred and forty-four eyes (126 patients) were consecutively included in our study. The mean preoperative IOP was 20,4+/-6,4mmHg. After the phone call, only five patients were examined before the first planned control at Day 5. For 3 of them the examination revealed the presence of a hyphema and their topical treatment was changed. The others two patients had no medical modifications. At Day 5, the mean IOP was 10,6 +/- 5,9 mmHg. Thirty-two eyes (22,2%) needed a change in their treatment at Day 5. The mean IOP at Day 21 was 12,9 +/- 4,6 mmHg. Our success rate (IOP<21mmHg with no topical) at day 21 was 95,6%.
Conclusions
We replaced the Day 1 control with a phone call. We didn't notice a substantial rate of complications. The criteria of success of a filtering glaucoma surgery vary according to the different articles in the literature. Our success rate seems to be similar to those we find in the literature and may suggest that the control at Day 1 is not necessary if the surgery is not complicated.

• 3571

Contact lens and ocular surface - After all, its still a foreign body

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Summary
Contact lenses, as indicated by the name, are in direct contact with the ocular surface. CL are swimming within the tear film, between eye ball & palpebral conjunctiva - in the middle of the Ocular Surface Unit. Interactions thus have direct impact on tear film & tissues with the risk of potential side effects (for details please see: WWW.OSCB-BERLIN.ORG).
One main impact is increased mechanical friction by the ´additional structure´. Friction increases during eye movements and blinks when the lid border moves over the contact lens rim and along its anterior lens surface. Limited diffusion of nutritients can occur through the lens, particularly the supply with oxygen is critical for the cornea that depends on gas diffusion – Modern materials have meanwhile decreased this risk. Chemical impacts occur by the lens material or by solutions for lens cleaning & storing. CL are a fantastic medical device for sports and cosmetics which makes them tempting for many patients with refractive errors, not to tell about higher order aberrations that can only be compensated by a contact lens. Still, contact lens fitters & users must be aware of advantages and disadvantages of contact lens wear and both must be balanced in the individual patient.

• 3572

Results of the Scleral Lens in Current Ophthalmic Practice (SCOPE) survey

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Summary
An IRB approved, internet based, 19 question survey was administered via email to 4,633 eye care providers. A total of 989 responses were collected representing a total of 84,735 patients. 723 responses from individuals living in 14 countries who had fit at least 5 patients with scleral lenses were analyzed. A summary of findings from this survey will include descriptions of lens characteristics, recommendations for wear time, disinfection systems, types of solutions used for insertion, demographic characteristics of fitters and incidence of complications.

• 3573

Contact lens related corneal infections

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Summary
Since Czechoslovak chemist Otto Wichterle introduced soft contact lenses in 1961 the achievements of the manufactures and success in marketing increased dramatically. Unlimited availability of purchasing contact lenses in the internet and optic shops, slot machines and supermarkets gave a huge incomes for the industry, however restricted patients from the professional and verbal information regarding wearing particularities, risk factors and proper, at least annual examination by the ophthalmologist. Therefore number of contact lens wearing complications, related to bacterial, fungal and parasitic infections started constantly to grow. In this course we will update guidelines of the conservative treatment, timing and surgical approach of curing such sight- threating conditions. Clinical cases supplemented with high quality photo, video and pathology slides material will be discussed.

• 3574

How to deal with Keratokonus – are there contact lens related problems in sclerals?

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Summary
Scleral lenses have become a popular early treatment choice for patients with keratoconus. In a recent SCOPE (Scleral Lenses in Current Ophthalmic Practice: an Evaluation) study group finding, 34% of practitioners, of 629 survey respondents, chose scleral lenses as their first treatment option for patients with corneal irregularity. Among all treatment choices for corneal irregularity, scleral lenses ranked second only to corneal rigid gas permeable lenses, from those responding. The SCOPE study group then polled a group of keratoconus patients wearing scleral lenses. Of 79 keratoconus patients reporting scleral lens wear in both eyes, 85% were somewhat or very satisfied with their vision. However, these patients also reported experiencing cloudy vision (59%), lens discomfort (67%), and difficulty with lens handling (63%) at some time over the previous two years.

• 3575

Ocular surface reconstruction in severe contact lens associated pathology

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Summary

Limbal stem cells insufficiency (LSCI)
can be primary (PLSCI) or secondary. (SLSCI). LSCI can be total or partial. Sings and symptoms of LSCI are: decreased visual acuity, photophobia, pain, and corneal epithelial defects leading to the loss of transparency. Conjunctivilzation of the cornea is a symptom sine qua non of total SLSCI. 5- 15% cases of SLSCI are after contact lenses wearing. The LSCI in long term contact lens wearers is caused by oxygen level reduction, mechanical irritation and / or inflammatory etiology of corneal limbus. Treatment includes the use of topical corticosteroids, cyclosporin A application of preservative free artificial tears eye drops. Surgical treatment includes: the autologous or allograft limbal stem cell transplantation. Autologous cultured limbal stem cell transplantation is a new method with standardized number of transplanted limbal stem cells. All surgical options of treatment will be discussed.

• 3581

Toric lens implantation in cataract surgery : risk factors of post-operative lens rotation, analysis of 50 cases

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Purpose
Toric lens implantation in cataract surgery has improved with the help of automatic alignment methods, which can determine the immediate postoperative angle with great precision. However, unpredictable misalignment sometimes occurs in the following days. The goal of our study is to identify risk factors of toric lens rotation within the first month of implantation.
Methods
We conducted a prospective, monocentric, descriptive study of 50 eyes in 26 patients operated for cataract by a surgeon experienced in toricity, and implanted a Zeiss Asphina709 implant, during September and October 2016. The intraoperative lens alignment was determined by conjunctival recognition with the Callisto system (Zeiss), coupled with the IOL Master 700 (Zeiss). Lens alignment at one month was determined by blinded double reading on slit lamp photographs using EyeSuite (Luneau). Axial length (AL), anterior chamber depth (ACD), lens thickness (LT), and white to white (WTW) distance were measured with the IOL Master 700.
Results
All implants were aligned as planned at the end of surgery. The average postoperative lens rotation at one month was 4.4° (+/-4.85). There was no statistically significant correlation between implant rotation at one month and AL (p=0.46), ACD (p=0.18), LT (p=0.75), WTW (p=0.67), Age (p=0.57), or Gender (p=0.11).
Conclusions
Our study was not able to identify significant risk factors for postoperative toric implant rotation. Our low average rotation and small sample size may explain why statistical significance was not reached. A larger prospective study is underway. Our study underlines the difficulty to predict which patients will show toric implant rotation and highlights the importance of viscoelastic management at the end of surgery. Understanding and controlling those risk factors may help achieve better refractive results in the future.

• 3582

Optical properties shape visual cortical population receptive fields after cataract surgery independently from subjective quality of vision

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Purpose
To study the impact of changed optical properties on cortical population receptive fields (pRF), psychophysical function and participant reported quality of vision after cataract surgery.
Methods
We studied 30 patients after recent bilateral sequential cataract surgery, using functional magnetic resonance imaging and pRF modelling methods to assess pRF sizes across early visual regions. Ophthalmological and psychophysical evaluation was also performed, and a quality of vision questionnaire was obtained.
Results
We found that subjects with worse optical properties had larger pRF sizes. pRF sizes in the primary visual cortex were also larger for operated subjects with worse contrast sensitivity (p=0.038). Surprisingly, patients who were more bothered by dysphotic symptoms showed lower pRF size fitting interception (p=0.012) and pRF size fitting slopes (p=0.020), showing that objective and subjective quality of vision may dissociate.
Conclusions
Optical properties of the eye influence PRF sizes and both dissociate from subjective quality of vision, suggesting that patients with better cortical resolution may have augmented dysphotic perception, and consequently more visual complaints, in spite of improved optical quality.

• 3583

Prevention of selenite-induced cataractogenesis by sildenafil in rats

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Purpose
To evaluate the effect of sildenafil on selenite-induced cataract formation in a rat model.
Methods
Twenty-six Wistar rat pups were divided into four groups. Seven pups received only selenite on postpartum day 10 (group 1), 7 pups received selenite and additional high dose sildenafil on postpartum day 10 (group 2), 6 pups received selenite and additional low dose sildenafil on postpartum day 10 (group 3), and 6 pups received only saline (group 4, control). All pups were examined for the presence of cataract under the microscope, starting from the day their eyes opened. Nitrite oxide metabolites, advanced oxidation protein products and total sulfhydryl levels were evaluated in both serum and lenticular samples.
Results
In group 3, the extent of lens opacification was significantly less than that of selenite-injected untreated rats (group 1) ($p < 0.05$). None of the rats in group 4 developed any lens opacity. In lenticular samples, nitrite oxide metabolites level was statistically lower in group 3 compared to group 1 ($p < 0.05$). In serum, advanced oxidation protein products and total sulfhydryl levels was statistically lower in group 3 compared to group 1 ($p < 0.05$).
Conclusions
Low dose sildenafil appears to inhibit selenite-induced cataractogenesis in the rat model, and this seems to be caused by the prevention of oxidative damage.

• 3584

Visualization of the light field of multifocal intraocular lenses using a dual wavelength approach

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Purpose
To implement a setup which allows simultaneous visualization of the far and near distance light field of multifocal intraocular lenses (MIOL) with two different wavelengths.
Methods
We used two different laser systems (532 nm and 405 nm) in junction with Powell lenses to create vertical laser lines. One laser line was collimated to simulate far distance imaging while the second laser line was diverging simulating near distance imaging at approximately 0.3 m distance. The MIOL was placed in a glass cuvette filled with balanced saline solution which was doped with two different fluorophores. The fluorophores were chosen to have a large Stokes shift and good separation between their excitation and emission bands. Image acquisition was performed with a slit lamp bio microscope and a digital single reflex camera. We investigated three different IOL types: a bifocal MIOL, a trifocal MIOL and an extended depth of focus IOL.
Results
We found that Propidium iodide and Fluorescein were appropriate fluorophores. Propidium iodide was excited at 532 nm and showed a red fluorescence while Fluorescein was excited at 405 nm showing the green fluorescence. Both lasers required a high power of approximately 30 mW in order to create a visible fluorescent reaction in the cuvette. All three MIOL types provided a good separation between far and near distance light. The regions of overlapping light fields were visible as yellow fluorescence.
Conclusions
In contrast to the previously published setups using a single wavelength with collimated excitation light and axially separated far and near distance foci the current setup allows superposition of the far and near distance foci which is more realistic compared to the situation in the eye. The dual wavelength approach enables an easy optical separation of far and near distance light.

• 3585

Robotic surgery - a new way to perform cataract surgery

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Purpose
To demonstrate the feasibility of robot-assisted simulated cataract surgery
Methods
We performed cataract surgeries on a Kitaro cataract wet lab training system using simultaneously the DaVinci Xi robotic surgical system and a phacoemulsification system. For each procedure, duration and successful completion of the surgery with or without ocular complications were assessed.
Results
Procedures were successfully performed on 27 lens nuclei. Feasibility of robot-assisted simulated cataract surgery is confirmed. The DaVinci Xi system provided the intraocular dexterity and operative field visualization necessary to perform the main steps of the phacoemulsification procedure: corneal incisions, capsulorhexis, grooving, cracking, quadrant removal and infusion-aspiration of the viscoelastic. The intervention of a second surgeon was required for the intraocular injections of viscoelastic, balanced salt solution and intraocular lenses. Mean operative time was 26 minutes. All lens nuclei were removed. Inadvertent enlargement of the main corneal incision caused by the phaco hand piece was observed in 2 cases.
Conclusions
Experimental robot-assisted cataract surgery is technically feasible using the new DaVinci Xi robotic Surgical System combined with a phacoemulsification machine.

• 3621

Contribution of microglia and complement activation to glaucoma progression

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Summary

Glaucoma results in decline and loss of retinal ganglion cells (RGCs), and is associated with microglia and complement activation, with correlation between early microgliosis in the optic nerve head and later optic nerve pathology. Inhibiting microglia activation can protect RGC axons, implicating microglia in glaucoma pathogenesis. Thus, microglia and innate neuroimmune events are critical components of glaucoma. Since microglia express receptors for multiple complement factors, we have investigated how the complement pathway contributes to glaucoma and microglial responses. We tested the therapeutic effect of limiting complement C3 activation using ocular gene therapy. We utilized CR2-Crry, which is the soluble rodent-specific complement inhibitor (sCrry) linked to a complement receptor 2 (CR2) targeting moiety. This was packaged into an AAV2 vector and delivered to the eyes of DBA/2J mice by intravitreal injection. AAV2-CR2-Crry-treatment was highly neuroprotective, with significant preservation of retinal ganglion cells and improved optic nerve integrity. Molecular analysis showed significant shifts in the gene expression profile of FACS-sorted myeloid cells, including upregulation of several potentially protective cytokines.

• 3622

Contribution of microglia-mediated neuroinflammation to retinal degenerative diseases

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Summary

Glaucoma is characterized by optic nerve damage and retinal ganglion cell (RGC) loss. The onset of the disease is accompanied by microglia reactivity and neuroinflammation. Hence, therapeutic strategies designed at reducing microglia reactivity may offer therapeutic benefits to manage glaucomatous damage. We have been evaluating the ability of adenosine A2A receptors (A2AR) blockade in the control of retinal neuroinflammation and neuroprotection in experimental models of glaucoma.

The pharmacological blockade or the genetic inactivation (siRNA in microglial cells or A2AR knockout animal) prevent microglia reactivity, retinal neuroinflammation, and RGC loss. Also, the treatment with a selective A2AR antagonist reverts inflammation and protects the retina. Furthermore, the intake of caffeine, a non-selective antagonist of adenosine receptors, affords protection to the retina and prevents microglia reactivity.

Our results open the possibility for the use of A2AR antagonists as therapeutic options in glaucoma.

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• 3623

Characterizing microglia activation: a spatial statistics approach to maximize information extraction

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Summary

Microglia play an important role in the pathology of CNS disorders, however, there remains significant uncertainty about the neuroprotective/degenerative role of these cells due to a lack of techniques to adequately assess their complex behaviour in response to injury. This talk briefly describes a novel technique for microglia analysis, combining improved immunohistological image analysis with spatial statistical techniques (Ripley-K function and Dixon's χ2-test). Using this approach, a comprehensive set of morphological parameters describing microglia activation status was developed to characterise microgliosis in a murine optic nerve injury model. In addition to monitoring global changes in microglia density, nearest neighbour distance, and regularity index, cluster analyses based on changes in soma size and roundness were used to yield novel insights into the behaviour of different microglia phenotypes. These methods should be considered a generic tool to quantitatively assess microglia activation status, to profile these phenotypic changes into microglia subpopulations, and to map their spatial distributions in virtually every CNS region and disease state.

• 3624

Ocular inflammation as a motor for axonal regeneration in the optic nerve

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Summary

Retinal ganglion cells (RGCs) normally fail to regenerate injured axons and die upon axotomy. However, induction of intraocular inflammation (IS), which is associated with an activation of retinal astrocytes and microglia transforms RGCs into a regenerative state. It delays neuronal degeneration and enables axon growth into the injured nerve. CNTF, LIF and IL-6 released from retinal astrocytes have been shown to be critical for this stimulation. However, the role of microglia has not yet been investigated in this context. Using a pharmacological approach based on CSF1R inhibition we show that almost all microglia are eliminated in murine retinae and optic nerves without affecting peripheral monocytes/macrophages or other cells of the visual system. We surprisingly found that the time course and extent of RGC degeneration after optic nerve crush remained unaffected despite the presence of apoptotic RGC remnants after microglia depletion. In addition, microglia depletion neither affected the induction of regeneration associated genes upon optic nerve injury nor the increased regenerative potential of RGCs upon IS. Thus, microglia are not essentially involved in RGC degeneration or axonal regeneration after acute optic nerve injury.

• 3625

"Inflammaging" in the zebrafish visual system

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Summary

Appropriate modulation of neuroinflammation upon central nervous system (CNS) damage is known to trigger a regenerative response, but the underlying cellular and molecular mechanisms remain elusive. Zebrafish possess high regenerative abilities, yet, also gradually age. They are ideally suited to study the contribution of neuroinflammation to successful regeneration, also in an aging context.

First, we followed the inflammatory response in fish subjected to optic nerve crush (ONC) and revealed a timed induction and resolution of microglia/macrophage (Mi/MΦ) activation. Next, both immunostimulatory/suppressive paradigms indicated that, as in mammals, axon regeneration is stimulated by an induced inflammatory response. Studies addressing Mi/MΦ activation and polarization state will provide further insights. In a second approach, we investigated whether an aged cellular environment affects neuronal survival/axonal regeneration. Detailed analyses in aged fish revealed altered numbers and distributions of Mi/MΦ, indicative of 'inflammaging,' as well as a significant delay in axon outgrowth after ONC. Ongoing studies suggest phenotypic changes of senescent Mi/MΦ underlie this decelerated regeneration capacity in the aged zebrafish CNS.

• 3631

Why should you buy a Shack-Hartman aberrometer for your everyday practice ?

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Summary
Quality of vision is a new comprehensive set of measures that determines visual performance at near, far and in variable light conditions. Good vision is no longer defined by 20/20 vision. The necessity of evaluating vision beyond Snellen acuity has led clinicians and vision scientists to utilize contrast sensitivity, wavefront aberrometry and straylight measurement in most clinical trials related to vision.Recently,the advent of 3D movies and 3D TVs brought us new challenges regarding 3 3 Dimensional Quality of Vision.In this course, experts will share with you their experience on this new frontier of modern ophthalmology

• 3633

Emerging applications of adaptive optics retinal imaging

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Summary
Adaptive optics (AO) is an optical technology used in astrophysics to compensate the turbulences of the atmosphere which alter the quality of the images.
That principle has been applied to various image modalities (OCT, SLO, Flood, etc) permitting the observation of the retina's finest structures at the microscopic scale. The rtx1 is the first, and until now, the only compact AO retinal imaging medical device available on the market. Based on an en-face near infrared imaging approach, the rtx1 allows to observe the cone photoreceptors mosaic, the lumen and the walls of the retinal arterioles, and the pores of the lamina cribrosa. It is now possible to detect the early signs of diseases and to follow-up the effect of a treatment.
Thanks to its ergonomy for the patient and the user, the rtx1 is more and more adopted by clinical research centers worldwide to investigate various medical fields. We will present here recent results in the field of ophthalmology but also in translational research using AO retinal imaging to investigate pathologies in cardio-vascular and neurological diseases.
Conflict of interest
Any post or position you hold or held paid or unpaid:
Employee of Imagine Eyes

• 3634

High resolution anterior segment OCT and lamellar corneal surgery

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Abstract not provided

• 3641

Small fatal choroidal melanomas: A survey by the European Ophthalmic Oncology Group

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Purpose
To assess retrospectively characteristics of smallest choroidal melanomas that metastasized.
Methods
Ten ocular oncology services submitted data anonymously through a secure website. Eligible were patients with a choroidal or ciliary body melanoma <3 mm in thickness and <9 mm in diameter that developed metastases. Of 57 patients submitted, 49 fulfilled all eligibility criteria.
Results
At treatment, median age was 57 years (range, 26-81), tumor thickness 2.3 mm (range, 0.4-3.0) and diameter 7.2 mm (range, 3.0-9.0). Fifteen tumors (31%) were observed before treatment, and 13 of them grew a median of 0.5 mm (range, 0.1-1.2) in thickness and 1.0 mm (range, 0-3.0) in diameter in a median of 7 months (range, 2.5 months-5.8 years). Fifty-seven percent were >2 mm in thickness, 62% had subretinal fluid, 77% caused symptoms, 51% had orange pigment, and 79% a margin within 3 mm of the optic disk (25%) touched disk margin). The number of high risk characteristics was 0 for 10% of the tumours and ranged 1-5 for 12%, 29%, 31%, 14%, and 4%. Local recurrence developed in 18% of eyes. By study design, all developed metastatic melanoma. Cumulative incidence estimate for metastasis developing was 14% (95% CI, 6-25) by 2 years, 51% (95% CI, 36-64) by 5 years, and 86% (95% CI, 72-93) by 10 years after treatment. Median relapse-free survival was 4.5 years.
Conclusions
Ten percent of the smallest choroidal melanomas that metastasized had no high risk characteristic for growth. One third was followed for growth, which may or may not have influenced outcome. We found only 5 melanomas in 10 centres that were <4.5 mm (3 DD) in diameter and none that was <3 mm and metastasized.

• 3643

Absence of nuclear Programmed cell death 4 as an indicator of poor prognosis in uveal melanoma patients

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Purpose
Uveal melanoma (UM) is the most frequently occurring intraocular malignancy in adults. Arising from the uncontrolled proliferation of melanocytes in the choroid, ciliary body and iris, UMs have a strong propensity to metastasise to the liver, where they are fatal. In a previous study, proteomic examination of UMs at either a high or low risk of developing metastasis identified the down regulation of Programmed Cell Death 4 (PDCD4) levels with increasing metastatic risk.
Methods
This study examined PDCD4 protein expression and subcellular localisation in UM patient samples by immunohistochemistry (IHC). 165 primary (PUM) and 18 metastatic UM (MUM) samples with full clinical, histological and genetic data were included in the study. Slides were assessed and scored according to (A) percentage of tumour cells with cytoplasmic PDCD4 expression; (B) intensity of cytoplasmic staining and (C) percentage of PDCD4 positive tumour nuclei.
Results
In PUM and MUM samples, PDCD4 was localised primarily to the cytoplasm. An equal percentage of primary and metastatic samples expressed nuclear PDCD4 (28%). Loss of nuclear PDCD4 was strongly associated with factors associated with a poor prognosis, in particular, monosomy 3 (p=0.014) and loss of nuclear BAP1 (p=0.012). PUMs with nuclear PDCD4 in ≥10% of tumour cells had an improved survival time compared with PUMs with <10% nuclear expression of PDCD4 (p=0.105).
Conclusions
The tumour suppressor PDCD4 shuttles between the nucleus and cytoplasm to exert its effects in normal cells. In PUM samples, an absence of nuclear PDCD4 localisation was associated with a poor outcome. Further functional studies are necessary to determine how PDCD4 localisation influences UM cell behaviour.

• 3642

miRNA profiling of uveal melanoma exosomes as a metastatic risk biomarker

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Purpose
Uveal melanoma (UM) is the most common primary intraocular malignancy in adults. It is a highly aggressive cancer in which nearly 50% of patients die from liver metastasis. UM patients can be divided into 3 groups based on their genetic profile and disease free survival; the low risk, intermediate risk and high risk tumours. Recently, we have shown that high risk patients can be identified based on the expression of five miRNAs. Since tumour tissue is not always available and biopsies are not without risk, it is important to develop a method that can identify high risk patients in a non-invasive manner. Exosomal miRNAs are an excellent candidate for this application.
Methods
Exosomes were isolated from the cell culture medium of a non-metastatic and high risk metastatic UM cell line by ultracentrifugation and were characterized by western blot, electron microscopy and Nanosight Tracking Analysis (NTA). RNA was isolated from exosomes by the Qiagen RNeasy micro kit and quantified by an Agilent bioanalyzer. Subsequently, miRNA expression was measured by Taqman miRNA qPCR assays.
Results
All exosome samples isolated from cell medium showed expression of CD81. Bioanalyzer confirmed the absence of ribosomal RNA and an abundance of small RNAs. qPCR analysis shows changes in the expression of some classifier miRNAs in exosomes extracted from cell lines. Showing that the classifier miRNA signature in UM cells partially overlaps with the miRNA signature in exosomes secreted by UM cells.
Conclusions
These exosomal miRNAs show great promise as a reliable predictor of disease free survival in UM. Next step is to detect these exosomal markers in blood of UM patients as this will enable us to provide all UM patients with a prognosis in a non-invasive manner.

• 3644

Nestin expression in primary and metastatic uveal melanoma

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Purpose
Nestin, a member of the intermediate filament protein family, has been described as a putative cancer stem cell marker (CSC) in a variety of tumours. In particular, increased Nestin expression is associated with an aggressive and primitive tumour phenotype as well as a poor prognosis in cutaneous melanoma. In this study, we examined the expression of nestin in primary (PUM) and metastatic uveal melanoma (MUM) samples, and correlated the findings with histological, clinical and survival data.
Methods
Nestin expression was assessed by immunohistochemistry in 141 PUM and 26 MUM samples; 11 of the PUM cases were matched with their corresponding metastases. The percentage of tumour cells staining positively for nestin was scored by three independent observers. Statistical analysis of all data was performed with SPSS
Results
Increased levels of nestin in PUM samples were associated with known poor prognostic parameters, including epithelioid cells (p<0.001), closed loops (p=0.001),increased mitotic count (p<0.001), monosomy 3 (p=0.007) and chromosome 8q gain (p<0.001). Positive staining was identified in both the cytoplasm and membrane of tumour cells. PUM with nestin expression levels above a cut-off value of 10% (as determined by ROC analysis) were associated with a significantly reduced survival time (Log rank, P=0.002). In the MUM, a higher nestin percentage combined with poor prognostic markers led to a shorter survival time following the development of metastases.
Conclusions
In conclusion, increased nestin expression in PUM is an independent predictor of a tumour phenotype associated with metastatic progression and reduced survival time at metastasis.

• 3645

Protein kinase inhibitors for targeting tumor-initiating cells in uveal melanoma

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Purpose

Uveal Melanoma (UM) is the most common intraocular tumor in adults. Surgery and brachytherapies have improved survival rates, but up to 40% of patients develop liver metastases.

Mutations in the Gαq family members GNAQ and GNA11 are present in 80% of UM tumors whereas BRAF mutations are much less common. Consequently, Protein Kinase signaling pathways are dysregulated and specific targets can be identified for precise therapeutic approach. On the other hand, it has been proposed that tumors contain a specialized subset of cells defined as tumor-initiating cells (TICs) that may be responsible for de novo resistance to drugs and metastatic disease. Thus, targeting TICs may be imperative for achieving a cure.

Methods

To this end, we performed an in vitro screening using the Screen-Well® Kinase Inhibitor Library (BML-2832-0100) on TIC-enriched populations of UM cells harboring either GNAQ /GNA11 or BRAF mutations.

Results

These UM-TICs have the capacity to self-renew and generate tumor spheres (melanospheres) in low-adherent culture conditions. Furthermore, they display stem cell-like features such as high expression of CD133, CD44, Nestin or ABCB5 specific markers. The metastatic ability of OMM-2.5-enriched TIC cells is currently explored in vivo after their orthotopic injection into the uvea of HL-SCID mice.

Our results revealed that metastatic and TIC-enriched populations were more resistant to antiproliferative effects of kinase inhibitors. Several kinase inhibitors such as Tyrphostin 51 (EGFRi), DES (PKCi), DRB (CK2i) and ML-9 (MLCKi) differentially affected growth and survival of TIC-enriched population from parental cell line Mel270.

Conclusions

Taken together, we showed that EGFR, MAPK, PKC and PI3K signaling pathways are activated in TICs and their respective inhibitors may represent attractive therapeutic candidates for metastatic UM.

• 3646

Macular features assessed by optical coherence tomography-angiography after proton beam therapy for choroidal melanoma

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Purpose

To characterize the macular features of patients treated with proton beam therapy for choroidal melanoma (CM), using the optical coherence tomography-angiography (OCTA).

Methods

Observational, retrospective, study included patients treated with proton beam therapy for a small CM. All the patients had undergone a full exam including: visual acuity, optical coherence tomography (OCT B-scan) and OCTA (Spectralis Heidelberg, Germany) focused on the 10 central degrees. Only patients that had received 100% of the dose to the macula were included. Vascular features of both plexuses, of the choriocapillaris and the choroid were analyzed in OCTA.

Results

37 patients had undergone an OCTA following proton beam therapy for a small CM. Only 17 patients (9 men and 8 women) that had 100% of the dose to the macula were included in this study. The mean age of the patients was 56.6 years (28-86). The mean follow-up duration was 35.8 months (11-72 months). The mean tumor thickness was 3.39 mm (1.3-7 mm). 13 patients (76.5%) had a clinical radiation maculopathy, 8 patients (47.1%) had macular cysts on OCT B-scan. All the patients (100%) had abnormalities on OCTA. Cysts were found in 9 patients (52.9%) mostly in the deep capillary plexus. The loss of the choriocapillaris was observed in 15 patients (88.2%). Choroid vessels were diminished (by size and density) in the macular area in 13 patients (76.5%). .

Conclusions

OCTA permits earlier detection of micro vascular alterations on both plexuses that the post radiation origin is highly probable du to the important doses receivedPatients treated with proton beam therapy for CM with 100% of the dose to the macula, present some alterations at both plexuses but also a vascular rarefaction of the choriocapillaris and of the choroidal vessel.

• 3651
Primary mitochondrial optic neuropathies

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Summary
Primary mitochondrial optic neuropathies are a genetically heterogeneous group of conditions, with autosomal dominat, recessive, X-Linked and mitochondrial inheritance. These optic neuropathies are usually caracterized by bilateral, symmetrical, painless reduced visual acuity, color vision defects, central or centro-caecal scotoma and optic disc pallor. The dominant (dominant optic atrophy, DOA) and the mitochondrial forms (Leber's hereditary optic neuropathy, LHON) are the commonest. The most frequent gene mutation responsable for DOA is the OPA1. OPA 1 is also associated with the allelic condition syndromic dominant optic atrophy, DOA+ syndrome.

• 3652
Retinal involvement in mitochondrial diseases

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Summary
Purpose: To describe the retinal phenotypes of mitochondrial conditions.
Methods: A case presentation format will be used to illustrate different retinal conditions due to mitochondrial mutations. Both clinical and electrophysiological phenotypes as well as genotypes will be discussed.
Results: Phenotypes and genotypes of mitochondrial diseases leading to retinal involvement are very different. The degree of retinal involvement is very variable, both between families and within the same family.
Conclusions: Retinal involvement of mitochondrial disease is very diverse. Specialised imaging, psychophysics and visual electrophysiology are important tools to estimate severity of involvement.

• 3653
Chronic progressive external ophthalmoplegia

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Summary
Chronic progressive external ophthalmoplegia (CPEO) is a slowly progressive extraocular muscle disorder characterized by bilateral, usually symmetrical, limitation of eye movements and ptosis. This classical manifestation of mitochondrial disease can develop either in isolation or more frequently, in association with other multisystemic features (CPEO plus). An expanding list of nuclear-encoded mitochondrial genes is now known to cause CPEO phenotypes, predominantly in the context of multiple mitochondrial DNA (mtDNA) deletions, but also as part of mtDNA depletion syndromes. This genetic heterogeneity can result in diagnostic delays, which is further compounded by the clinical challenges inherent in distinguishing CPEO from other disorders that also present with external ophthalmoplegia and ptosis. Corrective ptosis surgery can be a highly effective treatment and alleviating symptoms of diplopia can make a significant difference to the patient's quality of life.
Conflict of interest
Any consultancy arrangements or agreements:
GenSight Biologics

• 3654
Neurological involvement in mitochondrial eye diseases

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Summary
The most frequent mitochondrial eye diseases are Leber's Hereditary Optic Neuropathy (LHON) and Dominant Optic Atrophy (DOA). They are both characterized by optic atrophy due to retinal ganglion cell loss. Extra-ocular features have been described in both diseases. In particular, neurological involvement has been reported even though, for some of the neurological features in LHON, the possibility of a chance association is still debated.
In LHON the main neurological features are: 1) Multiple Sclerosis "like" phenotype 2) Movement disorders including dystonia, parkinsonism and myoclonus 3) Peripheral neuropathy 5) Migraine 6) Hearing loss 6) "LHON-MELAS-Leigh" overlap.
In DOA, the "plus" subtype is a well-recognized entity characterized by the occurrence, over the decades, of optic atrophy and sensorineural deafness, polyneuropathy and myopathy with chronic external ophthalmoplegia, and in some families Parkinsonism and dementia. DOA "plus" is typically associated with missense mutations affecting the OPA1 GTPase domain, and skeletal muscle is remarkable for COX deficient fibers and mtDNA multiple deletions. More recently, a Multiple Sclerosis "like" phenotype has been described also in DOA.

• 3655

Patient management – genetic testing and practical considerations

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Summary

Mitochondrial diseases frequently manifest with ocular signs involving the optic nerves, extraocular muscles and retina; therefore, the ophthalmologist is, in many cases, the first specialist consulted. During the last decade, it has been shown that even disorders originally thought to be an isolated ocular entity may display a broad spectrum of overlapping phenotypes affecting multiple organs. This makes genetic counselling challenging. Ophthalmic examination using state of the art imaging, such as optical coherence tomography and autofluorescence, may identify subclinical disease, therefore ophthalmologists can play an important role in guiding further investigation and molecular testing. It is becoming apparent that clinical classification should be associated with the underlying genetic defect to improve our understanding of genotype-phenotype correlation for these conditions. Supported by AZV 16-32341A

• 3661
Anatomy and physiology of the anterior eye segment

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Summary
Non-invasive, non-contact imaging methods are essential for diagnostics and therapeutic interventions at the anterior eye segment. Given by the properties of the ocular tissues, optical modalities like optical coherence tomography and confocal microscopy are ideally suited for visualizing the morphology of the anterior segment of healthy and diseased eyes with resolutions in the micrometer range.
Furthermore, advances in light source technology allow for high resolution imaging of functional parameters as for example the precorneal tear film thickness and, based on the sample reflectivity, also the evaluation of the tear film lipid layer. The presented cases show the potential of the techniques to help in clinical decision-making and follow-up after treatment and surgical intervention, respectively. The results indicate that the technological progress in the OCT field and new imaging developments can help to gain a novel insight in the physiology and pathophysiology of the human anterior eye segment.

• 3662
Doppler OCT - functional imaging in the retina

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Abstract not provided

• 3663
OCT Angiography

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Summary
OCT has become already a standard diagnostic tool in ophthalmology. Despite its continuous improvement in performance, its tissue specificity is still limited, as the contrast mechanism relies on local backscattering changes only. Functional extensions of OCT, in particular Doppler OCT and angiography partially mitigate this limitation. Doppler OCT provides quantitative blood flow in a depth-localized manner. Abnormal changes in total retinal blood flow have been related to major retinal diseases and their assessment might therefore be an early biomarker of disease onset. Recent developments overcome the necessity to determine the Doppler angle for flow quantification. Fast OCT sequences resolve the pulsatile blood flow in circumpapillary vessel cross sections, that allow to determine the total retinal perfusion in reliable manner. OCT Angiography (OCTA) has gained much attention, due to its easy operation, and impressive vascular detail. It operates in a fully non-invasive manner, directly on OCT data, and as such as naturally co-registered. Several examples are given to highlight recent developments to improve speed, field-of-view and penetration depth.
Conflict of interest
Any research or educational support conditional or unconditional provided to you or your department in the past or present:
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• 3664
Multifunctional OCT for preclincial imaging

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Summary
Functional extensions of optical coherence tomography (OCT) expand image contrast and enable quantitative measurements of optical tissue properties, improved segmentation of tissue morphology and the assessment of physiological parameters. In this presentation, we will discuss applications of multifunctional OCT including high-resolution polarization-sensitive OCT and OCT angiography for preclinical studies of ocular disease models.

• 3665

Photoacoustic imaging and its preclinical application in ophthalmology

LIU M

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Summary

Photoacoustic imaging is an emerging optical imaging technique featuring optical illumination and acoustic detection. Short laser pulses deposit their energy in optical absorbers where light energy is converted to acoustic energy. Therefore photoacoustic imaging is a direct way of absorption mapping in 3D. Since absorbers, or chromophores, have unique absorption spectra, spectrascopic photoacoustic imaging can distinguish different absorbers by wavelength unmixing. In preclinical and clinical settings, photoacoustic microscopy, one major modality in photoacoustic imaging, can be used for ophthalmic imaging. Without the use of contrast agents, two absorbers can be distinguished: melanin and hemoglobin. Even though the application of photoacoustic microscopy in ophthalmic imaging is relatively new and still in its primitive phase, here we can see how photoacoustic microscopy can reveal the details of blood vessels and melanin in the eye. We will also discuss the potentials of photoacoustic imaging for ophthalmology.

• 3671

The earliest eyes on Earth

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Summary
Vision had to start somewhere. During the Precambrian Era, life existed in a quiet gloom where most creatures were blind. There was no need to be camouflaged, warn off predators or seduce a partner with bright patterns. Then, at the beginning of the "Cambrian Explosion", 540 million years ago, life opened its eyes. Given the tremendous adaptive advantage conferred by sharp vision for avoiding predators and locating food, there must have been tremendous evolutionary pressure to elaborate and refine visual organs. Through well-preserved Cambrian fossils (Trilobites, Anomalocaris and Fuxianhuia protensa) we will see the evolution of vision through the world's oldest eyes. With very well-developed compound eyes, these earliest animals had a complex visual system. With up to 16,000 lenses in each eye, some of these animals saw their world with exceptional clarity whilst hunting in well-lit waters. Only a few arthropods, such as modern predatory dragonflies, have similar resolution. We will show extraordinary fossils to reveal exquisite details about the earliest eyes on Earth.

• 3672

Eye of Horus

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Summary
Horus was the Egyptian god of light, the son of Osiris and Isis. He was regarded as the rising sun, born afresh daily and the symbol of renewed life. In cultures that practiced magic eyes were the symbol of great importance. The ability to see enables to experience and explore the surrounding world and interact with it. In ancient cultures stars especially the sun and the moon were called the eyes of heaven. The sun was the face or eye of Indian solar deity Surja, the eye of German deity Odin or Iranian deity Ahuramazda. The right eye of Egyptian God Horus represents the sun, left eye the moon. In The "Book of the Dead" (around 1500 B.C.) which is a collection of spells which enable the soul of the deceased to navigate the afterlife, it is written: the eye of god Horus gives eternal life and protects me when it is closed". The eye of god Horus became the symbol of the power of healing and revival. It was believed that a talisman representing the eye of Horus has the power to protect from charm and therefore was used by witch doctors for healing session and during funeral ceremonies.

• 3673

The eye according to Byzantines medical writers

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Summary
The scientific foundation of ophthalmology as a medical specialty can be located in the Alexandrine period, since it is there we find evidence of diagnosis and therapy in the systematic knowledge of the eye. Many of the documents from that period have been lost, but the knowledge was preserved in the writings of Galen (129-216 AD) and his successors. Byzantine medicine (324-1453 AD) preserved ancient medical knowledge and transferred it either directly, or via an Arabic translation, into Latin. This was the natural connection between antiquity and the Renaissance, one that has been greatly appreciated
in studies of the history of medicine. This study presents a detailed analysis of early Byzantine medical sources and the ancient medical tradition upon which they drew. There
follows a discussion of knowledge relating to the eye, its clinical description, diagnosis and treatment.

• 3674

Artistic depictions of the eyes and blindness throughout history

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Summary
Sight has always been the fundamental means by which we human beings relate to our environment and to each other. We use our eyesight to perceive, to understand, and to ascertain the truth. For thousands of years, artists have depicted the theme of blindness and have portrayed its transforming effects. The eyes of the blind are frequently illustrated no differently from those of other, presumably sighted, figures. In addition, since neither most artists nor observers are ophthalmologicly sophisticated, with rare exceptions, it is highly unusual for the artist to depict authentic ocular pathology. The various methods of artistic representation of blindness are given with numerous examples. While it is clear that the artistic renderings of blindness, depicted across various media of expression, are extremely varied, there have been some amazing constants throughout recorded history, even though medical understanding of, and our ability to restore, vision, has undergone almost incomprehensible change. Oscar Wilde said: "…art imitates life." It is clear that the fear of blindness and the appreciation of our precious gift of sight, as depicted in art, have changed little over the ages.

• 3675

The evolution of oculoplastic operations

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Summary

Although oculoplastic surgery has only recently been recognized as a subspecialty, the early origins of the interrelationship between plastic surgery and ophthalmology, trace back to the 22th century B.C. Minor eyelid operations performed by Babylonian and Assyrian physicians as well as eyebrow stitching descriptions, contained in the Egyptian Papyrus, serve as the earliest surgical attempts at oculoplastic surgery. Other ancient civilizations also provided accurate descriptions of a number of eyelid diseases, including their surgical treatment. During the Greco-Roman period, several local flaps, e.g. the double-pedicled and the V-Y advancement flap, were first described. Byzantine physicians compiled, standardized and enriched the medical knowledge of their Greco-Roman predecessors, contributing with the surgical treatment of trichiasis, lagophthalmos, ectropion, hydatids, epicanthus, pterygia, lacrimal fistulae and eyelid adhesions. The following centuries, a variety of surgical techniques were developed. Thus, modern oculoplastic surgeons, have incorporated numerous reconstructive procedures into their practice, ranging from simple local flaps to complicated mucosal or composite flaps and selective microvascular procedures.

• 3681

Lifetime Study in mice: radiation-induced cataract

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Summary

We did a lifetime study in irradiated and control mice with a follow up time until 24 months post irradiation with repeated in vivo analysis of the lens density and the retina. Mice of different genetic constitution (wild-type, Ercc2+/-) were acutely whole body irradiated with low doses of ionising radiation (0, 63, 125 and 500 mGy) and a low dose rate (63 mGy/min). Lens opacification was analysed monthly by Scheimpflug imaging and the retinal fundus and thickness was analysed by OCT. At different time points (4 and 24 hours, 12, 18 and 24 months post irradiation) mice were sacrificed and eyes were analysed by histology and immunohistochemistry.

Mice of all groups, even the DNA repair helicase deficient mice (Ercc2+/-), did not develop clinically relevant radiation-dependent lens opacities. Only an age-dependent increase of lens density was identified. Consequently, no major morphological changes were visible in the eye histology of all mice. Immunohistochemical staining against DNaseIIb revealed no differences between the groups as well as 8-OHG staining resulted in similar ROS levels in all irradiation groups. However, non-irradiated Ercc2+/- mice showed an increased level of oxidative stress compared to wild-type mice.

• 3682

Radiation-induced cataracts

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Summary

The radiosensitive nature of the lens has been increasingly reported, although the exact mechanistic details of the radiation response pathways for cataractogenesis are unclear. Radiation-induced DNA damage and the subsequent impairment of repair pathways within the lens epithelium are involved. Here, two distinct regions of the murine lens epithelium have been analysed for their differences in double strand break (DSB) repair responses to ionising radiation. The responses of epithelial cells located at the anterior pole (central region) have been compared to those in other locations, including the proliferative compartment, and including the very periphery of the monolayer (peripheral region). Described here are the responses between the two regions, across four strains, over a low dose (0 – 25 mGy) X-irradiation range up to 24 hours. Damage visualised through biomarker 53BP1 staining was present across the epithelium, repair kinetics appear non-uniform. Epithelial cells in the central region have significantly more 53BP1 positive foci. In this study, BALB/c were identified as the most suitable strain for low dose ionising radiation exposure investigation.

• 3683

The role of the Shh signaling pathway in radio-induced cataractogenesis

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Summary

Besides the well-known role in cancer, Shh signaling pathway direct cell proliferation, cell fate determination and EMT, remaining largely expressed in the stem cell compartment of adult tissues. Recently, we proposed Ptch1+/- mice as a relevant radiation-induced cataract mouse model. These mice, develop cataract with a very high incidence (45.2%) and short latency after irradiation with 3 Gy of x-rays, when radiation is delivered during the early stage of postnatal lens development. Molecular analyses suggest that Shh and TGF-ß signaling cooperate to promote Ptch1-associated cataract development by activating EMT and converging on Nanog. Furthermore, using a range of decreasing radiation doses to assess the cataract response in these mice, nonlinear biological responses were observed using doses ≤ 1 Gy, with a suggestion for borderline effects at 2 Gy, both for gross cataract development and for activation of the genetic pathways involved in the molecular pathogenesis of Shh-associated cataract.

These findings highlight a novel function of Shh signaling unrelated to cancer and provide a new animal model to investigate the molecular pathogenesis of cataract formation.

• 3684

Radiation-induced cataracts

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Summary

The eye lens is not only a radiosensitive tissue, but also one where the response to ionising radiation (IR) is cell location specific. Moreover this behaviour affects the emergent properties of the cells in the lens epithelium causing deregulation of the normally geometrically constrained epithelial cells as that transition from the germinative zone to the meridional rows at the very periphery of the lens. Epithelial cells in the germinative zone are, however, much slower than either the central epithelial cells or isolated blood lymphocytes from the same animals in their repair of double strand breaks (DSBs). Here we describe the emergent cell behavior of peripheral lens epithelial cells that affects the "roundness of the lens". This is an example of a nonlinear biological response induced by low dose IR exposure. It is a consequence of a non-uniform increase in cell proliferation in the lens epithelium. The measurement of epithelial cell density and cell proliferation rates in the lenses of IR exposed animals is a key underpinning technology. We present a rapid imaging method to measure cell proliferation and density in the IR exposed lens and determine how IR affects the emergent properties of cells in the lens epithelium.

• 3711

The pre-Descemets corneal layer (Dua's layer): Controversy and clinical applications

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Abstract not provided

EVER 2017 SATURDAY SEPT 30

• 4111

Surgical management of diabetic macular edema - For

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Summary

Diabetic retinopathy may require surgical management in case of vitreomacular interface disorders. Indications and prognostic factors will be discussed.Furthermore, after many anti-VEGF without any reduction of diffuse macular edema, surgical approach may be proposed. In histopathological analysis, myofibroblasts have been detected and cause the contraction of vitreoretinal interface disorders affecting visual acuity. Removal of epiretinal membrane associated with ILM peeling is essential in these cases in order to eliminate the contractile elements.

• 4112

Surgical management of diabetic macular edema - Against

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Summary

Diabetic macular edema (DME) is the leading cause of visual impairment in patients with diabetes mellitus. Disruption of the blood-retinal-barrier has been implicated to the pathogenesis of DME. In addition, vascular endothelial growth factor (VEGF) and other inflammatory mediators have been found to be major contributors to angiogenesis and to increased vascular permeability, leading to DME.

Although surgical management of DME has been proposed as a treatment option, since it releases vitreous traction at the macula and improves oxygenation of the posterior segment, complications and persistence of macular edema postoperatively put this treatment modality in suspicion. In fact, eyes with refractory edema and no observable traction seem less likely to improve after surgical treatment. Moreover, in the majority of cases, there is no functional improvement, despite the encouraging anatomical results.

Nowadays, anti-VEGF agents still remain the standard of care in the management of DME, while intravitreal steroids gain interest as well. In cases, in which DME coexists with vitreoretinal interface pathology, pars plana vitrectomy in selected cases may be useful.

• 4113

Ocriplasmin in the treatment of vitreomacular traction - For

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Summary

Enzymatic vitreolysis for the treatment of vitreomacular traction (VMT) and small macular holes with traction instead of pars plana vitrectomy is a hot debate currently.

Ocriplasmin may give a fast and easy solution to the VMT and small macular holes with traction with minimal patient's discomfort and only trasient side effects.

Pars plana vitrectomy the only alternative management to the above mentioned retinal diseases it is an invasive procedure, may be traumatic to the macula, and carries a risk of post-operatively complications such as an epiretinal membrane, nerve fiber layer defect and cataract formation.

Therefore enzymatic vitreolysis should be considered as a strong treatment option.

• 4114

Ocriplasmin in the treatment of vitreomacular traction - Against

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Summary

Ocriplasmin is an enzyme that dissolves vitreal proteins as well as possibly proteins associated with visual function in the retina, choroid, and lens. The MIVI trials concluded that intravitreal Ocriplasmin was superior to an injection of placebo in altering the vitreoretinal interface of affected eyes, although it was accompanied by some, mainly transient, ocular adverse events. There are anecdotal reports of adverse events as well as early reports in the literature of previously unreported side effects, such as enlargement of the macular hole, zonular instability, and localised non-rhegmatogenous retinal detachment. A recent BEAVRS survey in the UK reported lower macular hole closure rates and higher than expected adverse events. Furthermore, there have been conflicting views on the safety of Ocriplasmin with changes in the ellipsoid zone seen on OCT and changes seen on ERG indicating photoreceptor damage. The practical question asked by the retina specialist is the following: observe, inject or operate? Increased numbers of real world experience with Ocriplasmin and post marketing surveillance studies are needed.

• 4115

Anti-VEGF intravitreal injections in the management of radiation maculopathy - For

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Summary
Radiation maculopathy is a sight threatening complication of radiation treatments for tumours of the eye and surrounding tissues. Many treatments have been tried for radiation maculopathy to variable success and the choice of agent depends on a judgement of risk to benefit. The use of lasers and steroids has become less prominent in recent years. Current first line has become anti-VEGF injections, after the success in other macular disorders that are prone to neovascular or exudative vasculopathy. Large prospective and retrospective series and case controlled studies show efficacy in maintaining or improving visual acuity and reducing the extent of macular edema. In addition, the preventive use of anti-VEGF injections will also be discussed.

• 4116

Anti-VEGF intravitreal injections in the management of radiation maculopathy - Against

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Summary
Radiation maculopathy (ischaemic or oedematous) is a dose-dependent complication after radiation therapy associated with vascular decompensation caused by radiation damage. It develops primarily in patients treated for choroidal melanoma or other intraocular tumours following plaque brachytherapy or proton beam radiotherapy though it has been reported following epimacular brachytherapy for AMD patients or regional radiotherapy in other cases of malignant neoplasia.
Though anti-VEGF treatment has been proposed in the management of radiation maculopathy there are inherent problems in its use. The pharmacokinetics of anti-VEGF necessitate repeated, and an increased number of intravitreal injections. The efficacy of anti-VEGF has been most robust when used preventively
Alternative treatments include macular laser, triamcinolone acetonide injections and more recently dexamethasone implants. The former had good anatomic results and the latter have comparable results with anti-VEGF agents in smaller series with less injections. Dexamethasone implants also had a more favourable outcome in cases non-responsive to bevacizumab. Laser could still have an important preventive role especially in the treatment of ischemic areas.

• 4121

Effects of docosahexaenoic acid on the viability of human tenon's fibroblasts

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Purpose
Excessive scarring of the conjunctiva is the major cause of failure of the surgical treatment for glaucoma. The activation of human Tenon's fibroblast (HTFs) is supposed to be responsible for wound healing and scar formation. Antimetabolites are used to inhibit subconjunctival fibrosis but these molecules may lead to serious complication. Previous studies have shown that omega-3 polyunsaturated fatty acids (PUFAs) such as docosahexaenoic acid (DHA) have anti-inflammatory, anti-proliferative and anti-angiogenic properties. The aims of this study were to evaluate DHA as a potential inhibitor of human Tenon's fibroblasts.
Methods
Primary HTF cells were obtained from patients during glaucoma surgery and were cultured in DMEM medium. After stimulation with TGF-β2, HTFs were treated with MMC (0.01 mg/mL) and different concentrations of DHA (50, 100 and 200 µM) for 48 hours. Lipid profile of HTFs was determined by gas chromatography, cell proliferation by Ki67 assay, cell migration was evaluated by videomicroscopy and cell toxicity by MTT assay. The expression α-SMactin and MAPK p38, ERK, JNK in their non-phosphorylated and phosphorylated forms was determined by western blotting.
Results
MMC reduced proliferation, migration compared to control but showed important toxicity suggested by the increased respiratory rate of mitochondrie in cytotoxicity assay and confirmed by a G2 arrest in cell cycle. DHA had no significant impact on cellular viability. DHA at 200 µM showed an efficacity similar to MMC. A reduction of the ability of cells to migrate was observed with DHA in a dose-dependent manner. DHA efficiently dicreased α-SMactin expression of myofibroblasts. Proteins from the Smad signaling pathway could not be observed.
Conclusions
These findings indicate that DHA inhibits migration and differentiation of HTFs to myofibroblats.

• 4122

Effects of Caveolin-1 ablation in the inner retina under healthy and experimental glaucoma conditions

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Purpose
Variations in Caveolin1/2 (Cav1/2) gene loci has been identified a risk factor in glaucoma. Cav-1 is the prominent signature protein of caveola and is implicated in various signal transduction pathways. Cav-1 ablation has previously been shown to impair the retinal function and our study established that it is involved in regulation of BDNF/TrkB signalling in the retinal ganglion cells. This study aimed to investigate the role of Cav-1 specifically in the inner retina in both healthy and experimental glaucoma conditions.
Methods
Cav-1-/- and the age matched wildtype mice were used in the study (n=32). Experimental glaucoma model was generated by weekly intracameral microbead injections to induce high intraocular pressure (IOP) for 2 months. Retinal functional changes were assessed by electroretinogram (ERG) and positive scotopic threshold response (pSTR) recordings. H&E staining carried out on retinal sections to evaluate histological differences in retinal laminar structure.
Results
Cav-1-/- mice showed significantly lower pSTR amplitudes when compared with WT mice (n=18, p<0.05). ERG amplitudes in Cav-1-/- were smaller than WT mice as reported previously. Following 2 months of elevated IOP (Control, 10.81±0.4; High IOP 25.71±3.2 mmHg), WT mice demonstrated a significant decrease in pSTR amplitudes (n=8, p<0.05) while the Cav-1-/- mice showed a less fall in the pSTR. Histological assessment of glaucomatous retinas also revealed significantly greater decrease in the number of cells in ganglion cell layer in WT compared to Cav-1-/- mice (n=16, p<0.05).
Conclusions
Cav-1 plays a critical role in the maintenance of inner retinal integrity under normal conditions. Cav-1 ablation was associated with functional and structural protection of the inner retina under chronically elevated IOP conditions.

• 4123

Global histone modifications predict the outcome of glaucoma surgery

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Purpose
Conjunctival and subconjunctival fibrosis at the surgical site influences the outcome of glaucoma surgery. Since glaucoma surgery initiates a cascade of events that leads to up- or downregulation of various genes and the subsequent release of cytokines and growth factors, we analyzed global histone modifications at the site of glaucoma surgery and their relationship with the outcome of glaucoma surgery.
Methods
44 patients who were scheduled to undergo glaucoma surgery were enrolled in this study. A 4 × 4 mm section of Tenon's tissue with overlying conjunctiva was cut from the eye at the margin of the incision. Primary rabbit anti-histone antibodies were applied in humidified chamber at the following dilutions: H3 K9 K14 K18 K23 K27Ac at 1:200, H4 K5 K8 K12 K16Ac at 1:200, H3 K4diMe at 1:800 (Abcam), and H4 R3diMe at 1:25 (Millipore). The sections were counterstained with Harris's haematoxylin, dehydrated, and mounted.
Results
Using histochemical staining, we determined the number of cells that were positive for histone acetylation and demethylation of histones H3 and H4. The patients were divided into high- and low-acetylated or -methylated groups accordingly. The low-acetylation group for H3 K9 K14 K18 K23 K27 and H4 K5 K8 K12 K16 had poorer surgical outcomes based on Kaplan-Meier plots. The preoperative intraocular pressure was significantly related to acetylation of both H3 K9 K14 K18 K23 K27 and H4 K5 K8 K12 K16 in univariate and multivariate regression analyses.
Conclusions
Our findings suggest global histone modifications in the conjunctival and subconjunctival tissues predict glaucoma surgery outcomes. A low acetylation status indicated a poor prognosis for glaucoma surgery. Prognostication using histone modifications might have implications for epigenetic therapy to improve glaucoma surgery outcomes.

• 4124

Inflammatory changes in aqueous induced by diabetes in open angle glaucoma patients

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Purpose
Comparative changes of inflammatory cytokines expression in open angle glaucoma and diabetes.
Methods
A cross-sectional study: 87 eyes, from 87 patients, distributed in 4 groups: 24 eyes from healthy subjects, 26 eyes from diabetic patients, 16 POAG eyes and 21 eyes from diabetic glaucoma patients. Aqueous was collected during conventional cataract surgery. 21 inflammatory markers were quantified and compared between groups using a Luminex® Performance Assay multiplex kit based on flowcytometric methods. Data on patient demographics, duration of glaucoma/diabetes, intraocular pressure as well as duration of anti-glaucoma therapy were collected for correlations and prediction models.
Results
Molecules like CXCL5 (p=0.008), CXCL8 (p=0.048), IL-1α (p=0.005), IL-2 (p=0.015) and TNFα (p=0.041) were found significantly higher if diabetes was present in POAG patients. Based on the same pathogenic pathway (TNFα stimmulation, Th1 lymfocytes), a prediction model was created for each glaucoma group. As such, levels of CXCL5, CXCL8, IL-1α and IL-2 could highly predict TNFα level for the POAG patients (r2=0.842, p=0.000), whereas for the diabetic glaucomatous patients the prediction level was inferior (r2=0.618, p=0.034). Therefore, we tested a second inflammatory model for this category. Presence of diabetes induced collateral stimmulation of TNFα via elevated GM-CSF expression (stimmulation via Th2 lymfocytes). Molecules like TNFα, G-CSF and VEGF were significant predictors for a GM-CSF augmented expression (r2=0.758, p=0.018) in this group; moreover a lineary dependence between GM-CSF and TNFα was noted. No other parameter was signifficant in these models.
Conclusions
Inflammatory reaction in glaucoma patients was based on TNFα overexpression, induced either directly (POAG) or indirectly via collateral pathways GM-CSF mediated (diabetic POAG).

• 4125

Early signs of microglial activation in mice retinas contralateral to experimental glaucoma: quantitative analysis of cells number, processes retraction and reorientation

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Purpose

To quantify retinal microglia signs of activation after 24 h of unilateral laser-induced ocular hypertension (OHT) in OHT-eyes and their contralateral eyes.

Methods

Albino Swiss mice were divided into two groups, naïve (n=6) and lasered (n=6). Retinal whole-mounts were immunolabeled with anti Iba-1 to quantify the: i) number of microglial cells in the photoreceptor layer (PRL), outer plexiform layer (OPL) and inner plexiform layer (IPL); ii) the area of the retina occupied by Iba-1+ in the nerve fiber layer-ganglion cells layer (NFL-GCL) and; iii) the arbor area of microglial cells in the OPL and IPL. iv) the number of microglial vertical processes connecting the OPL and PRL.

Results

In OHT eyes and contralateral eyes had no significant differences in cell number with respect to naïve. OHT eyes presented a significant decrease in microglial arbor area in the OPL in comparison with control ($p<0.01$) and in the IPL in comparison with control and contralateral eyes ($p<0.01$ and $p<0.05$ respectively). However the retinal area occupied by Iba-1+ cells in the NFL-GCL was significantly increased: i) in both contralateral and OHT eyes with respect to control ($p<0.01$ in both instances); and ii) in OHT eyes with respect to contralateral eyes ($p<0.05$). In contralateral untreated eyes, the number of microglial vertical processes connecting the OPL and PRL were significantly increased in comparison with control and OHT eyes ($p<0.01$ and $p<0.05$ respectively).

Conclusions

At 24h, laser-induced OHT produces a reactive non-proliferative microgliotic response both in OHT eyes and in contralateral untreated eyes. Whether this response favors neuroprotection or neurodegeneration needs to be clarify.

• 4126

Qualitative early signs of microglial activation in mice retinas contralateral to experimental glaucoma

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Purpose

To analyze qualitative retinal microglia signs of activation after 24 h of unilateral laser-induced ocular hypertension (OHT) in OHT-eyes and their contralateral eyes.

Methods

Albino Swiss mice were divided into two groups, naïve (n=6) and lasered (n=9). Retinal whole mounts were immunolabeled with antibodies against Iba- 1 and MHC-II.

Results

Both in OHT eyes and in contralateral eyes Iba-1+ cells: i)had morphological signs of activation, being these more intense in OHT eyes than in the contralateral eyes. Iba-1+cells showed hypertrophy, soma displacement both in their own retinal layer and towards the nearest one and in some instances, reoriented microglial processes from being parallel to being perpendicular to the retinal surface. ii) were dystrophic in some instances in the photoreceptor layer (PRL); iii) in the outer plexiform layer sent processes to the PRL and this was mainly found in contralateral eyes; iv) overall, did not up-regulate the expression of MHCII .

Only in OHT eyes MHCII+ rounded cells were observed in the nerve fiber layer-ganglion cell layer, being more numerous in the peripheral superior zone of the retina and near the optic disc. These cells were surrounded and phagocyted by numerous ameboid Iba-1+ cells. In addition, beneath the retinal areas where this event was occurring, microglial cells of the inner plexiform layer and outer plexiform layer oriented their processes towards those areas and surrounding them.

Conclusions

At 24 h after unilateral OHT, microglial features of activation were observed not only in OHT eyes but, interestingly, also in the contralateral untreated eyes. Whether this activation favors neuroprotection or neurodegeneration needs to be clarify.

• 4127

Aqueous inflammatory proteasome in open angle glaucoma in Caucasian patients

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Purpose

Primary open-angle glaucoma is characterized by loss of retinal ganglion cells and their axons, resulting in optic nerve cupping and visual field loss. Until now, no specific cause was attributed to POAG development, but multiple pathogenic theories have been approached, beside IOP elevation and aging.The aim of this study was to assess the inflammatory and immune dysregulation theory in POAG.

Methods

We included in a cross-sectional study 40 eyes, from 40 patients: 16 eyes with POAG and 24 eyes from healthy subjects. Aqueous was collected during conventional cataract surgery. 21 inflammatory markers were quantified and compared between groups using a Luminex® Performance Assay multiplex kit based on flowcytometric methods.

Results

Mean age in POAG group was 75.69+/-5.54 years vs 72.33+/-11.26 years in controls ($p=0.23$). Mean IOP in healthy controls was 14.21+/-2.68 mmHg compared to 18.19+/-4.3 mmHg in glaucoma patients, controlled by 3+/-0.87 topical substances. Mean MD level in POAG group was -13.59+/-9.35 dB, whereas PSD mean level was 4.25+/-4.22dB. Cytokines expression in glaucoma patients compared to healthy controls was found significantly different for CXCL5 ($p=0.008$), CXCL8 ($p=0.048$), IL-1α ($p=0.005$), IL-2 ($p=0.015$) and TNFα ($p=0.041$). Therefore, a prediction statistical model for these cytokines was created. All markers point out a common inflammatory pathway that triggeres TNFα release. A mathematical model proved that CXCL5, CXCL8, IL-1α and IL-2 can accurately predict TNFα level in this study (r square=0.842, $p=0.000$).

Conclusions

Our results show that in POAG patients there is an increased production of inflammatory cytokines in aquoeous humor. Moreover our statistical predictions point out TNFα molecule and its signalling pathways as the determinant pathogenic pathway involved in the inflammatory compound of POAG caucasian patients.

• 4128

Association of apolipoprotein E with a risk of primary open-angle glaucoma

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Purpose

Glaucoma is classified as a neurodegenerative disorders. It is characterized by loss of retinal ganglion cell (RGC) and changes in the structure of the optic nerve. The exact mechanism of RGC death is multifactorial and unclear. Many reports have focused on the possible role of apolipoprotein E (APOE) in the development risk of glaucoma.

Methods

The study involved 30 patients with primary open-angle glaucoma (POAG) and 30 age-matched healthy subjects. Material for the study was the whole blood and the aqueous humor. The main goal of this study was to assess the expression level of APOE in whole blood and serum of patients with POAG compared with a control subjects without glaucoma. Moreover, we evaluated the expression level of APOE protein in the aqueous humor in POAG patients. The level of mRNA expression was determined by QRT-PCR and the protein level was evaluated by ELISA. The statistical analysis was performed using the non-parametric Mann-Whitney U test.

Results

The results of APOE mRNA expression level in the blood have shown no statistical differences between POAG patients and control subjects ($p>0.05$). However, the analysis of protein level in the serum has showed a higher expression of APOE of POAG patients compared with the control group ($p \leq 0.05$; 5106.07 ng/ml vs 4294.70 ng/ml). Additionally, we have observed a tendency to increase in concentration of APOE in the aqueous humor in POAG patients (262.12 ng/ml) compared with controls (173.83 ng/ml).

Conclusions

Our research suggests that altered level of APOE may be related to the development of primary open angle glaucoma.

• 4131

Topo- and tomographical keratoconus indices in case of progression

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Summary
Especially in an early stage topography and tomography are perfect tools for diagnosis of keratoconus. Corneal crosslinking requires a documented progression of keratoconus. In this talk we would like to address the Instrument-based documentation of keratoconus progression for qualifying a Patient for corneal crosslinking in case of keratoconus. Special focus is given to the TMS-5, the CASIA2 and the Pentacam.

• 4132

Application of OCT in diagnosis and treatment of keratoconus patients

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Summary
OCT optical coherence tomography is a noninvasive imaging modality. Morphological and morphometric data can be obtain using this technique.
Cross-linking is a method commonly used in reducing the progression of keratoconus and severe infectious diseases of the cornea. OCT can be useful in qualification patients for cross-linking, during surgery and in the management of patients after cross-linking. Different OCT systems (time- domain, spectral domain and swept source) will be presented on the basis of clinical examples.

• 4133

Crosslinking and corneal biomechanics

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Summary
This presentation will demonstrate data on corneal biomechanics measured with the CORVIS ST (Oculus GmbH, Wetzlar, Germany) to evaluate normal corneas, non-crosslinked and crosslinked corneas. Characteristics of biomechanical parameters are explained.

• 4134

Crosslinking in infectious corneal ulcers and Terrien marginal degeneration

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Summary
Corneal collagen crosslinking (CXL) is an established safe and effective option in the treatment of early keratoconus. This presentation reviews the published evidence and personal experience with CXL in special indications.
The intrinsic toxicity of the oxidative CXL process, normally causing a temporarily acellular corneal stroma to a certain depth, implies an antiseptic potential on bacteria, fungi and amebae. This has been applied to refractory corneal infections with varying success. While most available evidence is anecdotal, some prospective studies appear to confirm the usefulness of CXL as an antimicrobial treatment.
CXL in keratoconus is usually applied to the central cornea and aims at preventing the progression of ectasia, with minor effect on curvature and refraction. However, our experience with CXL in cases of peripheral ectatic conditions such as Terrien's disease shows that, beyond stabilization of the process, a marked improvement in astigmatism is possible with a persistent effect after a long term follow up. The possible implications on the mechanism of action of CXL and the pathogenesis of ectasia will be discussed.

• 4135

Crosslinking in infectious keratitis- experimental and clinical data

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Summary

The effect of crosslinking (CXL) on human corneal cells, microorganisms and on viral, bacterial, mycotic and acanthamoeba keratitis is summarized. Keratocyte and human endothelial cell viability decreases significantly at 0.1% riboflavin concentration ($P<0.01$) while the percentage of CD34 ($P<0.01$) and alpha-SMA positive keratocytes ($P<0.05$) increases. CXL may be effective against Staphylococcus aureus, Staphylococcus epidermidis and pseudomonas aeruginosa in vitro, even if they are metichillin, oxacillin or penicillin resistant. In clinical practice, CXL may be used as an alternative treatment option in bacterial, mycotic and acanthamoeba keratitis, if they are therapy resistant.

• 4141

Preliminary results: Comprehensive national retinoblastoma cohort in Finland - RB1 mutation spectrum

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Purpose
Retinoblastoma (Rb), a malignancy of developing retina, emerges almost always after biallelic mutation and inactivation of tumor suppressor gene RB1. In heritable Rb, a child carries germline RB1 mutation. Identifying this will help in future risk management and family planning. Recently, we have made an effort to create a comprehensive national register for Rb. DNA sequencing for mutations in RB1 is being offered to every patient not previously tested and the results are included in the register.
Methods
Of the 226 Rb patients registered in the Finnish Retinoblastoma Register until January 2016, 72 have so far underwent germline DNA testing and 40 patients from 32 unrelated families tested positive for mutation. RB1 mutation detection methods varied depending on the time period. Mutations were checked for pathogenicity from the Leiden Open Variation Database (http://rb1-lsdb.d-lohmann.de).
Results
RB1 mutations comprised 90% of heritable (bilateral, familial or both) Rb and 10% were sporadic unilateral tumors (unifocal or too advanced to assess focality). The distribution of mutation types was 46% nonsense, 15% frameshift, 15% splice site, 3% large indel, 8% missense, 13% chromosomal deletions and none promoter. Two novel mutations (c.1A>C and c.2042_2203+?del) were detected. Five mutations (13%) had been reported only once and nine mutations (23%) three times or less.
Conclusions
The frequencies of the type of mutation in the RB1 gene in the preliminary results of our national cohort expectedly follow the mutation spectrum described worldwide.

• 4142

Outcome of Retinoblastoma Patients Treated According to the University Hospital of Siena Guidelines

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Purpose
To analyze the results of Retinoblastoma (Rb) treatment according to the University Hospital of Siena guidelines in terms of complete ophthalmoscopic remission (COR) of disease.
Methods
A total of 109 eyes of 87 patients were enrolled from September 2013 to November 2016. The mean patient age at diagnosis was 22.8 months (± sd 20.5 months). Sixtysix/109 eyes (60.55% of cases) were unilateral, 42 (38.53%) bilateral. Thirtyfive/109 (32.11%) were classified as low stage (A-C of ICRB classification), 36 (33.03%) as D stage and 31 (28.44%) as E stage. Interventions: Conservative treatment with intravenous (IV) chemotherapy (CHT) and/or intrarterial (IA) CHT, both as first or second line therapies; primary or secondary enucleation.
Results
Fourtysix/109 eyes (42.20%) received primary IV CHT, 40 (36.70%) primary IA CHT and 22 (20.1%) were enucleated at diagnosis. Twentyfive eyes (22.9%) were treated with secondary IA CHT (for failure of IV CHT, the majority being bilateral cases), 4 (3.6%) with second line IV CHT (mainly thermo-CHT after IA CHT). Twentythree/109 eyes (21.1%) were secondary enucleated. Globe salvage with COR of disease has been obtained by 53/109 eyes (49% of all cases, 60.9% of the treated ones), in particular: by the 32.5% of the eyes treated with primary IV CHT, by the 52.5% of those treated with primary IA CHT and by the 60% of the eyes treated with secondary IA CHT. Mean follow-up is of 21.9 months (± sd 16.9 months).
Conclusions
These results confirm the efficacy of our guidelines for Rb treatment. Particularly we obtained a better ocular salvage rate (p>chi2=0.0007, Mantel Cox Comparisons) for the cases treated with secondary IA CHT than with primary IA CHT. This observation demonstrates the efficacy of IA CHT even in recurrences of Rb after primary IV CHT, if early detected with a close follow-up.

• 4143

A case of misdiagnosed diffuse infiltrating retinoblastoma

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Purpose
The aim of this case report is to describe a case of a 19 months old female with diffuse infiltrating retinoblastoma in her right eye misdiagnosed as corneal dystrophy in another center. Diffuse infiltrating retinoblastoma can lead to anterior segment seeding with pseudohypopion, pseudoialitis and parsplanitis, intraocular hemorrhage confusing it with uveitis, unexplained vitreous hemorrhage, hyphema or endophalmitis.
Methods
In October 2016 the girl was observed at our Ocular Oncology Unit at the University of Siena. At ophthalmoscopic examination in her right eye she presented hyperemia, corneal edema, endothelium alterations, flocculi in the angle, iris neovascularization, and hematic clots (3-10 h). At fundus examination there were not retinal masses , but cloudy vitreous and vitreous deposits inferiorly. The left eye was normal. B scan echography documented thickened retina and vitreous deposits . RMI excluded extraocular disease.
Results
The eye was enucleated and the diagnosis of diffuse infiltrating retinoblastoma was confirmed.
Conclusions
Diffuse infiltrating is the least common growth pattern of retinoblastoma and often the most difficult to recognize clinically. It grows diffusely within the retina .Any child with signs of uveitis, hyphema, hypopion, vitreous hemorrhage and ialitis should be evaluated for retinoblastoma.

• 4144

Orbital recurrence of uveal melanoma after 45 years from enucleation

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Purpose
A 52-year-old woman who had undergone enucleation of the left eye at the age of 7 years for posterior uveal melanoma , had no further problems until 45 years later, when she developed a multifocal malignancy of the ipsilateral orbit.
Methods
Case report
Results
MRI documented the presence of nodular multiple masses in the anophthalmic socket suggesting possible metastatic disease. Hepatic examination and ultrasound evaluation , CT scan of the thorax and bone scintigraphy excluded other sites of metastatic lesions. She underwent excissional of the 3 distinct tumors , 2 inferiorly and one superiorly in the anophthalmic socket. After surgery she received proton beem radiotherapy in the anopthalmic socket for a total of 4.600rads.
Histopathology documented malignant melanoma of the orbit characterized by epitheliod cells.
Conclusions
The long interval between recognition of the primary tumor and enucleation and the appearance of clinically manifest metastatic disease in the ipsilateral orbit is the longest reported in the literature to date.
A similar case of metastatic choroidal melanoma to the contralateral orbit 40 years after enucleation has been reported by Coupland(1996)

• 4145

A review of orbital tumors in adult Portuguese population

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Purpose
To determine the types and frequency of orbital tumors from patients referred to the Orbital Department.
Methods
Retrospective consecutive case series. All cases of histopathologically or radiologically verified orbital tumors from a major tertiary referral hospital in Lisbon, were reviewed from a 9-year period. The distribution of patient's age and sex; and tumor's pathology, origin and location in the orbit were determined.
Results
Consecutive series of 71 patients. Median age at tumor's diagnosis was 52y-o (from 0 to 92 y-o), and 65% of the patients were females. The most common clinical features at presentation included proptosis in 33 patients (33%), low vision in 24 (34%), a mass in 15 (21%) and pain in 12 (17%). The mean duration of symptoms was 3,3 years (from 1month to 20 years) before referral. Orbital tumor were malignant in 37 patients (52%) and benign in 34 (48%). The most common tumors were in the extraconal area: malignant lymphoma in 8 patients (11%) and squamous cell carcinoma in 4 (5%); in the intraconal area: meningioma in 9 patients (12%), cavernous hemangioma in 8 (11%), metastases in 7 (10%); and in the lacrimal gland malignant lymphoma 7 (10%) were the most common.
Conclusions
A variety of tumors can involve the orbit. In our series 48% were benign and 52% were malignant. Regardless of the location the most common tumors were malignant lymphoma and cavernous hemangioma. Symptoms that are associated with orbital tumors include: proptosis, orbital mass, decreased vision and pain.

• 4146

Adult orbital precursor B-lymphoblastic lymphoma with involvement of the extraocular muscles

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Purpose
To report a very rare case of a precursor-B Lymphoblastic lymphoma (pre-B-LBL) with periocular muscle involvement in an adult. The clinical, histopathological, and genetic findings will be reported.
Methods
Case report, Immunohistochemistry, FISH, and ArrayCGH.
Results
A 56-year-old male experienced sudden onset of left sided ptosis and diplopia. Pain was not prominent. The patient had complete remission of an abdominal pre-B-LBL. On examination, proptosis and a left sided third cranial nerve palsy was found. After a few days, mydriasis without rapid afferent pupillary defect developed. MRI showed thickening of the medial and inferior rectus muscles. A biopsy of the inferior rectus muscle was obtained for histopathological examination. Histologically, an infiltrate of immature lymphocytic tumour cells was seen within the orbital skeletal muscle tissue. The tumour cells were small and presented with fine blastic nuclear chromatin along with small peripheral nucleoli. The tumour cells stained positively for CD10, CD79a, PAX5, and BCL-2. The Ki-67 proliferation index was 90%. These findings were consistent with a TdT-negative pre-B-LBL relapse. FISH was negative for BCR/ABL, MLL-rearrangement, and ETV-6-break. ArrayCGH was performed. A bone marrow biopsy confirmed systemic involvement. The patient was immediately started on NOPHO High Risk chemotherapy, followed by orbital radiation and awaits allogeneic bone marrow transplantation. The patient has no light perception in his left eye.
Conclusions
This is the first reported case of a very rare rapid growing orbital pre-B-LBL in an adult.

• 4151

CLP-PEG scaffold development: towards conjunctival tissue engineering

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Abstract not provided

• 4152

Corneal mesenchymal stem cell derived exosomes: new therapeutic option for corneal wound healing

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Abstract not provided

• 4153

Corneal thinning post crosslinking: fact or fiction? Solving the mystery by in-vivo measurements of corneal refractive index

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Abstract not provided

• 4154

Discovering and elucidating the role of non-coding defects in the CHM region in the pathogenesis of choroideremia

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Abstract not provided

• 4155

Evaluation of blood retinal barrier breakdown in non-infectious uveitis through an endothelium transcriptomic approach

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Abstract not provided

• 4156

Exploring the role of cis-acting non-coding variation in inherited blindness: the ABCA4 gene in Stargardt disease as a model

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Abstract not provided

• 4157

Immunomodulatory capacity of corneal derived MSCs and keratocytes

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Abstract not provided

• 4158

Incretins, a new target for neuroprotection in glaucoma therapy?

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Abstract not provided

• 4159

Inhibition of a hyperactive kinase signaling hub as a novel and integrative therapy for diabetic retinopathy

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Abstract not provided

• 4411

Transpupillary laser versus intravitreal Anti-VEGF for the management of acute ROP: where do we stand?

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Summary
According to ETROP, treatment-requiring ROP is any stage in zone I with plus, stage 3 in zone I without plus, and stage 2 + or 3+ in Zone II. Zone I disease and aggressive posterior ROP, APROP, still have reduced prognosis as to anatomical and functional outcome. The BEAT-ROP study compared Anti-VEGF therapy with Bevacizumab and traditional transpupillary laser therapy to treat zone I and posterior zone II disease in a randomized fashion. Since then many other reports were published, mostly non-randomized, and often not limited to zone I or posterior zone II disease. An important risk after anti-VEGF therapy are late recurrences due to persistent immature retinal vascularization. Optimal dosage is not yet known. Also, eventual long-term negative effects on neurodevelopmental features have been reported. On the other hand less myopia with anti-VEGF than with laser is claimed as a possible advantage, and also the ease of application not needing anesthesia. From all data it would appear that APROP still remains a major challenge irrespective of the mode of treatment. This paper will discuss the pros and cons for the various treatment options.

• 4412

Endoscopic vitrectomy for stage 4 ROP

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Summary
Introduction. Retinal detachment (RD) surgery in ROP is complex. Safe surgical access into the vitreous cavity is a challenge with a significant risk of requiring primary lensectomy with long term ocular morbidity risk. Endoscopic vitrectomy (Endo-Vit) is a novel surgical approach, enabling a different intraoperative surgeon's perspective that may addresses some of the surgical challenges. Purpose. To evaluate the efficacy and safety of Endo-Vit for traction RD in ROP. Setting. Great Ormond Street Hospital for Children, London. Methods. Single centre noncomparative consecutive series of surgery for stage 4 ROP. Inclusion criteria was stage 4A or 4B ROP, with stage 5 excluded. Results. Eighteen eyes of 14 patients were included. Mean gestational age, birth weight and follow-up were 25.3 weeks, 794g and 3 months, respectively. RD stage was 4A in 7 eyes, and 4B in 11 eyes. Median age at primary Endo-Vit was 45.8 weeks post menstrual age. Median number of surgeries was 1. Overall, primary retinal re-attachment was 89%, 100% in 4A, and 82% in 4B. None required primary lensectomy. Conclusions. Endo-Vit reduces the need for primary lensectomy in stage 4 ROP compared to standard techniques, with favourable anatomic outcomes.
Conflict of interest
Any consultancy arrangements or agreements:
Scientific Advisory Board of Beaver Visitec

• 4413

Surgery in ROP, when is not too late?

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Summary
Retinopathy of prematurity (ROP) is the leading cause of preventable blindness in the premature newborn, when there is retinal detachment (RD) in children with ROP, even in limited detachments, the severity and extent of the RD as well as the expedited treatment are key factors to limit the resulting visual disability.
The surgical treatment in children with RD due to ROP is aim to limit its extension, preserve anatomy as far as possible and facilitate visual rehabilitation. Advanced stages of ROP are poorly understood, this results in the lack of early detection of RD. Stages 4A and 4B have better prognosis if treated early, in stage 5 often the doubt exists if the anesthetic risk or the time and work necessary for the surgery are worth it since in most cases the anatomical and visual result is bad.
We will analyze the types of traction leading to RD, the planning of surgery, the use of pharmacological agents, the recommended time to perform the procedure, autor's recommendations to decide the type of procedure to be performed and the follow-up.
The surgical management of the advanced stages of ROP in an early form may allow in some cases to preserve vision in eyes with retinal detachments in which the macula is still redeemable.

• 4414

Novel gene based therapies for inherited retinal dystrophies in pediatric patients

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Summary
Gene based therapies for inherited retinal dystrophies have improved dramatically over the past 10 years. Clinical trials in patients based on the adeno-associated virus (AAV) mediated gene transfer of a correct cDNA copy of the mutant gene were started for several disorders, including early onset severe retinal dystrophy associated with mutations in the RPE65 gene, and juvenile retinoschisis due to mutations in the RS1 gene. Furthermore, optogenetic approaches and cell based therapies are on the verge to the clinical application. The highest expectations though have raised the recent development of genome editing strategies based on CRISPR-Cas endonucleases, which together with a template DNA enable the correction of the mutant DNA sequence ex vivo or in vivo in photoreceptor cells. In this lecture, an overview will be given on the current state of the art in gene based therapies for pediatric patients, and limitations and potential solutions will be discussed.

• 4415

Surgical treatment of Persistent Fetal Vasculature (PFV)

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Summary

Purpose: Persistent fetal vasculature (PFV), or persistent hyperplastic primary vitreous (PHPV), is a congenital ocular disorder caused by incomplete regression of the embryonic hyaloid vasculature (associated with cataract and glaucoma). Our aim is to overview primary surgical approaches in treatment of PFV with anterior disease based on literature review and two consecutive cases.

Methods: Review of published cohort studies and case reports was performed with PubMed Search engine (keywords: PFV, PHPV, lensectomy, vitrectomy, anterior disease). Two consecutive cases of unilateral PFV with anterior disease treated with lensectomy and vitrectomy were analyzed regarding surgery timing and surgical steps.

Results: Literature review showed limited follow-up (mean 22–76 months) in cohort studies, as well as variation of timing, surgical approaches, and correction of aphakia. During surgery protection of corneal endothelium, removal of capsular remnants and endodiathermy of the hyaloid artery are critical.

Conclusions: Timing of primary surgery in PFV and proper surgical intervention are crucial for the best visual outcome possible. Postoperative period has to include thorough monitoring of intraocular pressure and amblyopia treatment.

• 4421

Trabeculectomy - what I learned from my first 20 cases

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Summary
Trabeculectomy has existed for 40 years now and remains not only the Gold Standard in filtering surgery but also the most commonly performed Glaucoma surgery worldwide. However, this highly effective intraocular pressure (IOP) lowering procedure is a time consuming, multi-step surgery with a relatively steep learning curve. Accordingly, a begginer surgeon should be aware of the critical steps in pre-operative, intra-surgical and post-operative management in order to maximize results with a low risk profile. In this lecture, we will cover the tips and tricks a surgeon may experience when first starting on this surgery. We will cover the topics concerning pre-surgical assessment of the patient, type of anesthesia, wound construction, scleral flap and ostium design as well as wound closure and post-operative management. Additionally, the most common results and complications in the early post-operative period will be discussed.

• 4422

Glaucoma Drainage Device (tube) surgery - what I learned from my first 20 cases

ANAND N
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Summary
Glaucoma Drainage Device (tube) surgery - what I learned from my first 20 cases
Many glaucoma sub-specialists undergo intense fellowship training before embarking on independent practice but no experience specifically prepares you for the first months of your solo career. Additionally, tube surgery may not be ubiquitously used and competition from more traditional surgeries (e.g. trabeculectomy) and Micro-incisional Glaucoma Surgery (MIGS) can result in limited exposure to GDI surgery during the course of fellowships and insecurities when performing the first few cases independently. This part of the SIS will provide expert tips and genuine advice from young glaucoma consultants from across Europe who will share videos and experiences from their first few cases as solo glaucoma specialists. This will include tips on preventing and handling complications, the sharing of lessons and pitfalls to be expected, specific advice on how to handle complications and pearls on how to safely teach residents and fellows.

• 4423

XEN implant and UC3 - what I learned from my first 20 cases

VANDEWALLE E (1,2)
(1) UZ Leuven, Ophthalmology, Leuven, Belgium
(2) KU Leuven - University of Leuven, Ophthalmology, Leuven, Belgium

Summary
Starting with new glaucoma techniques gives a beginning surgeon some extra stress. In this session, we will go into more detail how to perform those techniques and to select the right patient for the right technique. We will elaborate more how to avoid pitfalls and how to handle complications intra- and postoperatively

• 4424

Ab interno glaucoma surgery - what I learned from my first 20 cases

AU L
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Summary
There are many abinternal glaucoma procedure nowadays, ranging from schlemm canal stenting to goniotomy; from suprachoroidal stenting to endoscopic cycloablation. Most of these procedure requires the use of intraoperative gonioscopy which is often a new skill for glaucoma specialist. this talk would focus of tips and tricks in acquiring accurate and reproducible intraoperative gonioscopy, methods to highlight schlemm canal and aids to help identify angle structures. It'd cover the techniques of istent, Hydrus stent, goniotomy with KDB knife, abinternal canaloplasty as well as Cypass suprachoroidal stenting. Careful case selection would be discussed to maximise surgical success and minimise risk and complications.
Conflict of interest
Any consultancy arrangements or agreements:
Consult for Allergan, Alcon, Santen, Ivantis, Glaukos
Any research or educational support conditional or unconditional provided to you or your department in the past or present:
Research with Allergan, Ivantis and glaukos
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person:
Allergan, Alcon, Santen, Ivantis, Glaukos, Eyetechcare
Any Lecture fee paid or payable to you or your department:
Allergan, Alcon, Eyetechcare, Glaukos

• 4425

Deep Sclerectomy - what I learned from my first 20 cases

MERCIECA K

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Summary

Deep Sclerectomy (DS) is a commonly performed procedure for many types of open angle glaucoma, particularly in mainland Europe. The procedure has also gained popularity throughout the UK over the last years, with more units and surgeons in different parts of Great Britain teaching and learning this technically challenging but very rewarding technique. Many glaucoma sub-specialists undergo intense fellowship training before embarking on independent practice but no experience specifically prepares you for the first months of your solo career. Additionally, DS may not be ubiquitously performed and competition from more traditional surgeries (e.g. trabeculectomy) and Micro-incisional Glaucoma Surgery (MIGS) can result in limited exposure (or none at all) to this type of procedure during the course of a fellowship and/or insecurity when performing the first few cases independently. This part of the SIS will provide expert tips and genuine advice from a newly appointed glaucoma consultants trained in DS and currently teaching the procedure within a large UK tertiary referral setting. The speaker will share videos and experiences from the first few cases as a solo glaucoma specialist. The course will include tips on preventing and handling complications, sharing of lessons and expected pitfalls, and pearls on how to properly and safely teach residents and fellows to perform this procedure.

• 4431

The suppression of local cytokine production in experimental models of injured cornea after stem cell treatment

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Purpose

Limbal stem cell deficiency (LSCD) is associated with the break of immune privilege of the cornea, a harmful local inflammatory reaction, production of cytokines and a failure of corneal regeneration. The corneal transplantation is not sufficient treatment. In the case of bilateral LSCD the only therapeutic option is an allogenic transplantation of limbal tissue or cultured limbal stem cells (LSCs) with a systemic administration of immunosuppressive medication. As an alternative, mesenchymal stem cells (MSCs) turned out to be a suitable source of autologous stem cells (SCs).

Methods

In this study MSCs were obtained from murine bone marrow. Flow cytometry was used to characterize the phenotypic markers of such MSCs. LSCs were isolated from limbal tissue by trypsin digestion. For in vitro experiments SCs were cultured in 48-well plates for 24 hours. Excised murine corneas were added into cultures and stimulated by proinflammatory cytokines, interleukin-1β (IL-1β), interferon gamma and by lipopolysaccharide or were pretreated with 0.25M NaOH for 20 seconds. After 48 hours of cocultivation of corneas with SCs, the expression of genes for inflammation cytokines and growth factors in the cornea was detected using real-time PCR. In in vivo experiments, SCs were seeded onto nanofiber scaffolds (allowed to adhere for 24 hours) and transplanted on the damaged (0.25M NaOH, 20 seconds) cornea.

Results

We showed that LSCs and MSCs have the ability to suppress the local expression of genes for IL-1β, tumour necrosis factor-α, vascular endothelial growth factor and inducible NO synthase in the damaged cornea in both in vitro and in vivo models and that transplantation of SCs supports corneal regeneration.

Conclusions

We suggest that MSCs can be a suitable substitute for ocular surface regeneration in cases when autologous LSCs are absent or difficult to obtain.

• 4434

Optical control of corneal nerve activity using chemical photoswitches

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Purpose

Photo-isomerizable small molecules (photoswitches) allow modulation of neural activity acting on native ion channels without requiring exogenous gene expression. DENAQ, a synthetic photoswitch, confers light-sensitivity to retinal ganglion cells in a mouse model of retinitis pigmentosa. However, there are no direct evidences on whether photoswitches can modulate electrical activity of neural structures located far away from the neuron cell body, such as corneal sensory nerve terminals. Our objective was to photo-modulate the activity of corneal cold sensory nerve terminals (CSNTs) in excised guinea-pig corneas pre-incubated with DENAQ.

Methods

Corneas were incubated with 2 mM DENAQ (40 min at 34ºC). Then, electrical activity of CSNTs was recorded extracellularly from corneas superfused at 34°C. A LED was used to deliver pulses of blue light (460 nm, 125 mW/cm2) to the perfused corneas. Light stimulation protocol consisted of 5 cycles of alternating 15s light/dark intervals.

Results

Blue light had no effect on the ongoing activity (OA) of CSNTs recorded from naïve corneas, not pre-incubated with DENAQ (7.4±0.4 vs 7.4±0.4 imp·s-1, dark vs blue light, n=8, p=0.79, paired t-test). In corneas pre-incubated with DENAQ, OA of CSNTs was significantly higher in the dark than under blue light (4.5±0.8 vs 2.3± 0.4 imp·s-1, p=0.001, n=8). OA of CSNTs under blue light was significantly lower in DENAQ pre-incubated corneas than in naïve corneas (p=0.013, t-test).

Conclusions

DENAQ produces a robust decrease of the spontaneous electrical activity of guinea pig corneal cold sensory nerve endings in the presence of blue light. Small molecules acting as chemical photoswitches may be potentially useful as drugs for patients with ectopic corneal nerve activity, such as in dry eye and ocular neuropathic pain.

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• 4433

Method for assessing the impact of residual roughness after corneal ablation in perception and vision

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Purpose

Despite theoretical models for achieving laser-based ablation smoothness (Invest Ophthalmol Vis Sci. 2017;58:2021–2037), methods do not yet exist for assessing the impact of the residual roughness after corneal ablation, in perception and vision. As solution, we propose a method to convert wavefront aberrations with associated roughness, to a visual point spread function (PSF), to calculate the polychromatic retinal image.

Methods

Using SCILAB (Scilab Enterprises, Versailles, France) patient-specific Zernike expansion coefficients and Pupil diameter were used to calculate the wavefront including chromatic compensation for the Red, Green and Blue channels (Optom Vis Sci 2003;80:6–14). Random noise was added to the calculated wavefront to simulate roughness in the cornea after laser ablation, within user-defined limits. PSF of the eye was calculated for Red, Green and Blue channels and the retinal image was determined, as weighted combination of different color channels. Several corneal roughness conditions were compared in terms of the calculated perceived image quality based on metrics like Michelson Contrast, Weber Contrast and Modulation Transfer Function.

Results

For a constant roughness term, reducing the pupil size resulted in sharpening the PSF and perceived retinal image. The impact of varying roughness in ablation could be quantified through the calculated image quality metrics, deteriorating dramatically with increasing roughness.

Conclusions

The proposed model can be used for quantifying the impact of residual roughness in corneal ablation processes at relatively low cost. This method can help compare different refractive laser platforms in terms of their associated roughness in ablation, indirectly improving the quality of results after Laser vision correction surgery.

Conflict of interest

Any post or position you hold or held paid or unpaid?:

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article. Shwetabh Verma and Samuel Arba Mosquera are employees at SCHWIND eye-tech-solutions, Kleinostheim, Germany.

• 4435

In vivo evaluation of voriconazole eye drops efficacy in a rat Acanthamoeba polyphaga keratitis model

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Purpose
Acanthamoeba keratitis is a sight-threatening infectious disease. Its effective and safe medical therapy remains highly debated. The aim of this study is to test in vitro and in vivo voriconazole as a potential antiamoebic treatment for Acanthamoeba keratitis.
Methods
In vitro sensitivity of Acanthamoeba polyphaga to voriconazole was assessed using a commercially available viability assay. In vivo, Sprague-Dawley male rats were injected in the left cornea stromal layer with trophozoites. Forty rats were divided into 3 groups, topically treated with 1% voriconazole eyedrop (hourly administrations for 3 days followed by every two hours for 11 days and followed every four hours for 7 days), orally treated with voriconazole (60 mg/kg/day), and control. At day 28, cornea and blood samples were collected and corneal scrapings were performed for bacterial and parasitological cultures and real-time PCR analyses. Paraffin-embedded corneas were analyzed. The plasma and corneal concentration of voriconazole was determined by high-performance liquid chromatography.
Results
In vitro, voriconazole inhibited Acanthamoeba polyphaga trophozoites proliferation with IC90 value of 6 µg/ml, however no cystical activity was found. Mean intracorneal concentration of voriconazole eyedrops after three days treatment was 5.6 +/- 4.4 ng / mg; after seven days treatment was 2.38 + /1.6 ng/mg; and after twenty one days treatment was 0.32 +/- 0.15 ng / mg. Clinical infection worsened in fewer rats between the 7th and the14th day post infection in the voriconazole eye drops group (1/10 rats) and the control group (9/10 rats) ($p = 0.001$).
Conclusions
Our findings support the potential use of voriconazole as anti-amoebic agents.

• 4451

Interventional controlled cross-sectional study assessing the correlation between optic nerve vessels anomalies, serum angiogenic factors and renal anomalies in children with Down syndrome

*POSTOLACHE, Lavinia(1)**
Huderf, Brussels, Belgium

Abstract not provided

• 4452

Metabolomics in surgical ophthalmological patients (MISO study)

*BARBOSA BREDA, João(1)**
KU Leuven, Neurosciences Department, Ophthalmology Lab

Abstract not provided

• 4453

Modulating synaptogenesis in mouse iPS derived 3D retinal cultures: a strategy to enhance neural circuit reconstruction post-transplantation

*GEORGES, Anouk(1)**
CHU, Liège, Belgium

Abstract not provided

• 4454

Neuroinflammation to rebuild neural circuits: unraveling the underlying molecular players

*BOLLAERTS, Ilse(1)**
KULeuven, Leuven, Belgium

Abstract not provided

• 4455

Ophthalmological screening and follow up of children with neurofibromatosis type 1

*CASSIMAN, Catherine(1)**
UZ St. Rafael, Ophthalmology, Leuven, Belgium

Abstract not provided

• 4456

Pathophysiological changes of the ocular surface as a result of scleral contact lens wear

*BEHAEGEL, Joséphine(1)**
UZ Brussel, Brussels, Belgium

Abstract not provided

• 4457

Peroxisomes and vision: exploring the importance of peroxisomal beta-oxidation for retinal integrity

*DAS, Yannick(1)**
KULeuven, Leuven, Belgium

Abstract not provided

• 4458

The eye as a miRror: targeting inflammatory miRNAs in age-related ocular diseases

*ROBLAIN, Quentin(1)**
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Abstract not provided

Posters

• T001

Nature-inspired Nrf2 activators in retinal pigment epithelial cells: a source for therapeutics in age-related macular degeneration

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Purpose
Age-related Macular Degeneration (AMD) is a severe neurodegenerative disease and a major cause of blindness in the elderly worldwide. Oxidative stress is a common feature of AMD pathogenesis, and a positive modulation of Nrf2 activity has been demonstrated to be protective. Natural products are generally a rich source of therapeutics; we recently combined polyphenols from curcumin and diallyl sulfide in new chemical entities to produce hybrids with anti-oxidant activity. To confirm Nrf2 pathway as a valuable therapeutic target, we studied the modulation of this cascade by our new hybrids.
Methods
The human retinal pigment epithelium cell line ARPE-19 was exposed to increasing concentrations of the new nature-inspired hybrids. Cell viability was evaluated by MTT assay. Nrf2 nuclear translocation and target gene expression were measured by Western blotting.
Results
New nature-inspired hybrids induce Nrf2 nuclear translocation and modulation of its target genes involved in phase II response in ARPE-19 cells. These molecules show a potency on Nrf2 activation profile comparable to that induced by the reference compounds curcumin and dimethylfumarate, the latter being currently used in clinic for multiple sclerosis.
Conclusions
The new nature-inspired hybrids show to be promising to counteract some features related to AMD pathogenesis, thus suggesting the potential use of Nrf2 activators as therapeutics.

• T003

Nrf-2 and PGC1-alpha deletion affects ultrastructural changes in retinal pigmented epithelium associated with the changes of oxidative stress and autophagy markers expression pattern in compound null mice

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Purpose
There is increasing evidence that NF-E2-related factor 2 (Nrf-2) and peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1α) participate in age-related retinal degeneration process. Our study aimed to provide de novo, in and ex vivo high-resolution imaging of eyes from different degenerative mouse models mimicking cellular changes observed in aged retinal pigmented epithelium (RPE).
Methods
The gross morphological alterations of eyes were analyzed by in vivo micro MRI. Oxidative stress marker (4-HNE) and the autophagy regulators (p62/SQSTM1, Beclin-1, LC3, Ubiquitin) were examined on thin wax sections by highly specific immunohistochemistry using semi-quantitative computer aided image analysis. Moreover accurate transmission electron microscopy ultrastructural assay was carried out to monitor the organelle changes in the RPE obtained from Nrf-2/PGC-1α knockout mice.
Results
Collectively, age-related autophagy decline and mitochondrial dysfunction was recorded in the RPE joined with upregulation of stress related biomarkers.
Conclusions
Taken together, our experimental data highlight for the first time that common deletion of Nrf-2 and PGC-1α might appear to have potential and broad applicability for retinal aging research.

• T002

Nrf-2 and PGC1-alpha deletion affects ultrastructural changes in retinal pigmented epithelium associated with the changes of oxidative stress and autophagy markers expression pattern in compound null mice

Kivinen N (1), Viiri J (2), Koskela A (3), Kettunen M (4), Koistinen A (5), Winiarczyk M (6), Kauppinen A (7), Kaarniranta K (8), FELSZEGHY S (9)

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Purpose
There is increasing evidence that NF-E2-related factor 2 (Nrf-2) and peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1α) participate in age-related retinal degeneration process. Our study aimed to provide de novo, in and ex vivo high-resolution imaging of eyes from different degenerative mouse models mimicking cellular changes observed in aged retinal pigmented epithelium (RPE).
Methods
The gross morphological alterations of eyes were analyzed by in vivo micro MRI. Oxidative stress marker (4-HNE) and the autophagy regulators (p62/SQSTM1, Beclin-1, LC3, Ubiquitin) were examined on thin wax sections by highly specific immunohistochemistry using semi-quantitative computer aided image analysis. Moreover accurate transmission electron microscopy ultrastructural assay was carried out to monitor the organelle changes in the RPE obtained from Nrf-2/PGC-1α knockout mice.
Results
Collectively, age-related autophagy decline and mitochondrial dysfunction was recorded in the RPE joined with upregulation of stress related biomarkers.
Conclusions
Taken together, our experimental data highlight for the first time that common deletion of Nrf-2 and PGC-1α might appear to have potential and broad applicability for retinal aging research.

• T004

Effects of HSP90 inhibitor TAS-116 on the inflammasome activation in ARPE-19 cells

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Purpose
Chronic inflammation is one of the key characters of Age-Related Macular Degeneration (AMD), the leading cause of blindness in the Western countries. The NLRP3 inflammasome contributes to the induction of inflammation. The heat shock protein, Hsp90 protects NLRP3 prior to its activation, and its removal releases the receptor protein for degradation. In this study, we tested the effect of the Hsp90 inhibition on the regulation of NLRP3 inflammasome in human ARPE-19 cells.
Methods
The experiments were carried out using IL-1α-primed ARPE-19 cells. Proteasomal degradation and autophagy were blocked with MG-132 and Bafilomycin A, respectively. TAS-116 was used as an Hsp90 inhibitor. The cytokine levels of IL-1β, IL-6, IL-8, and MCP-1 were measured from cell culture medium using the ELISA method. In addition, the activity of caspase-1 was measured by a commercial assay, and the levels of Hsp70 and Hsp90 were determined by the western blot technique from cell lysates. The toxicity of TAS-116 was assessed by measuring lactate dehydrogenase (LDH) levels from cell culture medium and using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay.
Results
According to our data, TAS-116 showed no toxic effects on ARPE-19 cells. TAS-116 decreased the secretion of IL-1β and IL-8 from IL-1a-primed RPE cells with dysfunctional intracellular clearance. The caspase 1 activity decreased along with the IL-1β levels. No changes were seen in the levels of IL-6 and MCP-1.
Conclusions
Our results suggest that TAS-116 is capable of reducing the NLRP3 inflammasome activation and the subsequent release of IL-1β and IL-8 in human RPE cells.

• T005

Autophagy induction decreases protein aggregation in response to polyphenolic pinosylvin and heat shock exposures in ARPE-19 cells

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Purpose
Impaired protein degradation and increased protein aggregation in retinal pigment epithelium (RPE) cells associate with the age-related macular degeneration (AMD) pathology. Heat shock proteins (Hsps) refold misfolded proteins and attempt to prevent the accumulation of detrimental cytoplasmic protein aggregates. Once Hsps capacity is exceeded the protein aggregates are secondarily degraded by autophagy or proteasomes. The Hsps and clearance mechanisms are important to prevent RPE damage and AMD development. We showed recently that stilbenoid polyphenol, pinosylvin has strong cytoprotective power against oxidative stress in ARPE-19 cells. Here, we investigated the effects of pinosylvin and/or heat shock on the regulation of autophagy in ARPE-19 cells in the protein aggregation model.
Methods
ARPE-19 cells were solely or simultaneously treated with 15 μM pinosylvin and/or heat shock at 42˚C for 30 min with or without proteasome inhibitor MG-132 (1 μM) or autophagy inhibitor bafilomycin A1 (50 nM) and followed up to 48 h. Autophagy markers p62/SQSTM1 (sequestosome 1), LC3 (microtubule-associated protein 1A/1B-light chain 3) and Hsp70 (heat shock protein 70) were analyzed by Western blotting (WB). Cytotoxicity was analysed by LDH assay.
Results
Inhibition of proteasomes with MG-132 or heat shock highly upregulated Hsp70, p62 and LC3 detected in WB. Simultaneous treatment with pinosylvin and heat shock showed stronger autophagy induction and cytoprotection rather than theirs single treatments during proteasome inhibition.
Conclusions
Combination of polyphenolic pinosylvin and thermotherapy may provide improved autophagy and cytoprotective response in RPE cells.

• T006

Loss of Nrf-2 and PGC1-alpha genes changes macromorphology of the eye and evokes microstructural and pigmentation pattern changes of the retinal pigmented epithelium

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Purpose
Nrf2 (NF-E2-related factor 2) and PGC1- α (peroxisome proliferator-activated receptor-gamma coactivator 1-alpha) regulate oxidative stress response in cells. Nrf-2 and PGC1-alpha double-knock-out (dKO) mice were used to monitor macro and morphological changes of eye, retina and retinal pigmented epithelium (RPE), respectively.
Methods
The mMRI and mCT imaging were carried out for mice aged at 6 weeks (mCT), 12 weeks and 12 months (mMRI). The retinal and RPE microanatomy and pigmentation were studied from HE-stained thin wax and toluidine blue-stained epoxy sections. Finally, cellular proliferation and pigmentation patterns were studied in the primary cell cultures.
Results
The dKO samples showed smaller body parameters and weight. mMRI, mCT assays indicated size differences and dysmorphic body features in the dKO mice. Moreover, dKOs exhibited reduced retinal full tickness joined with retained RPE morphology. The melanosomes of dKO RPEs were heterogeneous in shape morphology, but comparable in size to aged matched wild type melanosomes, respectively. However, there was a striking trend of increase in the density of melanosomes in RPE of dKOs that was convinced by the primary RPE cultures.
Conclusions
Nrf-2/PGC-1α knockout mice provide a novel model to study degenerative changes in retina and RPE.

• T007

Serum adiponectin associates with aging rather than neovascular AMD

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Purpose
To study whether adiponectin serum levels are changed in neovascular AMD. Adiponectin, secreted primarily by adipocytes, modulates cellular energy metabolism. Adiponectin participates also in retinal homeostasis and autophagy. Adiponectin receptors are abundant in RPE-choroid level. We have previously reported that ADIPOR1-gene variant associates with advanced AMD in Finnish population. Here, we evaluate the role of peripheral adiponectin in AMD.
Methods
After obtaining written informed consent, venous blood samples were collected from 145 neovascular AMD patients (mean age: 79.4 ± 6.1 years) and 90 controls (mean age: 74.6 ± 6.3 years) in a cross-sectional design. Other causes of macular oedema were excluded. Serum adiponectin levels were quantified using a commercial ELISA kit.
Results
Serum levels of adiponectin in neovascular AMD group (12.0 ± 9.5 μg/mL) did not significantly differ from levels in control group (11.1 ± 7.8 μg/mL; t-test p = 0.423). Adiponectin levels increased with aging (rs = .237, p = .01). Women had higher mean adiponectin levels (13.2 ± 9.4 μg/mL, n = 175) compared to men (7.8 ± 6.2 μg/mL, n = 70; t-test p = 0.001), but no difference was detected between AMD-patients and controls when analyzed separately by gender (women: 13.2 ± 8.6 μg/mL vs. 13.2 ± 9.9 μg/mL, respectively; t-test p = 0.959; men: 8.3 ± 7.5 μg/mL vs. 7.2 ± 4.0 μg/mL, respectively; t-test p = 0.439).
Conclusions
Our findings suggest that serum adiponectin levels are not altered in neovascular AMD. However, adiponectin may be considered more like a general serum biomarker of aging. As already known, gender can influence the adiponectin level in elderly.

• T008

Modulation of the rod outer segment aerobic metabolism diminishes the production of radicals due to light absorption

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Purpose
Oxidative stress is a primary risk factor for inflammatory and degenerative retinopathies. Irradiation with blue light of eye explants was shown to cause an oxidative stress, higher in the rod outer segment (OS) than in the inner limb, ultimately impairing the extra-mitochondrial aerobic metabolism of the OS. Here, to establish a correlation between the energy metabolism and phototransduction, the aerobic metabolism of purified bovine rod OS was assayed in function of exposure to either ambient or dim light.
Methods
Isolated bovine rod OS, purified by Fycoll/sucrose gradient were utilized. Production of Reactive Oxygen Intermediates (ROI) was evaluated by citofluorimetry, with dihydrorhodamine 123 (DHR) probe; ATP synthesis and oxygen consumption were assayed by luminometry or oximetry, respectively. When necessary, isolated OS were preincubated with 30 μM Resveratrol, for 15 minutes, or 5 mM Metformin, for 2 hours.
Results
Upon exposure to ambient light for 1 h, a significant increase in oxygen consumption as well as ATP synthetic ability by rod OS was observed, along with a consistent ROI production, with respect to dim light, i.e. the physiological rod conditions. Pretreatment with resveratrol, inhibitor of F1Fo-ATP synthase, or metformin, inhibitor of the respiratory complex I, significantly diminished the ROI production in vitro.
Conclusions
Data show for the first time the relationship between light and the rod OS metabolism. A production of ROI by the OS in vitro was also observed, positively correlating to light exposure. A beneficial effect of metformin and resveratrol was found, as modulators of ROI production, consistently with their inhibitory action on the complexes I and V of respiration, respectively. Data shed new light on the prevention of the cone loss secondary to rod damage due to oxidative stress.

• T009

Protective effects of sulforaphane on STZ-induced diabetic retinopathy via activation of Nrf2/HO-1 antioxidant pathway and inhibition of NADPH oxidase

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Purpose
To investigate the protective effects of sulforaphane, an Nrf2 activator, on streptozotocin (STZ)-induced diabetic retinopathy.
Methods
8 wk male C57BL/6 mice were intraperitoneally injected with streptozotocin (STZ, 45 mg/kg) for 5 consective days. Animals with fasting blood glucose higher than 13.89 mmol/L were considered diabetes and used for further study. Two weeks after STZ injection, animals were intraperitoneally injected with sulforaphane (12.5 mg/kg) for 8 wks, 3 times per week and retinas were harvested at the tenth-week. Reactive oxygen species (ROS) in retina were detected by DHE staining. The expression of heme oxygenase-1 (HO-1) and Nox2 in retina was detected by Western blotting. Immunofluorescent staining was used to detect the expression of RNA binding protein with multiple splicing (RBPMS) and choline acetyl transferase (ChAT), which could specifically mark the retinal ganglion cells (RGCs) and amacrine cells (ACs), respectively. Acellular capillaries in retina were observed by using periodic acid-Schiff and hematoxylin staining.
Results
The fasting blood glucose of the mice injected with STZ was increased rapidly, accompanied by significantly decreased body weight. STZ-injection induced increased ROS generation, increased RGCs and ACs loss, and increased formation of acellular capillaries, which could all be reversed by SF treatment. Meanwhile, HO-1 and Nox2 expression were increased by STZ-injection. SF treatment could further enhance STZ-induced HO-1 expression, whereas decreased STZ-induced Nox2 expression.
Conclusions
SF treatment could protect mice retina from STZ-induced oxidative stress and cellular damage, possibly through the activation of Nrf2 antioxidant pathway and inhibition of Nox2 expression.

• T010

Differential hypoxic response of human choroidal and retinal endothelial cells proposes tissue heterogeneity of ocular angiogenesis

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Purpose
To elaborate molecular differences between choroidal and retinal angiogenesis by generating and comparatively analyzing human primary choroidal and retinal endothelial cell (CEC and REC) lines.
Methods
Human CEC and REC were isolated by positive selection and cultured. Characterization was performed by immunostaining for endothelial cell (EC)-specific markers. Total RNA and protein were extracted from normoxic or hypoxic CEC and REC cultures. qPCR arrays were used to comparatively analyze CEC and REC, and expression differences were calculated by ΔΔCt method. Angiogenesis-related protein expression differences were investigated by western blot and proteome profiler, and were calculated by densitometry. Functional responses to hypoxia were analyzed by sprouting assay.
Results
Primary human CEC and REC lines stained positively for all EC markers and demonstrated high purity with similar staining and morphology. Under normoxia, CEC showed significantly lower expression levels for cell proliferation and vessel maturation genes and higher expression levels for inflammation-related genes when compared to REC. In response to hypoxia, CEC and REC displayed differential regulation for a multitude of angiogenesis-related genes and proteins. Furthermore, within the vascular endothelial growth factor (VEGF) family, CEC showed preferential upregulation for vascular endothelial growth factor A (VEGFA) while REC upregulated placenta growth factor (PlGF) levels. Sprouting was observed in normoxia, and was significantly by hypoxia.
Conclusions
Differential normoxic and hypoxic regulation of angiogenesis-related factors by CEC and REC outlines tissue heterogeneity of ocular angiogenesis and suggests that tissue specificity should be considered as a novel treatment modality for successfully overcoming choroidal and retinal angiogenic conditions in the clinic.

• T011

Human ex vivo model of iris angiogenesis

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Purpose
To assess iris angiogenesis using human explants and determine the role of hypoxia during iris neovascularization.
Methods
Human irises were isolated post-mortem from human research consented donnors. Explants were seeded onto extracellular matrix (ECM), and kept at normal oxygen concentrations (normoxia, 20% O2) or exposed to hypoxia (1% O2) in standard tissue culture conditions for 48 h. Iris angiogenesis was analyzed by quantifying the neovascular area. Furthermore, iris neovascular structures were characterized by immunofluorescence.
Results
Human iris ex vivo neoangiogenesis could be observed within 48 h after the explants were seeded onto ECM, and was defined as vascular sprouts and/or tufts. Vascular sprouts were more common in normoxia, while vascular tufts were mostly formed in hypoxia. A significant increase in vascular area was observed in irises exposed to hypoxia when compared to normoxia. Positive immunoreactivity to specific endothelial cell markers confirmed human iris neoangiogenesis ex vivo.
Conclusions
Our data shows the first human ex vivo neoangiogenesis assay, using iris. The method here presented could have potential use in testing pro- and anti-angiogenic drugs in an human ocular context.

• T012

A novel in vivo model of puncture-induced iris neovascularization

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Purpose
To assess iris neovascularization by uveal puncture of the mouse eye and determine the role of angiogenic factors during iris neovascularization.
Methods
Uveal punctures were performed on BalbC mouse eyes to induce iris angiogenesis. VEGF-blockage was used as an anti-angiogenic treatment, while normoxia- and hypoxia-conditioned media from retinal pigment epithelium (RPE) cells was used as an angiogenic-inducer in this model. Iris vasculature was determined in vivo by noninvasive methods. Iris blood vessels were stained for platelet endothelial cell adhesion molecule-1 and vascular sprouts were counted as markers of angiogenesis. Expression of angiogenic and inflammatory factors in the puncture-induced model were determined by qPCR and western blot.
Results
Punctures led to increased neovascularization and sprouting of the iris. qPCR and protein analysis showed an increase of angiogenic factors, particularly in the plasminogen-activating receptor and inflammatory systems. VEGF-blockage partly reduced iris neovascularization, and treatment with hypoxia-conditioned RPE medium led to a statistically significant increase in iris neovascularization.
Conclusions
This study presents the first evidence of a puncture-induced iris angiogenesis model in the mouse. In a broader context, this novel in vivo model of neovascularization has the potential for noninvasive evaluation of angiogenesis modulating substances.

• T013

The supportive role of interferon-γ in retinal differentiation of mesenchymal stem cells

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Purpose

Retinal disorders represent a serious health problem causing a decreased quality of vision or even blindness. There are currently no effective treatment protocols for these disorders. The promising approach for the treatment of retinal disorders is stem cell-based therapy. Mesenchymal stem cells (MSCs) are a perspective candidate due to their possibility to migrate to the site of injury, differentiate into multiple cell types and produce a number of trophic factors. In this study we analysed the potential of murine bone marrow-derived MSCs to differentiate into cells expressing retinal markers and tested the possibility to express neurotrophic factors by differentiated MSCs.

Methods

Flow cytometry was use to characterize the phenotypic markers of murine MSCs isolated from bone marrow. The retinal extract were prepared by homogenization of posterior segments of the mouse eyes and the supernatants were prepared by stimulation of spleen cells with Concanavalin A. MSCs were cultured with retinal extract and supernatants simulating the environment of retinal damaged for 7 days. The expression of genes for retinal markers and growth factors by MSCs was detected using real-time PCR.

Results

MSCs cultured with retinal extract and supernatant differentiated to the cells expressing retinal cell markers. To identify a supportive molecule in the supernatant from activated spleen cells, MSCs were cultured with retinal extract in the presence of various T-cell cytokines. The expression of retinal markers was enhanced only in the presence of IFN-γ, and the supportive role of spleen cell supernatants was abrogated with the neutralization antibody anti-IFN-γ.

Conclusions

The results show the supportive role of IFN-γ in differentiation of MSCs to the cells expressing retinal cell markers and the enhanced ability of differentiated cells to express growth factors.

• T015

The 8-fold quadrant dissection method for ex vivo human interventional retinal experimentation

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Purpose

Retinal research relies on animal and in-vitro models which lack many of the characteristics of human retina. We have instead established a reproducible ex-vivo model of primary retinal explants derived from human donor eye cups.

Methods

A dissection strategy performed independently by two investigators was designed to maximize retinal tissue whilst maintaining experimentally reproducible fragments of retina suitable for experimental purposes. The retina was divided into 4 quadrants through the fovea and equivalent distribution of photoreceptors between quadrants was confirmed with CD73 staining in 7 pairs of donor eyes with flow cytometry. In the 8 quadrants from each of the 7 donors, the standard error in proportion of photoreceptors was 0.8-2.3%.

Results

Cellular composition of free floating retinal explants were followed for 2 months in 10 retinas with quadrant dissection and 8 with random dissection. Explants could be maintained for 2 months with live populations of photoreceptors, ganglion cells and Müller cells detected by flow cytometry. In contrast, amacrine and horizontal cells, decreased by 90% at 7 days. Only quadrant dissection from the same patient showed reproducible and reliable proportions of cell populations between dissections at any time point. There was no statistically significant relationship between the proportion of any cell population and donor age, time after death, time to storage or time in storage.

Conclusions

The 8 fold quadrant dissection method from a single donor forms an attractive human experimental model for interventional testing in retinal research. We demonstrate the utility of this model in a simple neuroprotection study, showing that insulin protected against CoCl2 induced hypoxia in human photoreceptors.

• T014

Can optical coherence tomography be used in lacrimal gland imaging?

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Purpose

Introduction: Lacrimal gland is a serous gland, bi-lobed in shape, situated superolateral to the eye. The gland continually secretes tears which moisten, lubricate and protect the surface of the eye. Excess tears drain into small ducts which empty into the nasal cavity. Even in healthy subjects, the palpebral lobe is seen through the conjunctiva when the upper eyelid is elevated. The structural features of lacrimal gland are usually analyzed with ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI). Purpose of this study was to explore the possibilities of the lacrimal gland imaging using optical coherence tomography.

Methods

Patients and methods: Our study included 10 healthy subjects, aged between 25 and 30 years. Images of the palpebral portion of the lacrimal gland were made using optical coherence tomography, anterior segment module. We have obtained B-scans of the lacrimal gland, longitudinally and transversely to the exposed palpebral lobe. With the obtained images we analyzed structures of the lacrimal gland.

Results

Results: In this study we obtained photographs of the palpebral lobe of the lacrimal gland. We were able to identify conjunctiva, subconjunctival connective tissue, blood vessels, excretory ducts and glandular parenchyma.

Conclusions

Conclusion: Preliminary results of our study shows that optical coherence tomography offers a possibility of structural differentiation in attempt to analyse morphology of the lacrimal gland. With the development of modern technologies, such as OCT, analysis in vivo of ocular adnexa is placed directly into the domain of ophthalmologists, which, in cases of patients with systemic diseases, facilitates diagnostic process and treatment.

• T016

The investigation of the distribution of nerves, blood vessels and immune cells on the fresh human corneal surface using optimized protocols for immunostaining of flat mounted whole cornea

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Purpose

To present a reliable protocol for the immunostaining of flat mounted corneas and provide a map of the distribution of nerves, blood vessels and immune cells on fresh human corneal epithelium and conjunctiva.

Methods

Organ-cultured human corneas were used for our technique development. 15 fixatives and 5 antigen retrieval (AR) methods were assessed using 4 ubiquitous proteins with different, well-characterized subcellular localization: ZO-1 (membrane), actin (cytoplasm), hnRNP L (nucleosol) and histone H3 (chromatin). The distribution of nerves (Neurofilaments and tubulin β3), blood vessels (CD31 and α-SMA) and immune cells (CD45, CD4, CD8, CD68) in fresh human corneas (without any preservation in culture medium) was then investigated using these optimized protocols.

Results

0.5% paraformaldehyde (PFA) and pure methanol were selected as the most efficient fixatives. Using our optimised protocol, we revealed not only superficial cells (cytokeratin 3, E-cadherin), but also basal cells (ΔNp63, PAX6). Nerve fibers were mainly stained by tubulin β3 on epithelium and by Neurofilament on conjunctiva. CD31 stained only the capillaries situated at the limbus, whereas α-SMA stained all types of vessels on the corneal surface. Numerous immune cells were detected on conjunctival and capillary loops below the limbus. A few immune cells were observed on central epithelium.

Conclusions

Tissue fixation with 0.5% PFA or pure methanol, without any subsequent AR techniques, were found to produce the best results. Compared to IHC on cross sections, immunostaining of flat mounted cornea allows a precise localization of targeted cells through the full thickness of the corneal epithelium and conjunctiva. The distribution of nerves, blood vessels and immune cells on the corneal surface has therefore been mapped.

• T017

Remote ischemia affects the diameter of larger retinal vessels in normal persons

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Purpose
Remote ischemic conditioning (RIC) implies that repeated episodes of ischemia in one organ can protect another remote organ from the adverse consequences of ischemia. It remains to be elucidated whether the diameter response in retinal vessels can be used as a marker of RIC in general and whether the response can be used to predict the effect of RIC on the visual prognosis in diseases characterized by retinal ischemia.
Methods
In twenty normal persons aged 20-31 years the Dynamic Vessel Analyzer (DVA) was used to measure the resting diameter and diameter changes during isometric exercise and flicker stimulation before, immediately after, and one hour after RIC induced by transient ischemia in the left arm.
Results
The baseline diameter of retinal venules was reduced non-significantly immediately after ($p=0.07$) and significantly one hour after RIC ($p<0.009$), whereas the baseline diameter of arterioles was unaffected by the intervention ($p>0.61$). Arterial constriction induced by isometric exercise was significantly reduced immediately after RIC ($p<0.04$), but not one hour after RIC ($p>0.99$). None of the other diameter responsese were affected by RIC ($p>0.22$ for all comparisons).
Conclusions
The diameter of large retinal vessels is affected one hour after controlled transient ischemia in the left arm. This indicates that the diameter response of retinal vessels could be a potential marker of ischemic conditioning in the body in general. The potential of remote ischemic conditioning as an intervention on vision threatening retinal diseases where ischemia is a part of the pathogenesis should be investigated.

• T018

An educational information platform on the ocular surface and dry eye disease - OSCB-Berlin.org

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Purpose
The OCULAR SURFACE is an important part of the eye for the first steps of vision and thus for everything that comes later. The complexity and the ever-increasing wealth of new scientific findings makes it increasingly difficult for many to understand the ocular surface and its diseases – in particular DRY EYE DISEASE.
Methods
Experienced scientists have collected relevant research-based information, from the literature & own results and experience. It is intended to provide useful, reliable understandable information for all stake-holders from laymen & patients, over clinical practitioners to the fellow scientists in the field that is also suitable for academic teaching.
Results
This educational OSCB-WebSite- Homepage of the Ocular Surface Center Berlin (OSCB-Berlin.org) follows a newly developed didactic style that is image-driven in the user interface & content. Text is in parallel with images like a text book - but in addition the information is intensely cross-linked by hyperlinks and supplemented by Animations, so that the reader can enter from any starting point and dig deeper until the information interest is satisfied. The Website is based on pictographic images that illustrate the content. When it becomes more complex, static images are supplemented with Animations in the same style that make even complex content easily understandable. Every topic is covered in three different formats with increasing depth of information to satisfy different interest groups.
Conclusions
Conclusion. The new online INFORMATION PLATFORM on the OCULAR SURFACE and DRY EYE DISEASE covers many aspects of the ocular surface and its alterations with a focus on Dry Eye Disease. It contains reliable, science-based, unbiased information & constitutes a public information platform for all stakeholders in the field. and is supported by hundreds of colleagues world-wide.

• T019

A holistic dynamic concept on the pathophysiology in dry eye disease

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Purpose
Dry Eye Disease (DED) is still insufficiently understood because it is a complex alteration of the functional anatomy of the ocular surface. Current concepts are often oversimplified and a new realistic model is developed that reflects all relevant aspects.
Methods
. A NLM PubMed based review of the literature on DED was performed. Pathogenetic mechanisms were identified and arranged in a patho-physiologic hierarchy of causative relations that reflects clinical findings but is independent of assumed ´importance´.
Results
Basic primary causative factors for DED are structural and functional alterations of the ocular surface integrity. This concerns a deficiency of (A) tear component SECRETION by the secretory elements and of (B) tear FILM FORMATION by the eye lids and blinking mechanism. Together this leads to the two main pathologies of (1) TEAR FILM DEFICIENCY and thus insufficient permanent wetting of the interpalpebral surface that causes (2) the well-known SURFACE TISSUE DAMAGE that gives rise to signs and symptoms. Both pathologies are governed by several interacting secondary pathogenetic factors. Typical for the complex disease mechanism are self-enforcing vicious circles - in contrast to present over-simplified models they do not necessarily depend on inflammation and there are in fact several, different, interacting vicious circles instead of just one. The disease process is influenced by an impairment of regulatory systems (innervation, endocrine system, immune system) of the body & by negative internal and external risk factors.
Conclusions
This new holistic dynamic concept on the pathophysiology DED incorporates long established as well as new mechanisms in the pathophysiological order. It is complex but not complicated - intuitively understandable and suitable to assist basic scientist, patients, and clinical practitioner alike.

• T020

Macrogilal retinal cells show a bilateral early activation in a mouse model of unilateral laser-induced experimental glaucoma

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Purpose
To describe macroglial morphological features of activation after 24 h of unilateral laser-induced ocular hypertension (OHT) in OHT-eyes and their contralateral eyes.
Methods
Albino Swiss mice were divided into two groups, naïve (n=6) and lasered (n=6). Retinal whole-mounts were immunolabeled with antibodies against GFAP and MHC-II.
Results
With respect to naïve, OHT eyes and contralateral eyes showed different features of macroglial activation in some retinal areas: i) Müller cells were reactive and expressed GFAP; ii) astrocytes were more robust and had more primary and secondary processes; and iii) MHCII was up-regulated in astrocytes and in some Müller cells. In contralateral eyes, these signs were observed mainly in the periphery. In addition, in the OHT eyes: i) in some retinal vessels near the optic disc, the astroglial reactivity was so intense that the entire vascular walls were sheathed by astroglial cells; ii) in some areas of the retina, astrocytes and Müller cells formed glial scars. iii) MHC-II immunoreaction in astrocytes varied depending on the retinal area; in those in which MHC-II immunostaining was less intense, only astrocyte primary processes could be recognized;
Conclusions
At 24 h after unilateral OHT, macroglia showed features of activation not only in OHT eyes, but also in untreated contralateral eyes. Early up-regulation of MHC-II in macroglial cells in both OHT retinas and contralateral retinas, suggest an immune system-related inflammation early after the induction of ocular hypertension.

• T021

Assessment of the visual acuity, contrast sensitivity, color vision and visual integration in the Alzheimer's Disease progression according to the scale GDS

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Purpose

Alzheimer's disease (AD) is characterized by an accumulation of abnormal plaques and tangles in the brain with cortical atrophy most pronounced in the medial temporal and posterior temporoparietal regions. The process is estimated to begin years before the appearance of clinical symptoms. The aim of this work was to investigate the potential use of ophthalmological psychophysical tests as AD follow-up.

Methods

Twenty-six mild AD patients, 12 moderate AD and 32 controls underwent visual acuity (VA), contrast sensitivity (CS), colour perception tests and perception visual test (PDT). All patients were classified according the Global Deteriorate Scale (GDS).

Results

In comparison with control: i) patients with mild AD presented a significant decrease in the VA, in the CS (for all the spatial frequencies), in the blue colour perception and in PDT; ii) patients with moderate AD showed the same result as the mild AD, compared with controls, furthermore a significant increase of the total number of errors in the colour test ($p < 0.05$ in all instances). In comparison with mild AD, moderate AD patients had no statistical differences in CS, VA and PDT ($p > 0.05$) but significant differences in the colour perception (total number of errors and unspecific blue axis errors) ($p < 0.05$).

Conclusions

In comparison with the control group, patients with mild and moderate AD presented a statistically significant decrease in CS, for all the spatial frequencies (the higher the spatial frequency, the greater the loss of CS perception), and in the colour perception. Therefore AD patients, show alterations in the M, P, and K visual pathways. Psychophysical tests could be useful tools to diagnose support and follow-up in mild AD.

• T022

Thickness mapping of individual retinal layers and sectors by Spectralis SD-OCT in Autosomal Dominant Optic Atrophy

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Purpose

To assess layer- and location-specific retinal thickness deficits in autosomal dominant optic atrophy (ADOA) on Spectralis SD-OCT.

Methods

This cross-sectional study included 41 ADOA patients with OPA1 exon 28 (2826delT) mutation (age, 8.6-83.5 years; best-corrected visual acuity (BCVA), 8-89 ETDRS letters) and 55 mutation-free first-degree healthy control relatives (age, 8.9-68.7 years; BCVA, 80-99 ETRDS letters). Participants underwent routine examination and OCT with thickness analysis of the total retina, inner retinal layers and outer retinal layers. Individual segmentation was performed of the perifoveal retinal nervefiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer, outer plexiform layer, outer nuclear layer and peripapillary RNFL. Segmentation lines were moved manually to fit optimally with the borders between the layers. Combinations of layers and sectors were tested for their diagnostic significance. Statistical analysis was corrected for age, gender, spherical equivalent, axial length and family clustering in a mixed model analysis.

Results

The perifoveal RNFL, GCL, IPL and the peripapillary RNFL were all significantly thinner in ADOA patients than in healthy controls ($p < 0.0001$). No statistical difference was found for other layers. The largest deficit was found in the GCL (-49.9 %), and it reached its maximum in the "nasal inner macula" sector with a thickness deficit of -63 %. Attenuation of the peripapillary RNFL was most prominent temporally to the optic disc (-58.4 %).

Conclusions

In ADOA, retinal ganglion cells are most prominently missing in the nasal perifoveal area of the GCL, which together with the temporal peripapillary RNFL area serves as the strongest diagnostic OCT marker of ADOA.

• T023

Optical coherence tomograpy in cerebral amyloidosis

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Purpose

To correlate structural and vascular optical coherence tomography (OCT) parameters with cerebral amyloid burden in cognitive intact (Control) and mild cognitive impairment patients (MCI).

Methods

Controls and MCI patients were recruited from an ongoing longitudinal cohort of cognitively intact older adults and a memory clinic-based cohort of amnestic MCI patients respectively. Retinal nerve fiber layer (RNFL) thickness and parafoveal vessel density were measured using Angio-OCT. Amyloid burden was quantified on [18F] flutemetamol or florbetaben PET scans as standard uptake value ratio (SUVR) and categorized as positive (Aβ+) or negative (Aβ-). For statistical analyses, univariate correlation coefficients and one-way ANOVA with LSD post-hoc comparisons were performed.

Results

35 Controls (16 Aβ+, 19 Aβ-) and 28 MCI patients (20 Aβ+, 8 Aβ-) were recruited. Parafoveal vessel density and inferior RNFL showed a significant negative correlation with SUVR (spearmans $\rho = -0.296$, $P = 0.020$; and -0.336, $P = 0.008$ respectively). Inferior RNFL was significantly lower in the Aβ+ MCI group compared to the Aβ- Controls, Aβ+ Controls and Aβ- MCI patients ($P = 0.007$, $P = 0.023$ and $P = 0.015$ respectively) with no significant differences being found between the other subgroups.

Conclusions

This pilot study demonstrates that lower parafoveal vessel density values, as assessed with angio-OCT, are correlated with higher cerebral amyloid burden. The reduced inferior RNFL thickness in MCI, previously reported in other studies, appears to be confined to Aβ+ MCI patients. These findings provide further support for a potential role of OCT in the early diagnosis of Alzheimer's disease.

• T024

Changes in visual function and retinal structure in patients with manic-depressive illness or bipolar disorder

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Purpose

To evaluate changes in visual function and changes in the macula and in the retinal nerve fiber layer (RNFL) measured by spectral domain optical coherence tomography (SD-OCT) in patients with Bipolar Disorder.

Methods

30 eyes of 15 patients with Bipolar Disorder and 72 eyes of 36 healthy subjects were analyzed. All of them were evaluated for the best corrected visual acuity (VA) using the 100%, 2.5% and 1.25% saturation ETDRS test. The contrast sensitivity was evaluated with the Pelli Robson test and the CSV1000E test. The color vision was evaluated with the Farnsworth and Lanthony D15 tests. All participants were assessed with the SD-OCT to obtain macular thickness and retinal nerve fiber layer (RNFL) measurements.

Results

The patients with Bipolar Disorder presented lower VA in low contrasts (2.50% and 1.25%, $p < 0.05$). Significant differences in color vision were also found with the Lanthony Test in the AC CCi, CIndex and CCI indices ($p < 0.05$). There were no significant differences in contrast sensitivity with Pelli Robson or CSV1000E nor in the vision of color with the Farnsworth test. In the RNFL a significant thinning was observed in the temporal areas of the optic nerve (temporal, temporal superior and temporal inferior, $p < 0.05$) in patients with Bipolar Disorder compared to healthy patients. No differences were observed at the macular area.

Conclusions

Patients with Bipolar Disorder present alterations in the visual function as well as axonal loss measured by optical coherence tomography.

• T025

Macular thickness changes using spectral-domain optical coherence tomography automated layer segmentation in multiple sclerosis

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Purpose
We aim to study the role of automated layer segmentation in MS patients' management.
Methods
Retrospective study that included 39 patients (78 eyes) with confirmed diagnosis of MS and 35 healthy age-matched controls. Macular spectral-domain optical coherence tomography scans (SD-OCT, Heidelberg Engineering, Heidelberg, Germany) were obtained followed by automated retinal layer segmentation at the center of fovea and at a radius of 3 to 6mm from the superior, inferior, temporal and nasal sectors (ETDRS grid). Patients with MS were subdivided into two groups: 1) with known previous ON, 2) not known previous ON. Statistical analysis using two sample t-test was made to calculate significant results between groups with 95% confidence interval.
Results
Total central and inner layers macular thickness was significantly reduced in MS patients compared to control group ($p<0.05$) predominantly due to retinal nerve fibre (RNFL), ganglion cell (GCL) and inner plexiform layers (IPL) reduction in foveal, parafoveal and perifoveal sectors with exception of RFNL temporal sector. GCL and IPL were significantly reduced in foveal and parafoveal sectors between group 1 and 2 ($p<0.05$) while no significant RNFL reduction was observed between these groups.
Conclusions
Reductions in total central and inner layers macular thickness can be detected in MS eyes with or without a previous history of known ON. As many ON episodes are not clinically detected, OCT may act as CNS imaging tool documenting neuronal degeneration in MS patients.

• T026

Reduction in subfoveal choroidal thickness and peripapillary retinal thickness after high-dose melphalan therapy followed by autologous peripheral blood stem cell transplantation in a patient with POEMS syndrome

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Purpose
To determine whether high-dose melphalan therapy followed by autologous peripheral blood stem cell transplantation can reduce the serum level of vascular endothelial growth factor (VEGF), the peripapillary retinal thickness (pRT), and the choroidal thickness (CT) in a patient with the polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome.
Methods
A 39-year-old man with POEMS syndrome was given high-dose melphalan therapy followed by autologous peripheral blood stem cell transplantation. The peripapillary retinal thickness (pRT) and subfoveal CT was determined by spectral-domain optical coherence tomography (SD-OCT) to quantify the degree of optic disc edema and choroidal thickness. The pRT thickness was measured at the baseline and at 6 months after the treatment. The serum level of VEGF was also determined by enzyme-linked immunosorbent assays (ELISAs) at the baseline and at 6 months after beginning the treatment.
Results
At the baseline, the serum level of VEGF was 9960 pg/ml and the pRT was 1062 μm in the right eye and 963 μm in the left eye. At 6 months after the treatment, the serum level of VEGF was reduced to 333 pg/ml, the ODE was reduced bilaterally, and the pRT was decreased to 406 μm in his right eye and 358 μm in his left eye. The subfoveal CT was 439 μm in the right eye and 409 μm in the left eye at the baseline. Six months after the treatment, the subfoveal CT was decreased to 368 μm in the right eye and 364 μm in the left eye.
Conclusions
Our result showed that the peripapillary retinal thickness and subfoveal choroidal thickness were reduced in the optical coherence tomographic (OCT) images along with a decrease of the serum VEGF levels. We recommend OCT to monitor the changes in the signs of POEMS syndrome after treatments.

• T027

Retinal nerve fibre layer thickness associates with cognitive impairment and physical disability in multiple sclerosis

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Purpose
Reductions in the retinal nerve fibre layer (RNFL) have been indicated even in early-stages of multiple sclerosis (MS). The aim was to assess the potential of the RNFL quadrant measurements in differentiating disease phenotypes and their association with cognitive impairment and physical disability.
Methods
465 MS patients and 168 healthy controls (HCs) were included. MS subjects were divided in subgroups according to disease phenotype. All subjects underwent optical coherence tomography (OCT) examination of all retinal quadrants using Canon OCT HS-100. Associations were tested using linear mixed effect models.
Results
The global RNFL thickness was 6.4 μm thinner (95%CI -8.5 to -4.3, $p<0.001$) in relapsing-remitting MS (RRMS),
11.6 μm thinner (95%CI - 14.4 to - 8.8 μm, $p<0.001$) in secondary progressive MS (SPMS) and 10.7 μm thinner (95%CI -16.0 to -5.5, $p<0.001$) in primary progressive MS (PPMS) compared with HCs. Global RNFL and temporal quadrant showed high correlation to cognitive impairment and physical disability in MS.
Conclusions
We report that RNFL thickness reduction is significantly associated with physical and cognitive disability and OCT measurements are useful for axonal loss. We suggest the use of temporal quadrant RNFL thickness as a more sensitive outcome as oppose to the global RNFL thickness.

• T028

Swept-Source OCT utilised to compare the choroidal thickness of the peripapillary area between patients with Parkinson´s disease and healthy subjects

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Purpose
To evaluate and compare peripapillary choroidal thickness (PPCT) in patients with Parkinson´s disease (PD) and healthy subjects using swept-source optical coherence tomography (SS-OCT)
Methods
80 healthy subjects and 40 PD patients were examined using Deep Range Imaging (DRI) OCT Triton. An optic disc 6.0×6.0 mm three-dimensional scan was obtained to measure choroidal thickness. Five concentrical choroidal zones were established and used to compare PPCT between PD patients and healthy subjects: zone 1 corresponded to the optic disc area (thus not measured by the OCT), zones 2 to 5 were progressively farther from the optic disc
Results
PPCT was significantly thicker in PD patients compared to healthy subjects in all the zones ($p\leq0.0001$): 126.89 ± 11.23 μm vs 96.53 ± 9.55 μm in zone 2; 152.75 ± 16.00 vs 121.39 ± 12.10 μm in zone 3; 190.21 ± 12.16 vs 156.69 ± 12.44 μm in zone 4; and 213.21 ± 11.83 vs 186.64 ± 9.47 μm in zone 5. A similar pattern of choroidal thickness was observed both in PD patients and healthy subjects; it was thicker in temporosuperior region, followed by superior, temporal, nasal and inferior regions
Conclusions
PD patients show an increased peripapillary choroidal thickness compared to healthy subjects in all zones. Peripapillary choroidal thickness shows a concentrical pattern both in PD patients and healthy subjects, with increasing thickness moving away from the optic disc. The new SS-OCT could be useful to evaluate choroidal thickness, and it could be useful in clinical practice

• T029

Neuro-retinal changes evaluation in multiple sclerosis patients: 10 years follow-up

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Purpose
To analyze functional and structural changes in the retina and optic nerve (ON) in patients with multiple sclerosis (MS) compared to healthy controls (C) and after 10 years of follow-up.
Methods
Fifty eyes of patients with mild-moderate MS were evaluated and compared to 50 eyes of C at a baseline visit and at 10 years of follow-up. The following functional parameters were evaluated: best-corrected visual acuity (BCVA), color vision examined with the Ishihara test, and mean deviation of visual field (VF) analyzed using the Humphrey perimetry. The structural parameters of the ON were also studied using the NSITE axonal application of the optical coherence tomograph (OCT) Heidelberg Spectralis.
Results
No differences were found in the functional parameters in MS patients compared to C, neither at 10 years of follow-up ($p>0.05$). However a statistically significant decrease was observed in the structural parameters between C and MS patients at 10 years of follow-up: mean, nasal-inferior (NI), temporal-inferior (TI), temporal (T), temporal-superior (TS), papillomacular bundle and nasal/temporal (N/T) ratio thickness ($p<0.001$), but also in the axonal thickness, specifically in the mean, TI, T, TS, papillomacular bundle and N/T ratio thickness ($p<0.001$) measured with OCT in patients with MS after 10 years of disease progression. A higher functional disability using the Expanded Disability Status Scale was also recorded.
Conclusions
Axonal damage can be analyzed and quantified in the retina and ON using the OCT in MS. Patients with MS showed significant decrease in the retina nerve fiber layer at 10 years of follow–up compared to C and a progressive axonal death (without outbreaks) that could be detected and quantified using the OCT, but not with the functional tests (BCVA, color and VF).

• T030

Choroidal changes in patients with multiple sclerosis

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Purpose
To evaluate the peripapillar choroidal thickness in patients with multiple sclerosis (MS) and to compare it with age- and sex- matched healthy controls, using a swept-source optic coherence tomography (SS-OCT).
Methods
Fifty-one right eyes of patients with MS and 102 right eyes of healthy controls were analyzed. A 6X6 mm choroidal cube was scanned using the SS-OCT Triton device. This OCT showed 676 measurements that were later divided in four zones, from lower to higher choroidal thickness: the zone 1 corresponds to the optic nerve head (no choroidal measurements are given), the zone 2 corresponds to choroidal thickness between 120 and 179 microns, the zone 3 between 180 and 239 microns, and finally the zone 4 corresponds to a thickness higher to 240 microns.
Results
A similar concentric choroidal thickness pattern was observed in MS patients and healthy controls. The choroidal thickness was thicker in the superior region, followed by the temporal, nasal and inferior regions. The farther from the optic nerve, the thicker choroidal tissue was quantified. However, a statistically significant decreased of the peripapillary choroidal thickness in all the concentric zones was observed in patients with MS compared to healthy controls (134.02±16.59 µm in MS group vs 171.56±12.43 µm in the control group in zone 2; 182.23±20.52 vs 219.03±17.99 µm, respectively, in zone 3; and 223.52±10.70 vs 259.99±10.29 µm, respectively, in zone 4; $p<0.0001$).
Conclusions
Patients with MS showed thinner peripapillar choroidal thickness compared to healthy controls. The SS-OCT device could be useful equipment in clinical practice to evaluate the peripapillar choroidal tissue in such patients.

• T031

Reproducibility of the measurements taken with swept source optical coherence tomography

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Purpose
To evaluate the measurements reproducibility of the macular area and of the retinal nerve fiber layer (RNFL) taken with different protocols with swept source optical coherence toography (SS-OCT) Triton.
Methods
108 eyes from 108 healthy subjects were included whose macular thickness and RFNL thickness were analyzed by SS-OCT Triton (Topcon, Japan). To study the reproducibility of the device, three measurements were taken followed by different protocols: 3D (H) + 5LineCross and 3D Macular (H) protocols (macular thickness) and 3D Disc protocol (RNFL and optic nerve morphometric values). The coefficients of variation (COV) and intraclass coefficients (ICC) were calculated.
Results
A high reproducibility was obtained with mean COV by type of protocol used of 8.31±13.54% to 1±1, 6% being the less reproducible protocol for the measurement of RNFL 8.31±13.54%. The macular area data in all ETDRS quadrants (11.6% to 37%) were more accurate than those of RNFL (2% macular vs 8% RNFL). The ICC of the optic nerve morphometric values presented a range of 0.91 to 0.53, being the vertical diameter disk value the less accurate. The ICC values of the total macular thickness were the most accurate (0.963 to 0.839). Little variability was observed in the RNFL thickness (ICC 0.946 to 0.750).
Conclusions
There is a high reproducibility of the protocols performed with Triton OCT. The total value of the RNFL protocol is much more variable than the macular protocols, being the temporal quadrants less reproducible than the nasal ones. These results could influence negatively in the evaluation of patients with neurodenegerative diseases where the most affected area is the temporal one.

• T032

Choroidal thickness measurements around the optic disc in healthy subjects using Swept-Source optical coherence device

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Purpose
To measure the peripapillary choroidal thickness in an extensive area around the optic nerve and several established sections in healthy subjects using a swept-source optical coherence tomography (SS-OCT) device.
Methods
A total of 86 healthy subjects were included in the study. An optic disc 6.0×6.0 mm three-dimensional scan of the right eye was obtained using the Deep Range Imaging (DRI) OCT Triton. Centered in the optic disc a 26x26 cube-grid was generated to automatically measure the choroidal thickness. Seven choroidal zones were established and analysed: 3 superior (temporal, central, and nasal), 3 inferior (temporal, central, and nasal) and the optic nerve head
Results
Peripapillary coroidal thickness was significantly thinner in the central superior, nasal superior, and nasal inferior zones in healthy eyes. Choroidal thickness in the central superior zone was 156.17±80.89 µm; in the nasal superior zone was 168.34±73.45 µm and in the nasal inferior zone was 137.47±65.96 µm.
Conclusions
Peripapillary choroidal thickness in healthy subjects is higher in the temporal and superior zones around the optic disc. SS-OCT could be a useful tool to evaluate choroidal thinning.

• T033

Optical coherence tomography outcomes in patients with Friedreich ataxia

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Purpose

To compare the ETDRS macular thicknesses (MT), the ganglion cell complex plus inner plexiform layer thicknesses (GCC) and the peripapillary retinal nerve fiber layer (RNFL) thicknesses between patients with Friedreich ataxia (FA) and age-matched healthy individuals.

Methods

Seven FA patients and 19 age-matched controls were prospectively selected. All participants underwent a neurological evaluation, a comprehensive ophthalmological assessment and imaging with spectral domain Cirrus OCT (Carl Zeiss Meditec, Dublin, CA). Both eyes were included, left eyes were converted to a right eye format. The OCT parameters were compared between groups with the Mann-Whitney U test. A $p<0.05$ was considered significant.

Results

Mean age was 44.73±11.9 and best-corrected visual acuity (BCVA) was 0.97±0.1 for the control group, while mean age was 37.85±10.2 years and BCVA was 0.76±0.2 for the AF group. The central macular thickness was similar in both groups, but the macular thicknesses of the inner ring of the ETDRS grid, except the temporal area, were reduced in FA ataxia compared to healthy controls. The nasal and inferior thicknesses of the outer ring were also lower in AF patients. All the GCC measurements and the RNFL thicknesses around the optic disc, except the eight clock-hour position, were decreased in FA individuals.

Conclusions

In AF patients, the macular, GCC and RNFL thicknesses were lower than in healthy controls, presumably because of the loss of the ganglion cells. More studies are needed to evaluate the changes in the retina due to AF.

• T035

Correlation between electrophysiological test and visual dysfunction in multiple sclerosis patients

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Purpose

Evaluate best corrected visual acuity (BCVA), contrast sensitivity (SC), pattern electroretinogram (pERG), multifocal electroretinogram (mfERG), and multifocal visual evoked potentials (mfVEP) in multiple sclerosis (MS) and compare with healthy controls.

Methods

Fifty-eight eyes were included: 14 of healthy controls and 44 of subjects with MS (of whom 17 presented a previous episode of optic neuritis). The BCVA ETDRS was recorded at 100% contrast, 2.5% and 1.25%, CS with CSV1000 test (at 3, 6, 9 and 12 cycles per degree) and Pelli Robson. The pERG, mfERG and mfVEP electrophysiology tests were performed with the Roland Consult's Reti-port / scan device.

Results

Patients with MS showed a significant reduction of VA at 100% contrast ($p = 0.013$), 2.5% ($p <0.001$) and 1.25% ($p = 0.008$), CSV-1000 was also affected at 3 ($p = 0.017$), 9 ($p = 0.017$), and 12 cycles per degree ($p = 0.048$), and also Pelli Robson ($p <0.001$). The mfERG showed in MS patients a significant affectation for amplitude and latency at the inferonasal and superonasal quadrants ($p = 0.045$ and 0.042 respectively), and the overall values of the mfPEV sown abnormalities at N1 and P1 amplitudes ($p = 0.019$ and $p = 0.039$, respectively).

Conclusions

Patients with MS have a clear impairment of visual function in both psychophysical and electrophysiological tests.

• T034

Visual impairment in combined pathology: multiple sclerosis and pituitary adenoma

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Purpose

To study the changes of visual function in patients with combined pathology: multiple sclerosis and pituitary adenoma.

Methods

4 females from 18 to 41 years old were examined.They complained of decrement of visual acuity, pain with eye movement. We identified decrease in visual acuity from 0.01 to 0.1, visual field central defect.To exclude organic pathology, the patient was sent for MRI of the brain, confirmed the diagnosis: MS and pituitary adenoma. For identify the root cause of reduced visual acuity, patients were examined by Cirrus HD-OCT; Humphrey HFA II-750i; Microperimetry on MP-1, MRI of the brain and orbits.

Results

144 patients were examined in the S. Fyodorov "Eye Microsurgery" Complex, Moscow, 4 of them were diagnosed and confirmed a combined pathology:MS and pituitary adenoma. According ophthalmoscopy in three patients was marked optic disk hyperemia and swelling of the disc margin, one patient – temporal optic disk pallor. According microperimetry we received a decrease in overall photosensitivity from 8.3 to 11 dB. OCT: in 3 patients revealed a slight an increase average retinal nerve fiber layer thickness (A RNFL) from 110 to 113 μm. In 1 patient revealed a decrease A RNFL thickness to 76 μm. To confirm demyelinating cause of optic neuritis was scheduled MRI of orbits. In two patients were found nidus of demyelination in the optic nerve. Hormonal activity of pituitary microadenomas in the blood serum: cortisol from 350 to 400 mME/l, prolactin from 190 to 315 nmol/l.

Conclusions

Visual impairment caused by demyelinating process that is confirmed by special methods of examination. Identified pituitary microadenomas is hormone-inactive tumor, therefore they do not affect the clinical course of MS. Combined pathology requires a change in tactics of patient's management with the participation of the endocrinologist and neurosurgeon.

• T036

Multifocal electroretinogram and optical coherence tomography to evaluate parafoveal fixation

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Purpose

Spatial resolution of the human visual field changes depending on the distance from the fovea and fixation point. The visual field is divided in three areas: foveal, parafoveal and peripheral. The highest visual acuity (AV) is obtainded at the foveal area, covering approximately 2 °, then parafoveal area covers 2 ° to 5 °, and the peripheral vision from 5 ° to the edge of the visual field, but the AV decreases progressively in each area .

Methods

We analyzed two cases of parafoveal fixation by SD-Spectralis OCT (Heidelberg Engineering), Triton Swept-Source OCT (Topcon) and multifocal electroretinogram (mfERG) with RetiPort / Scan (Roland Consult). The structure and function of retinal cells have been correlated using OCT images and the three-dimensional map of mfERG.

Results

Case 1: Patient with 100% ETDRS VA equal to 0,0 in both eyes (OU), contrast sensitivity (CS) Pelli Robson 1,35 in right eye (OD) and 1,20 in left eye (OS), presents Parafoveal fixation <1°.

Case 2: Patient with previous episode of optic neuritis in OD and parafoveal fixation of 3° in OS, which presents VA ETDRS 100% of 0.7 in OD and 0.1 in OS, CS PelliRobson of 1,05 in OD and 1,20 OS.

Both cases present a reduced macular peak seen at the mfERG, and a fixation point out of the foveal at the OCT.

Conclusions

We can see how VA and CS decreases as the fixation eccentricity increases, as can be clearly seen in the three-dimensional mfERG map. CS seems to be the quickest parameter to be affected.

• T037

Visual function in multiple sclerosis patients treated with Fingolimob during two years of follow-up

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Purpose
To evaluate visual function changes in multiple sclerosis (MS) patients treated with Fingolimob during two years.
Methods
A total of 31 eyes of 16 MS patients that were going to start Fingolimob treatment were included. All of them underwent an ophtalmic examination including best corrected visual acuity (BCVA) using ETDRS optotype with 100%, 2,5% and 1,25% contrast; contrast sensitivity using CSV 100 E and Pelli-Robson tests and cromatic vision using Farsworth and Lanthony D15 tests. Quality of life was evaluated by the MSQOL questionnaire. The same protocol was repeated 2 years later.
Results
A significant reduction of visual acuity was observed after two years of follow- up in 2,5% (0,33±0,023 vs 0,39 ±0,16; p<0,001) and 1,25% (0,43±0,05 vs 0,54±0,22; p<0,001) contrasts. All CSV frequencies showed a significant decrease except 18cpd (3 cpd: 1,78 vs 1,73 ± 0,17; 6 cpd: 1,94 ± 0,17 vs 1,85 ± 0,24; 12 cpd: 1,69 vs 1,39 ± 0,37; p<0,001). A progresive reduction in chromatic vision (Farnsworth and Lanthony test, p<0,001) was also found. MSQOL-54 questionnarie result was significatly lower after two years in physical (p=0.023) and mental (p=0.032) health sections.
Conclusions
MS patients treated with Fingolimob present progressive changes in visual acuity, contrast sensivity, and chromatic vision. Visual function tests may be an useful tool to evaluate the progression of neurodegenerative diseases and treatment effectiveness.

• T038

Cabin pressure aboard commercial aircraft and non-arteritic ischemic optic neuropathy

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Purpose
To evaluate variations in pressurization of commercial aircraft at cruising altitude. Most aircraft are pressurized between 6,000 and 8,000 feet (ft.), depending on the type of aircraft and composite materials of the fuselage. Patients with NAION may note transient obscurations of vision in concert with low partial pressures of oxygen associated with high altitude.
Methods
Altimeters were used to measure the altitude and cabin pressure at cruising altitude aboard 83 commercial aircraft, including 38 narrow-body and 45 wide-body planes. Single-aisle aircraft with a fuselage width of 10-13 ft. were considered narrow-body, while twin-aisle aircraft with a fuselage width of 16-20 ft. were qualified as wide-body. There were six types of narrow-body and seven types of wide-body aircraft studied.
Results
The mean cabin pressure among all flights was 6,200 ± 970 ft. Narrow-body aircraft had a significantly greater mean cabin pressure of 6,634 ± 965 ft. compared to wide-body aircraft with a mean cabin pressure of 5,834 ± 818 ft. ($p < 0.001$). With respect to service date, newer generation aircraft had a mean cabin pressure of 5,999 ± 949 ft., which was lower than the mean cabin pressure of older aircraft 6,462 ± 946 ft. ($p = 0.03$).
Conclusions
Innovation in flight design has offered the ability for aircraft to fly at greater altitudes, while maintaining lower cabin pressures. Those at high risk of hypoxia induced complications such as NAION may consider aircraft type when air travel is required. Although all flights studied maintained pressurization below suggested United States Federal Aviation Administration (FAA) guidelines, the possibility for oxygen desaturation remains with current flight practices, especially in those at high risk.

• T039

Differences in onset between eyes in patients with Leber's Hereditary Optic Neuropathy (LHON)

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Purpose
Leber's hereditary Optic Neuropathy (LHON) is an inherited mitochondrial disease characterized by a painless, subacute loss of central vision with over 95% of affected patients harbouring one of three mitochondrial DNA (mtDNA) classical point mutations (m.11778G>A, m.3460G>A and m.14484T>C). The purpose of this study was to compare the age of disease onset and time interval between affected eyes by mutation.
Methods
Age of onset, unilateral versus bilateral presentation, interval between the first and second eye, and the mtDNA mutation were retrieved from two separate database registries consisting of 268 Italian and 71 U.S. patients.
Results
Clinical data from 300 LHON patients with classical LHON mutations were evaluated (m.11778G>A, n = 216; m.3460G>A, n = 40; m.14484T>C, n = 44. Bilateral eye involvement was clinically documented in 99.4% of cases with 50.3% of all patients demonstrating sequential onset. In these latter cases the median inter-eye delay was 12.8 weeks. Comparing the age of onset across mutation subtypes, the m.14484T>C mutation resulted in the lowest age at onset (19.2 ± 10.6 years) compared to m.11778G>A (25.8 ± 15.3 years) and m.3460G>A (20.9 ± 14.5 years) ($p < 0.05$). Interestingly, the m.14484T>C mutation exhibited more simultaneous than sequential onsets compared with the other two mutation subtypes ($p < 0.001$). Moreover, m.14484T>C showed a shorter and more reproducible interval between eyes (inter-eye onset range = 1–44 weeks) versus m.11778G>A (range = 1–2016 weeks) and m.3460G>A (range = 2–816 weeks) for sequential presentations.
Conclusions
The m.14484T>C mutation, though least penetrant, manifested at an earlier age and resulted in a smaller inter-eye delay interval range and higher incidence of simultaneous involvement compared to the other two classical mutations in LHON.

• T040

Clinical experience with idebenone in the treatment of patients harboring rare mutations related to Leber's Hereditary Optic Neuropathy (LHON)

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Purpose
LHON is a mitochondrial disease resulting in progressive, severe central vision loss, which in >95% of patients is characterized by 1 of 3 primary mitochondrial DNA mutations. However, further rare mutations have also been identified. To date the only treatment approved for LHON is idebenone, which is safe and effective at a dose of 900mg/day; however, there is little information about its use in patients with rare mutations.
Methods
The Expanded Access Program (EAP) assessed idebenone's therapeutic potential in patients with onset of symptoms within 1 year prior to enrollment, in a real-world setting. Efficacy was assessed as clinically relevant recovery (CRR) or clinically relevant stabilization (CRS). CRR is defined as improvement from off-chart to reading 5 letters on the ETDRS chart, or as an improvement of 10 letters. CRS is defined as maintenance of VA <1.0 logMAR (20/200).
Results
Of 111 patients, 7 carried a rare mutation (A14495G, C3461T, G13051A, G3958A, T14487C, T4216C and T11253C+A14970G). The median age was 16.7 years, 57% were female and the time since onset was 2.8 months at the start of treatment. Patients presented with best visual acuity (VA) from 0.2 to 1.3 logMAR, and 3 patients presented with both eyes <1.0 logMAR at baseline (BL). One patient had only BL data currently available while 6 provided follow-up data, with a median treatment duration of 9.2 months at last observation. All 6 experienced a CRR (10/12 eyes total) and the range for magnitude of recovery was between 2 and 13 lines on the ETDRS chart. The 2 eyes which did not experience CRR maintained VA <1.0 logMAR at last observation.
Conclusions
LHON patients harboring rare mitochondrial mutations who received early treatment with idebenone presented with moderate VA loss at BL and experienced a very favorable outcome. All patients showed recovery of vision.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Xavier Lòria is an employee of Santhera Pharmaceuticals

• T041

Idebenone is effective and well tolerated in Leber's Hereditary Optic Neuropathy (LHON): Long-term results of real world clinical practice

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Purpose
LHON is a mitochondrial disease resulting in progressive, severe central vision loss, which is caused by 1 of 3 mitochondrial DNA mutations in >95% of patients. Idebenone, at a dose of 900mg/day, is effective and safe in patients with LHON. Here, we report long-term treatment outcomes in real world clinical practice.
Methods
The Expanded Access Program (EAP) assessed idebenone's therapeutic potential in patients with onset of symptoms within 1 year prior to enrollment. Efficacy was assessed as clinically relevant recovery (CRR) or clinically relevant stabilization (CRS). CRR is defined as improvement from off-chart to reading 5 letters on the ETDRS chart, or as an improvement of 10 letters. CRS is defined as maintenance of VA <1.0 logMAR (20/200).
Results
85 patients carried one of the 3 most common mutations and had at least 1 post-baseline (BL) visual acuity (VA) assessment. At BL, median age was 23.6 years and median treatment duration at last observation was 17.3 months. A subset of 25 patients presented with VA <1.0 logMAR, from which 52% experienced CRS. CRR from nadir was observed in 51% of patients. The number of eyes which remained on chart increased from 51% at nadir to 67% at last observation, and those <1.0 logMAR increased from 7% to 27%. At BL, 9% of patients were <1.0 logMAR in both eyes, which increased to 23% following treatment. The proportion of patients with CRR increased with treatment duration, with approximately 50% observed up to 6 months, but extending up to 18 months. CRR and CRS were observed, to different degrees, regardless of mutation.
Conclusions
Idebenone has a good safety profile for the long-term treatment of LHON, and when initiated early, can stabilize good residual vision and prevent severe vision loss and blindness in a large proportion of patients. Maximal benefit may be achieved by prolonged treatment.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Xavier Llòria is an employee of Santhera Pharmaceuticals

• T042

Optical coherence tomography angiography of the peripapillary retina and optic nerve head in Wolfram syndrome

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Purpose
To evaluate the peripapillary and optic nerve head (ONH) microcirculation in patients affected by Wolfram syndrome and to correlate the results with the functional and anatomical conventional imaging: visual field (VF) and structural optical coherence tomography (OCT).
Methods
This study reports two cases of siblings with wolfram syndrome. They underwent a complete ophthalmological examination and an automated perimetry. A measure of peripapillary retinal nerve fiber layer (RNFL) thickness using a Swept- Source OCT was performed. Optical coherence tomography angiography (OCT-A) images were obtained using a Swept-Source DRI OCT Triton (Topcon Corporation, Japan). The scan size of optic disc area was 6 mm × 6 mm and he was divided into four layers, which were optic nerve head (ONH), vitreous, radial peripapillary capillary (RPC), and choroid layers. Peripapillary and nerve head vessels density were evaluated.
Results
The first case is a 57 years old female patient with a history of diabetes insipidus and deafness, suffering from bilateral progressive visual loss. On fundoscopic examination, she had bilateral optic atrophy. Her visual acuity was reduced to 0.4 on both eyes. Her visual fields demonstrated generalized constriction. There was a family history of similar conditions. Her brother, a 46 years old male has a similar course of disease. The two patients had sectorial (temporal and inferior) optic atrophy based on the RNFL thinning detected by OCT. OCT-A scans showed a decrease of the vascular network in the ONH and in the RPC layers corresponding to the sector of RNFL thinning.
Conclusions
Peripapillary and optic nerve head temporal and inferior microvascular network were reduced in Wolfram patients. These findings confirm the preferential involvement of the small axons of the papillomacular bundle in dominant optic atrophy.

• T043

Ophtara centers of expertise in France: Fostering collaborative research and patient care for rare eye diseases

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Purpose
The French National Reference Center on Rare Diseases in Ophthalmology OPHTARA was labeled in 2006. This expertise center (re-labeling in 2017) includes Necker coordinating site, 3 component sites (Paris University Hospitals) and 16 national competence centers. Necker is unique center for rare eye diseases and ocular surgery for children. OPHTARA ensures patient care (children and adults) and covers all rare eye diseases, mostly genetically determined. OPHTARA and ocular genetics laboratory provides optimal genetic diagnosis.
Methods
OPHTARA recent structure gathers together 20 centers of expertise (CEs) localized all over France and 2 overseas territories. The center is attached to the National HealthCare Network SENSGENE and it is unique consortium part of European Reference Network (ERN) EYE, accredited in 2016. Rare eye disorders were divided in 4 goupes: diseases of anterior/posterior segment, of lacrimal/eyelid/orbit/, panocular and syndromic.
Results
OPHTARA is incrementing a database for rare diseases CEMARA including actually 7600 registered patients (2008-2017). The refferal Center established an optimal overall patient management strategy. OPHTARA develops actions concerning patient diagnosis, monitoring and care, research, clinical trials, education, professional training and information for patients and their families. The reference center defines healthcare protocols and guidelines, being the contact for many patient's associations.
Conclusions
OPHTARA ensures a role of expertise, multidisciplinary care and follow-up of patients thanks to the specific recognized skills of HCPs experts in rare ocular diseases. The networking could lead to the gathering of the scarce expertise in France to ensure high quality care for rare eye disease patients. European dimension of OPHTARA health care is proved by ERN EYE integration.

• T044

Microperimetry by optic nerve atrophy

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Purpose
to develop an algorithm testing of patients with optic nerve atrophy by microperimetry with different types of functional disorders.
Methods
the study included 40 patients with bilateral atrophy of the optic nerve, age 33, 0 ± 1, 88 years, with confirmed diagnosis of multiple sclerosis. 11 patients had a history of monocular optic neuritis – the first group (11 eyes), 29 without a history of optic neuritis – the second group (29 eyes). Preliminary, a Humphrey HFA-75i survey was conducted on a 120-point testing program. Microperimetry was performed on the MR-1 (Nidek technologies, Vigonza, Italy). We selected a pattern, fixation target, stimulus, test mode. In some cases it is necessary an individual selection of study parameters.
Results
The authors developed an algorithm for testing patients with optic nerve atrophy due to multiple sclerosis. The first group (11 patients) - visus 0.1-0.4 - pattern macula 12° 10dB, stimulus Goldmann III, fixation target - single cross 4°. In the first group mean sensivity 8.21 ± 2.3 dB dB, central visual field defects and unstable fixation 91.81 ± 2.72%.The second group (29 patients) - visus 0.5-1.0 – pattern retina 40° 20dB, stimulus Goldmann III, fixation target – four crosses 4°. In the second group mean sensivity 15.32 ± 0.84 dB, central and paracentral visual field defects and stable fixation 91.81 ± 2.72%. The results of microperimetry differed depending on the size of visual field defects and visual acuity. Thus, in the group with low visual acuity, there was a lower central sensitivity and more significant defects of the central field of vision compared to the group with a high visual acuity.
Conclusions
in the "Eye Microsurgery Complex", Moscow, at the first has been developed an algorithm of microperimetry in patients with MS with different visual acuity and stability of fixation.

• T045

Clinical applications of a visual field perimeter with binocular video imaging

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Purpose
The majority of visual field testing equipment is designed for monocular tests only: most instruments do not have the capability to visualize both eyes simultaneously and many do not have a head rest position suitable for binocular testing. This presentation will focus on the clinical applications of the binocular visual field tests available on the MonCvONE perimeter.
Methods
Binocular testing is very important for functional evaluations. Extrapolation from monocular tests is inaccurate as phenomenons such as integration, suppression, ocular deviation, cyclotorsion, ... affect differently monocular and binocular vision.
The MonCvONE perimeter combines a binocular video sensor with the possibility of video recording to the possibility of controlling the exam with an interactive mode similar to the Goldmann perimeter.
Results
Clinical examples of binocular perimetry will be presented including - the evaluation of ptosis with a documentation of the gain in visual field area in relationship with the opening of the eye lids. - the assessment of low vision with the Esterman technique - the evaluation of drivers' visual field in agreement with the European Community directive - the evaluation of the field of single vision with the determination of a diplopia score
- the test of the visual field in young infants when eye occlusion and head immobility are not easily obtained
Conclusions
These examples demonstrate the clinical usefulness of binocular visual field testing with video recording
Conflict of interest
Any post or position you hold or held paid or unpaid?:
president of Metrovision
Any Stocks or shares held by you or an immediate relative?:
shares in Metrovision

• T046

Comparative investigation of compression optic neuropathy of Grvaves orbitopahty(GO) as emergency orbital decompression

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Purpose
Purpose: to investigate pre-operative clinical feature of Compression optic neuropathy of Grvaves orbitopahty(GO), which had necessities of emergency surgery as orbital decompression.
Design: Retrospective,observational ,case-control study.
Methods
methods: setting single institution. Patient population: Sevanty-two patients were performed orbital decompression as treatment of proptosis and compression optic neuropathy with GO. Observational procedures: the following were considered potential pre-operative clinical factors for emergency orbital decompression: patients's sex, patients's age, Disease duration, laterality of GO, laterality of surgery, treatment history of resistance of steroid pulse therapy, thyroid function, visual acuity, existence of central diplopia, asymmetry of proptosis, psychological history,smoking. Main outcome: potential pre-operative clinical factors for emergency orbital decompression
Results
Results: women ,high age, long Disease duration, laterality of GO, laterality of surgery, treatment history of resistance of steroid pulse therapy, unstable thyroid function, poor visual acuity, existence of centraldiplopia significantly influenced necessities of emergency surgery as orbital decompression($p<.050$). The other itmes did not significantly influence necessities of emergency surgery as orbital decompression($p>.050$)
Conclusions
Conclusion: This study revealed potential pre-operative clinical factors of Compression optic neuropathy of Grvaves orbitopahty(GO), which had necessities of emergency surgery as orbital decompression. This results will be helpful and deeply meaningful for physician, managing GO, planning additional surgical options

• T047

Prediction of ophthalmological problems in 6.5 year-old prematurely born children

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Purpose
The aim of the study was to describe the ophthalmological outcome at 6.5 years and to identify possible predictive factors visual problems at this age.
Methods
This is a prospective, population-based study, including all infants born ≤ 32 weeks gestational age (GA) in Uppsala County, Sweden, during 2004 to 2007. The children were screened for ROP in the neonatal period, visual tracking test were performed at 4 months tests of, and at 2.5 years, ophthalmological, visuospatial and cognitive testing were performed. At 6.5 years, 84 prematurely born and 64 children born at term participated in ophthalmological and visual testing. Of the preterm children, 24 (29%) had ROP and 9 had IVH 3-4 and/or PVL in the neonatal period.
Results
Mean visual acuity (VA) did not differ between preterm and full-term children, but a "subnormal" VA of ≤ 0.8 was more common in the preterm than the control group (31% versus 14%) ($p<0.05$). No prematurely born child was blind, but two had VA < 0.5. A contrast sensitivity of < 0.5 was more common (36% versus 19%, $p<0.05$) and strabismus was also more common in the pre-terms (8% versus 0%, $p<0.05$). Within the preterm group, logistic regression analyses revealed GA, ROP, PVL/IVH, and mild cognitive disability (Bayley III test), to be predictive factors for ophthalmological and visual problems at 6.5 years age.
Conclusions
Prematurely born children had an increased prevalence of ophthalmological problems at 6.5 years age. Treated ROP and early neurological problems were risk factors for later ophthalmological dysfunctions. This study also showed that reduced cognitive function at 2.5 years appeared to predict such problems.

• T048

Comparison of traditional training and push-pull training for the binocular visual function in anisometropic amblyopia

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Purpose
To compare the binocular visual function in anisometropia amblyopia used by Push-pull Training and traditional training.
Methods
A total of 64 children with anisometropia amblyopia were enrolled in our study and randomly divided into two groups. After wearing glasses to correct refractive errors in the first three months, the experimental group were treated with push-pull training, and the the control group were treated with traditional covering method and visual stimulation for a period of 6 months. Then binocular visual functio was measured by synoptophore and random-dot stereograms(RDS).
Results
The average visual acuity of the amblyopic eyes in the experimental group was increased 4.2±2.6 lines and the control group was increased 4.52±1.9 lines ($p>0.05$). The average score of far stereoscopic in experimental group increased 9.3±4.7 points and the control group increased 10.1±5.6 points($P>0.05$.)There was no statistical difference between the two groups.
The average score of large-scale RDS stereoscopic in experimental group increased 14.2±9.7points and the control group increased 12.1±7.5points ($P<0.05$). The average score of the acuity stereopsis RDS in experimental group was increased 19.3±10.2 points and the control group increased 13.5±8.4 points($P<0.05$). The average score of cross stereoscopic RDS in experimental group increased 14.9±6.8 points and the control group increased 11.8±5.7 points ($P<0.05$). The average score of uncross stereoscopic RDS in experimental group increased 17.1±7.9 points and the control group increased13.4±6.6 points ($P<0.05$). There was statistical difference between the two groups.
Conclusions
compared with traditional cover training methods, the push-pull training method can not only achieve the same visual acuity, but also establish better binocular vision function.

• T049

Visual status of patient with syndrome of Moebius

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Purpose
To analyze functional state of visual status in a patient with Moebius syndrome during 16 years of follow-up.
Methods
Retrospective analysis of clinical course of Moebius syndrome in a patient in the age 0.5 - 16 years.
Results
Parents appealed to the Institute because of unusual state of the child (lack of facial expressions and eye mobility). After the ophthalmologic and neurological examination, a diagnosis was made: Moebius syndrome. Underdevelopment of VII, IX, XII pairs of cranial nerves. Myopic astigmatism. At 10 years old facial asymmetry, exotropy with vertical component, positive traction test on both sides and lagophthalmus 3 mm at downgaze were noted. Best corrected visual acuity of both eyes is 0.2. Perimetry both eyes: concentric narrowing up to 40° from temporal and nasal sides, up to 20° from above and from below. Optic discs are pale, there are pigmentless sections of retinal dystrophy on the periphery and near the optic discs. Pleoptoortoptic treatment was carried out. As a result of regular courses of electrostimulation of extraocular muscles, by the age of 16, a tendency to insignificant motility of the eyes upwards appeared. Convergence was absent. Best corrected visual acuity decreased to 0.1 in both eyes. Significant help in diagnosis was provided by computer pupillography [Bushuyeva NN et al., 2003], which accurately records and measures pupil area. The initial size of the pupil area was: on the right eye 17.9 sq mm, and on the left eye 13.1 sq mm. After the flash, the pupil of the left eye narrowed to 3.7 sq mm and the right eye - to 15.2 sq mm.
Conclusions
Pupillography allows evaluating vegetative nervous system status in Moebius syndrome patients. Electrostimulation of extraocular muscles allows slightly improving ocular motility of these patients. Obtained data needs further investigations on larger number of patients

• T050

Magnetic resonance imaging features in moebius syndrome: a pilot study

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Purpose
To investigate with unconventional neuroimaging (UNI) the alterations of the brain structures in patients affected by Moebius Syndrome (MBS).
Methods
7 MBS patients underwent MRI evaluation of the brain and the brainstem with 3.0T MRI through volumetric sequences (FLAIR 3D, BRAVO, CUBE T2); high resolution T2 imaging (FIESTA) and Diffusion Tensor Imaging (75 directions, ST: 3 mm) were also performed to better evaluate all cranial nerves. Data analysis and full-brain tractography were obtained using Functool software. We measured the dimensions of the brainstem in MBS patients and compared the obtained values with the AIRO's (Italian Association of Radiation Oncology) standard data.
Results
Brainstem resulted abnormal when compared to controls; in particular we found an hypoplasia of both the midbrain (6 cases) and the medulla (3 cases). In all the cases the VI and VII cranial nerves resulted hypo- or aplasic; fiber tracking and color coding in the DTI analysis showed a lack of uniformity in the brainstem and in the cerebellar peduncles. We also found a prevalence of abnormal transverse pontine fibers colonizing the cortical spinal tracts bilaterally (6 cases). We documented: thinner corpus callosum (4 cases), reduction of the internal auditory meatus and cisterna magna (1 case).
Conclusions
Our data show new relevant alterations of the brainstem in MBS patients investigated with UNI; we suppose that this could be related to a misdirection of the axonal guidance paths during the embryogenesis secondary to the abnormal development of the VIthand VIIth cranial nerves nuclei. We also found anomalies in the supratentorial region which need further investigations. A correlation of the features herein observed with the ophthalmological pattern of MBS may provide further insight in the pathogenesis of this disease.

• T051

Clinical features of strabismus and nystagmus in bilateral congenital cataract

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Purpose
The prevalence and clinical features of strabismus and nystagmus, and the factors affecting onset of strabismus and nystagmus were evaluated in the patients with bilateral congenital cataract.
Methods
58 patients, 116 eyes who had lens removal for the treatment of bilateral congenital cataract between January 1999 and January 2011 were evaluated. According to the preoperative and postoperative ocular alignment, patients were divided into 3 groups (Orthotropia/Orthotropia, Orthotropia/Strabismus, and Strabismus/Strabismus). Age at cataract surgery, and associations of nystagmus and primary intraocular lens (IOL) implantation with strabismus were analyzed.
Results
6 patients (10.3 %) had strabismus preoperatively and 11 patients (19.0 %) developed postoperative strabismus. Thus, total 17 patients (29.3 %) had strabismus postoperatively. Exotropia was more common than esotropia both preoperatively and postoperatively. 18 patients (31.0 %) had nystagmus postoperatively and sensory nystagmus was the most common type. Of the 18 patients with nystagmus, 10 patients had strabismus and exotropia was more common than esotropia. When there was nystagmus, postoperative visual acuity was poor. In the ortho/strabismus group, age at cataract sugery was significantly younger and postoperative nystagmus was more common and the rate of no primary IOL implantation was higher than the other groups.
Conclusions
In patients with bilateral congenital cataracts, exotropia and sensory nystagmus may be common. Age at surgery was earlier, the rate of no IOL implantation was higher and nystagmus was more common in postoperative strabismus onset group. And if there is nystagmus, poor visual prognosis may be seen. Therefore, careful observation should be needed in these patients.

• T052

Treatment with prism glasses for overcorrection after surgery for exotropia in children

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Purpose
To determine the effect of prism glasses and factors affecting treatment in children wearing prism glasses for overcorrection after surgery for exotropia.
Methods
The medical records of 43 patients who wore prism glasses for overcorrection after exotropia surgery and were followed up more than 1 year were reviewed retrospectively. Patients with overcorrection after surgery for exotropia were treated with occlusion of one eye and correction of hyperopia, and the prism glasses were prescribed if esotropia persists. The strength of prism glasses was adjusted based on alignment. We evaluated the effect of prism glasses according to the starting age of prism glasses, type of surgery, refractive error, occlusion after wearing prism glasses and overcorrection of the strength of prism glasses.
Results
Twenty one patients (48.8%) took off prism glasses. Among 22 patients who still wear prism glasses, the strength of prism was decreasing in 10 patients, maintained in 8 patients and increased in 4 patients. Only 1 patient underwent surgery for consecutive esotropia. In patients who began to wear prism glasses under the age of 10, the rate of took off prism glasses or the rate of decreased in the strength of prism was higher than in patients who began to wear prism glasses aged 10 or older (p=0.007). All patients who underwent unilateral recession and resection took off prism glasses or decreased the strength of prism glasses (p=0.026).
Conclusions
Among 43 patients who needed prism glasses to treat overcorrection after exotropia surgery, 72% took off prism glasses or decreased the strength of prism glasses. Only 1 patient needed second surgery for consecutive esotropia. Treatment with prism glasses for overcorrection after exotropia surgery is very useful and can lower the frequency of second surgery.

• T053

Comparison between over-glasses patching and conventional patching for children with moderate amblyopia : a prospective randomized clinical trial

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Purpose
To investigate efficacy of over-glasses patching treatment for amblyopic children using visual function improvement and Amblyopia Treatment Index (ATI) changes.
Methods
In a randomized multi-center controlled clinical trial, 107 children younger than 7 years with moderate amblyopia (visual acuity in the range of 20/40 to 20/100) were included to receive treatment with either a conventional patching or an over-glasses patching. The patients were prescribed 2 hours of patching per day for the sound eye. Best-corrected visual acuity (BCVA) was investigated and ATI questionnaires were collected from parents at 5 weeks and 17 weeks after the initiation of treatment. We compared the changes of visual acuity of amblyopic eyes and ATI scores in two groups.
Results
At 17 weeks, the mean visual acuity of amblyopic eye improved 3.2 lines in the conventional patching group and 2.7 lines for a new patching method that fit over eyeglasses (p=0.345). A similar proportion of subjects in each group had improvement of ≥ 2 lines (conventional patching group 67% vs. new patching group 67%, p=0.372) or had 20/25 or better amblyopic eye acuity (27% vs. 22%, respectively, p=0.531). There was not also a different treatment burden in each group as measured with the Amblyopia Treatment Index. The questionnaire number 11 (with statement, "Treatment makes the child's eye or eyelids red") was the only item having significantly different score between two groups (mean 4.0±0.9 vs. 2.8±1.0 at 5 weeks, p<0.001 and mean 4.0±1.1 vs. 3.0±1.0 at 17 weeks, p= 0.001, respectively, for conventional vs. over-glasses patching).
Conclusions
Over-glasses patching treatment is a useful option for amblyopia treatment when the patients suffer from adverse effects of using conventional patching.

• T054

A method for a rapid objective measurement of eye deviation angle in both strabismus and phoria

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Purpose
Strabismus is usually treated by corrective surgery of the extraocular muscles, the parameters of which mainly depend on the misalignment measurement and hence on its precision. The current strabismus angle measurement (prism cover test) hasn't changed since the eighteenth century. This test is time-consuming, cumbersome, severely limited by the child's cooperation, subjective and highly dependent on the examiner's skill and experience. Studies have shown a very high inter-examiner variability in measurement results. Moreover, the angle of strabismus itself may vary over time and the current low-efficiency test does not allow for multiple testing of the same patient, thus reducing the test's accuracy. Increasing the measurement accuracy and efficiency may reduce the number of reoperations and will improve results of strabismus surgery, prism prescriptions and orthoptic therapy and monitoring.
Methods
We are evaluating the accuracy and repeatability of NovaSight's novel strabismus angle measurement method using an automatic and objective system based on eye tracking, in comparison to the prism cover test results.
Results
A group of 23 adult subjects (average age 26.8±4.6 years) with eye deviations, heterotropia and heterophoria, were tested by both the automatic and the manual tests in a masked fashion by two experienced optometrists. The clinical trial results show a high correlation of over 88% between the presented automatic test and the golden standard prism cover test while a significant difference in standard deviation was found, the repeatability of the automated test is twice as high as that of the manual test.
Conclusions
The system increases the examination accuracy and thus may reduce the number of strabismus reoperations. The system also reduces chair time significantly and has the potential to become the new standard of care.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Company employee

• T055

Redistribution within retinal layers of the central fovea in preterms with developmental arrest

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Purpose
The aim of this study was to characterize thickness changes of foveal layers in preterms with or without signs of immaturity compared to control subjects through analysis of optical coherence tomography (OCT) B-scan images.
Methods
Selected eyes from 8 young adults with a history of prematurity (24-33 weeks of gestation) and 5 controls were imaged using conventional and directional OCT. Retinal layer thickness analysis was performed at selected temporal eccentricities defined by the individual distance between two landmarks for each case, the foveal center (FC) and the foveal rim (R).
Results
The use of an FC/R landmark transformation enabled comparisons of thickness profiles and area calculations from inter-individual B-scans at corresponding landmark positions in both controls and preterms. Reflectometric and manual segmentation measurements showed increased thickness of inner retinal layers (IRL) and photoreceptor cell body and axon/pedicle layers within the central fovea. Thickness and areal differences between controls and preterms with signs of developmental arrest showed a marked redistribution of IRL and the layers of photoreceptor cell bodies, axons and pedicles/synapses within the central fovea. This is in line with incomplete displacement of these layers from the foveal center. Since no changes of photoreceptor inner and outer segment thickness were observed the maturation of the photoreceptor segment layers seems to be within normal limits.
Conclusions
Our landmark-based analysis of OCT images using reflectometry and manual segmentation provides complementary findings in comparisons of normal and immature foveal structures. The thickness increase in the outer nuclear, Henle fiber, outer plexiform and post-receptor layers in preterms with signs of arrested foveal development indicate a marked redistribution of cells.

• T056

Enhanced visual attentional modulation in patients with inherited peripheral retinal degeneration in the absence of cortical degeneration

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Purpose
Studies concerning the effects of peripheral retinal degeneration on visual cortical structure and function are scarce. Our work aimed to determine the effect of peripheral retinal dystrophy caused by Retinitis Pigmentosa on brain function and structure using magnetic resonance imaging, taking into account the effect of the preserved visual field extent and the disease onset age.
Methods
We included thirteen patients and twenty-two matched controls. We analyzed cortical responses under attentional demands and passive viewing conditions while presenting a visual stimulus covering the central and paracentral visual field. Responses were studied in the visual cortical areas (V1, V2 and V3) and also in two cortical regions of interest corresponding to the preserved and the damaged visual field. The cortical thickness of visual areas was also measured
Results
We found that cortical visual responses under attentional demands were increased in patients with larger degeneration of visual field. Moreover, activation during the task condition was increased for patients in both cortical regions corresponding to the preserved and the damaged visual field, specifically in patients with severe visual field loss. These findings were observed in presence of preserved visual cortical structure.
Conclusions
We conclude that Retinitis Pigmentosa patients have enhanced visual attentional modulation despite their retinal degeneration, while cortical structure remains intact (with an relative increase in V2 thickness in patients with RP in early stages). The unmasking of feedback signals from higher level visual regions involved in attentional processes may explain the increased cortical responses. These findings are relevant in the context of the design of strategies for treating retinal diseases.

• T057

Slit lamp assessment of relative afferent pupillary defect

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Purpose
To demonstrate the accuracy of slit lamp assessment of relative afferent pupillary defect (RAPD) in patients with asymetric optic neuropathy.
Methods
40 eyes of 20 patients with asymetric optic neuropathy and no obvious RAPD in swinging flashlight test were evaluated on slit lamp. The asymetric optic neuropathy was confirmed by fundus examination, retinal nerve fiber layer thikness on OCT, visual field examination, visual potentials and/or brain and orbit MRI.
The horizontal pupillary diameter in the affected (or more affeted) eye was measured and compared to the horizontal pupillary diameter of the fellow eye using the width of the slit lamp beam. Both diameters were measured in millimeters and compared.
Results
There was a quantified anisocoria and RAPD each time when asymetric optic neuropathy was present. In other words, with the same slit lamp beam width (the same light intensity) the affected (or more affected eye) had a larger pupillary horizontal diameter.
Conclusions
Slit lamp assessment of RAPD is simpler, quicker and more accurate than standard assessment using swinging flashlight test especially when anisocoria is not obvious.

• T058

Case of IgG4-related eye disease accompanied by compressive optic neuropathy

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Purpose
We report a case of IgG4-related eye disease accompanied by a compressive optic neuropathy.
Methods
A 76-year-old woman had hypothyroidism with thyroid ophthalmopathy and was followed at the Kimitsu Central Hospital from July 2015. On October 2016, her right exophthalmos worsened, and a lago ophthalmic keratitis developed in the right eye on February 2017. MRI showed enlargements of the extraocular muscles, and blood tests showed high levels of serum IgG4 (446 mg/dl). On February 27, 2017, her visual acuity decreased to 0.01 OD, and she was referred to the Chiba University Hospital.
Results
At the first visit, her visual acuity was counting finger OD, and Goldmann perimetry showed a lower right visual field defect. Ocular movements in the right upper field was severely limited because of a lesion that occupied the upper orbit. She was diagnosed with IgG4-related eye disease accompanied by compressive optic neuropathy.She underwent two cycles of steroid pulse therapy with intravenous antibiotics. Two months later, her decimal visual acuity improved to 0.4 OD, and the ocular movements and the visual field defect were markedly improved. The logo ophthamic keratitis also improved, and the oral prednisolone was tapered to 20 mg. No side effects of the steroid therapy was observed.
Conclusions
When thyroid ophthalmopathy is markedly exacerbated, ophthalmologists should consider IgG4-related eye disease that can be masked by lesions associated with thyroid ophthalmopathy.

• T059

Spectral-domain optical coherence tomography of optic nerve after closed eye injury

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Purpose
Purpose: to research optic nerve in the early period of closed eye injury by spectral-domain optical coherence tomography.
Methods
32 patients with closed eye injury and transparent eye media were examined. The age of the patients was 41,5+ 2,7 years. The examination was performed 4,01+0,37 days after the injury. Visual acuity of the injured eye was 0,65+ 0,06. After examination by automated static perimetry 8 patients were diagnosed with paracentral scotoma, 4 - with scotomas in Bjerrum zone, 7 - with peripheral scotomas, 2 - with central scotomas. In 11 cases no scotomas were registered. Spectral-domain optical coherence tomography (SD-OCT) of both injured and healthy eyes was performed at the optical coherence tomograph RTVue-100 OCT (Optovue, Fremont,USA). Optic nerve heads (ONH) and retinal nerve fiber layers (RNFL) were examined with estimated diameter of 3,45 mm around disc center.
Results
Statistical analysis of morphometric parameters of ONH and RNFL based on SD-OCT data showed that in the early period in comparison with the healthy eye the injured eye has ONH edema resulting in ONH volume increase (0,43 + 0,02 and 0,29 + 0,02 mm3; p=0,008), rim volume increase (0,21 + 0,01 and 0,17 + 0,01 mm3; p=0,03), rim area increase (1,64 + 0,05 and 1,25 + 0,04 mm2; p=0,03), ONH area increase (2,12 + 0,07and 1,89 + 0,06 mm2; p=0,01), cup volume decrease (0,08 + 0,01 and 0,13 + 0,02 mm3; p=0,04) and cup area decrease (0,48 + 0,06 and 0,63 + 0,07 mm2; p=0,03). In addition to this RNFL thickness increase (111,12 + 2,04 and 106,75 + 1,59; p=0,007) was noted.
Conclusions
We detected a significant increase in the volume of the optic nerve head and an increase in the thickness of the nerve fiber layer of the retina on all 32 eyes in the early period after a closed eye injury

• T060

An intraocular foreign body detection using swept-source OCT

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Purpose
To describe a case report of a 35 years old metal worker with a corneal ulcer in his right eye treated with an antibiotics ointment by a primary care doctor that presented blurry vision two days later.
Methods
Examination of the anterior chamber by slit lamp, tonometry was used to determine intraocular pressure, funduscopy, Swept-Source OCT and CT scan were performed.
Results
The patient right eye presented intense epibulbar and tarsal hyperemia, and it had a 1x1mm corneal ulcer, positive in the fluorescent test, and an iridium hole below. Tyndall 2+ and IOP of 18mmHg. No cataract was detected. Funduscopy examination showed a moderate amount of vitreous hemorrhage. A CT scan, retinography and a Swept-Source OCT were performed and they revealed an intraocular foreign body located in the optic nerve area. The foreign body was removed via pars plana vitrectomy 23G surgery, requiring a magnet a demarcating laser. After four months the patient has a 20/20 visual acuity with no cataract.
Conclusions
This case underlines that although CT scan is considered the "gold standard" for the detection, localization and characterization of intraocular foreign bodies, new image techniques as Swept-Source OCT can be a non invasive and accurate search tool in cases of intraocular foreign body.

• T061

Can the retina be used to diagnose and plot the progression of Alzheimer's disease?

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Purpose
Alzheimer's disease is a neurodegenerative disease and the most common cause of senile dementia. The fact that the diagnosis can only be definitively made postmortem, or when the disease is fairly advanced, presents a serious problem if novel therapeutic interventions are to be devised and used early in the course of the disease. Therefore there is a pressing need for more sensitive and specific diagnostic tests with which we can detect Alzheimer's disease in the preclinical stage. In this presentation we describe the work of a systematic review,addressing the question whether the retina can be used to make a specific and early diagnosis of Alzheimer's disease.
Methods
This review was written during the EVER fellowship,2016 in the School of Optometry and Vision Sciences .All human and animal reviews, clinical and comparative studies, published in any language in the past 5 years from March 2011 were studies. 36 suitable papers were choosen after screening.
Results
With improvements in retinal imaging techniques like OCT, Doppler, FLIO and FLES, which are non invasive and inexpensive, the early diagnosis of AD is possible. Dynamic vessel analysis, retinal oximetry and adaptive optic retinal imaging are recent advances in retinal imaging, which provide a detailed analysis of the retina. Retinal vasculature screening may be a method for population screening of AD. With curcumin and immunotherapy the progression of the disease can be monitored and treatment can be planned, which is highly promising.
Conclusions
A high degree of clinical suspicion is needed to correlate problems in cognition with the changes in the eye, particularly the retina, pupil and ocular movements, so that the disease can be detected early and managed in the prodromal phase. The definitive diagnosis currently requires a combination of many biomarkers.

• T062

The proportion of microsaccadic overshoot and the influence of accomodation on the quantitative measures of microsaccades in fourteen normal test persons

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Purpose
In normal test persons to 1) quantify the proportion of microsacadic overshoot, and 2) to investigate if accomodation have an influence on the quantitative measure of microsaccades.
Methods
Fourteen healthy adults (mean age 31.2 years, range 16-50 years) all with a visual acuity of 1.0 or better with no previous eye diseases were investigated. Mean ametropia was -1.0 diopter. Microsaccades were quantified binocularly using an infrared recording technique (Eye Link 1000) during fixation at a distance of 40 centimeters and 6 meters. Accomodation was measured at 40 centimeters and 6 meters using an open field autorefractor (Shin Nippon SRW-5000).
Results
The mean proportion of microsaccadic overshoot during fixation at 40 centimeters and 6 meters was 75.8% and 146.1% larger than the normal "classic" microsaccadic amplitude, respectively. The relation between the "classic" microsaccadic amplitude (x) and the proportion of overshoot (f) could be fitted to a negative exponential curve. The best curve fit at 40 centimeters (R2=0.88) was f=3.02°exp(-6.00°x) and at 6 meters f=3.10°exp(-6.21°x) (R2=0.98). The mean "classic" microsaccadic amplitude (±SD) at 40 centimeters was 0.334 ± 0.140 degrees and 0.256 ±0.073 degrees at 6 meters. The microsaccadic amplitude ±SD including overshoot at 40 centimeters and 6 meters was 0.486 ± 0.209 degrees and 0.411 ± 0.101 degrees, respectively. Accomodation (in diopters) at 40 centimeters was positively correlated to the mean "classic" microsaccadic amplitude.
Conclusions
The proportion of microsaccadic overshoot is larger for smaller microsaccades when fixating at both near and far targets. Microsaccades seems to be influenced by accomodation.

• T063

Correlations of retinal thickness with frequency-doubling technology perimetry in older healthy subjects

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Purpose
To evaluate correlations of macular and peripapillary retinal nerve fiber layer (pRNFL) thickness with frequency-doubling technology (FDT) perimetry in older healthy subjects.
Methods
The observational, transversal, and comparative study examined 65 healthy eyes of 33 young subjects (22.0±2.1 years) and 32 older subjects (62.2±3.9 years). All eyes underwent inner and outer macular-segmentation (Treatment Diabetic Retinopathy Study macular regions) and peripapillary retinal nerve fiber layer (pRNFL) thickness measurements using spectral domain optical coherence tomography (iVue SD-OCT), and the FDT testing with N-20 full-threshold protocol.
Results
The fovea thickness decreased in the inner retina (p= 0.03), and increased in the outer retina (p= 0.025) in the older group. The inner macular-segment of the 3 mm zone was thinner (p= 0.002) in the older subjects. The 5 mm zones of inner and outer macular-segments and pRNFL thickness showed no significant differences with age. The FDT sensitivity was significantly lower in the older group, but the mean of mean deviation (MD) and pattern standard deviation (PSD) were not significantly different between age groups. PSD values were within the normal limit range (0-6 dB) in both groups. Only the PSD of FDT showed a significant negative correlation (R=-0.387, p=0.028) with the outer macular-segment thickness of the peripheral ring in older subjects.
Conclusions
The FDT pattern standard deviation increased as the outer macular-segment thickness of peripheral ring decreased in healthy older subjects.

• T064

Timing of changes in the entropy of the electroretinogram with glaucoma

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Purpose
The Photopic Negative Response (PhNR) of the electroretinogram (ERG) has been shown to be reduced in glaucoma in clinical studies and animal models. Its slow and noisy nature makes the implicit time of the negative going peak of the response difficult to define, most studies have focussed on the amplitude of the response rather than its timing. In this study, we estimate the timing of changes in signal entropy in a normal and glaucoma cohort from the ERG with the PhNR stimulus.
Methods
The left eyes of 21 glaucoma patients (age 34-86 mean 66.4) and 18 normal aged matched controls (44-84 mean 60.7) were tested. ERGs were measured with the LKC RetEval device with the integrated skin electrodes using a red flash stimulus (4ms) on a blue background (10cd/m2) after preadaptation using the mini-Ganzfeld. B-wave amplitude and implicit time were measured with the device software. Entropy analysis was performed in R on each raw sweep with a sliding window of 150 samples. The window was advanced in increments of one sample. The entropy at each window timepoint was averaged for all the sweeps. The terminal rise in entropy was detected by finding the maximum of the first derivative after filtration with the Komolgorov Zurbenko adaptive (kza) filter.
Results
There was no difference between the glaucomas and controls in the implicit time of the b-wave (31.1ms vs 30.6 ms p=0.66) or its amplitude (19.3 vs 17.0 mv p=0.18). The timing of the rise in entropy after the b-wave was significantly different with the glaucoma cohort rising sooner (74.7ms vs 79.8ms p =0.04). The gradient of the entropy rise was not significantly different.
Conclusions
The entropy rise after the flash stimulation corresponds to the end of the electrical activity evoked by the stimulus. The difference in glaucoma may be due to a relative loss of peripheral ganglion cells.

• T065

Across-frequency impairment in seeing a temporal gap

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Purpose
To assess the effects of employing separate spatial frequencies for leading and trailing markers on detection of a temporal gap between the two markers.
Methods
Twelve normal observers were tested to measure gap detection thresholds. Gaussian-windowed sinusoidal gratings were used for markers bounding a gap and thresholds were determined using an adaptive tracking procedure. Spatial frequencies of the leading and the trailing markers were orthogonally manipulated to be either 2 or 4 cpd. The trailing markers were tilted slightly clockwise from the vertical leading markers in order to isolate the effects of frequency change from those of pattern change. In separate blocks of trials, four combinations of the leading and trailing frequencies were tested.
Results
With markers of identical frequency, gap thresholds were higher for 4 cpd than for 2 cpd markers, replicating well-established findings of impaired temporal resolution with increasing spatial frequency. Gap thresholds for markers of different frequencies were even higher than the 4-cpd within-frequency thresholds.
Conclusions
Seeing a temporal gap becomes difficult when spatial frequency change is introduced between gap markers. We propose that temporal processing across different spatial frequency channels leads to impaired gap detection.

• T066

Changes in the electromyography of the lateral and medial muscles after the electrostimulation treatment of lateral muscles in children with convergent concomitant strabismus

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Purpose
It is known that physiotherapeutic treatment of convergent concomitant strabismus with electrostimulation of extraocular rectus muscles is applied. Assessment of changes in the electromyography of the muscles after the course of treatment was not carried out, due to absence of a method of surface electromyography (SEMG) of the rectus muscles.To identify changes in the SEMG before and after electrostimulation of the external rectus muscles in children with concomitant strabismus the work was done
Methods
Electrostimulation of the lateral rectus muscles of both eyes was performed using the Amplipulse-5 apparatus in a standard procedure in 12 children (24 eyes) with convergent concomitant strabismus with deviation 12- 24pr.dptr. SEMG was done with the M-TEST-2 electromyograph, according to the method developed by us earlier. Patients were examined before and after treatment.
Results
Amplitudes of the biopotentials of the SEMG of the lateral rectus muscle decreased slightly after treatment (11,55 ± 2,3 mV ÷ 10,64 ± 0,7 mV, p> 0.05), while the frequency increased significantly (49, 7 ± 3,6Hz ÷ 63,18 ± 8,2Hz, p <0.05). Ranges of the SEMG biopotential amplitudes and frequency of the medial rectus muscle decreased slightly after treatment (11.48 ± 0.5 mV ÷ 10.2 ± 0.9 mV, 101.96 ± 5.6 Hz ÷ 94.7 ± 19, 5 Hz, p> 0.05). Deviation became less in average on 12,2±4,6 pr.dptr. en with concomitant strabismus.
Conclusions
The method of surface electromyography allows estimating changes in the biopotentials of of the external rectus of the eye before and after electrostimulation (amplitude, frequency). Electrostimulation treatment decrease the imbalance between the lateral and medial rectus muscles biopotentials of SEMG in children with a convergent concomitant strabismus.

• T067

The time course of contrast sensitivity recovery after a pigment bleaching is delayed in subjects with abdominal obesity

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Purpose
The abdominal obesity is an anthropometric marker associated with inflammation and age-related macular degeneration (AMD). We examined the association between mesopic contrast recovery dynamics and abdominal obesity in older adults with normal macular health.
Methods
29 eyes of 29 healthy subjects (47 - 70 years) divided in two groups: a group without abdominal obesity (waist-to-height ratio (WHtR) < 0.5; n = 15) and a group with abdominal obesity (WtHR ≥ 0.5; n = 14) were examined. The recovery of contrast sensitivity for sine-wave gratings of low spatial frequency (1 cycles per degree) and low mean luminance (0.1 cd.m-2) was measured within the central retina for 6 minutes in darkness after photo-pigment bleaching. Sensitivity recovery functions were fitted to an exponential decay function. The time constant for recovery (tau, seconds), elevation and final contrast thresholds (CT) were calculated. The intersession repeatability of the method was determined by the Bland-Altman coefficient of repeatability (COR). Visual acuity (VA), body mass index (BMI) and WtHR were obtained.
Results
The mean tau was 42 s slower in the group with abdominal obesity (83.84 ± 35.78 s) than in the group without abdominal obesity (41.94 ± 13.70 s) (p <0.001). The mean elevation and final CTs did not vary significantly between groups. Forward stepwise regression analysis revealed that tau was independently correlated with WtHR (r = 0.74; p < 0.0001), but not with BMI, CT, VA or age. There was no significant relationship between WtHR and CTs. Intersession repeatability of recovery measurements was high (tau, COR= ± 16 s).
Conclusions
The time constant for contrast sensitivity recovery after a pigment bleaching increases with abdominal obesity in eyes of older adults with normal macular health. Testing for the combination of these factors would allow for early detection of AMD.

• T068

AMD drusenoid deposits "L", lipid type: morphology, volume, evolution analysis with morphology-structural software

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Purpose
To study AMD Drusenoid Deposits "L", Lipid type, with morphology-structural software and see all the input of this software on their morphology, volume, evolution knowledge and understanding
Methods
166 eyes of 83 patients, 30 men, 53 women, with AMD Drusenoid Deposits "L", Lipid Type (soft Drusen, Drusenoid PED "L"). Deposits were evaluated by Autofluorescence, IR imaging, OCT (Spectralis HRA-OCT, spectral domain OCT) and Morphology-Structural software (M-S software). ETDRS visual acuity (VA), complete ophthalmic examination with Fundus exam were added. M-S software let: grading (semi-automatized Drusenoid deposit volume and contours analyze, 3D deposit reconstruction); measurements (volume(in µm3), density (grey levels of deposits)(Statistic moments of pixel intensities: mean, median, minimum, maximum, average, standard deviation, skewness and kurtosis), structure (structural measures, texture parameters),(Haralick texture measurements for distances of 1 to 10 pixels), composition (differential density calculation). Grading, measurements (volume, density) let analyze Drusenoid Deposit "L", their evolution, 4 years follow-up
Results
M-S software allows AMD Drusenoid Deposits "L", Lipid Type (soft Drusen, Drusenoid PED) analyze, follow-up: topography, volume, density, evolution, for each cut, layer, eye, patient, and patient to patient. Therefore M-S software enable Drusenoid Deposits comparison, evolution for each patient and patient to patient. So M-S let assay AMD progression, assess evolution Drusenoid deposits "L" to atrophy and its occurrence period and intensity
Conclusions
Morphology-Structural Software contribute to and improve AMD Drusenoid deposits "L", Lipid type, study and knowledge, therefore AMD understanding.

• T069

AMD drusenoid deposits "P", protein-cellular type: volume, morphology, evolution analysis with morphology-structural software

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Purpose
To study AMD Drusenoid deposits "P" with morphology-structural software and see all the input of this software on their morphology, evolution knowledge and understanding
Methods
310 eyes of 155 patients, 61 men, 94 women, with AMD Drusenoid Deposits "P", Protein-Cellular Type (Pseudovitellifom AMD,Cuticular drusen,Subretinal drusenoid deposits(SDD),Drusenoid PED,"P"). Deposits were evaluated by Autofluorescence, IR imaging, OCT(Spectralis HRA-OCT,spectral domain OCT) and Morphology-Structural software (M-S software). ETDRS visual acuity(VA), complete ophthalmic examination with Fundus exam were added. M-S software let: grading (semi-automatized drusenoid deposit volume and contours analyze,3D deposit reconstruction); measurements (volume(in µm3), density(grey levels of deposits)(Statistic moments of pixel intensities: mean,median,minimum,maximum ,average,standard deviation,skewness and kurtosis), structure (structural measures, texture parameters),(Haralick texture measurements for distances of 1 to 10 pixels), composition(differential density calculation). Grading, measurements(volume,density) let analyze Drusenoid deposit "P", their evolution,4 years follow-up
Results
M-S software allows AMD Drusenoid Deposits "P", Protein-Cellular Type (Pseudovitellifom AMD, Cuticular drusen, Subretinal drusenoid deposits (SDD), Drusenoid PED, "P") analyze, follow-up: topography, volume, density, evolution, for each cut, layer, eye, patient and patient to patient. Therefore M-S software enable Drusenoid Deposits comparison, evolution for each patient and patient to patient. So M-S let assay AMD progression, assess evolution Drusenoid deposits "P" to Neovascular complication and its intensity and occurrence period
Conclusions
Morphology-Structural Software contribute to and improve AMD Drusenoid deposits "P",Protein-Cellular type, study and knowledge and so AMD understanding.

• T070

Effect of microglia suppression on branch retinal vein occlusion in mice

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Purpose
Activation of retinal microglia seems to have an influence on the outcome of retinal degenerative diseases. Recent studies show that systemic colony stimulating factor-1 receptor (CSF-1R) inhibition ablates microglia in the mouse central nervous system. However, the role of microglia inhibition in ischemic retinal disease remains unclear. The present study aims at investigating the effect of microglia depletion in vivo in experimental branch retinal vein occlusion (BRVO).
Methods
Cx3cr1gfp/+ mice, specifically expressing green fluorescent protein (gfp) on microglia/macrophages, were fed with the CSF-1R inhibitor PLX5622 in mouse chow for two weeks before laser-induced BRVO. Following BRVO, one group of animals was continuously treated with PLX5622 for three more weeks (PLX5622 group), while a second group was switched to normal diet (PLX5622 cessation group). Anatomical changes in the retina and gfp+ cell distribution were monitored weekly with optical coherence tomography and scanning laser ophthalmoscopy autofluorescence imaging (AF), respectively. Every week, 2-3 animals of each group were euthanized for histology. Retinal whole mounts stained for iba-1 (microglia/macrophages) and brn3a (ganglion cells) were compared to in vivo AF images.
Results
Accumulation of gfp-expressing cells in the area affected by BRVO was observed shortly after the laser in both groups. However, this accumulation was less pronounced in the PLX5622 treated group. Surprisingly, ganglion cell numbers were significantly decreased in the PLX5622 cessation group compared to the PLX5622 Group.
Conclusions
The data provided here showed that CSF-1R inhibition has a protective effect on ganglion cells after experimental BRVO. Thus, such inhibitiors may be a promising tool for modulation of retinal microglia and could be proven a useful target for ischemic retinal diseases.
Conflict of interest
Any Stocks or shares held by you or an immediate relative?:
M.S. Zinkernagel is holding equity in Novartis
Any research or educational support conditional or unconditional provided to you or your department in the past or present?:
D.Kokona receives grant support from Bayer
PLX5622 rodent diet was provided without financial support under a Materials Transfer Agreement with Plexxikon Inc., Berkeley, CA, USA.
M.S. Zinkernagel received financial support from Allergan, Bayer, Heidelberg Engineering, Novartis
Any Lecture fee paid or payable to you or your department?:
A. Ebneter received honoraria from Bayer for lectures

• T072

Inflammatory markers but not symptoms are a strong predictor of temporal artery biopsy outcome – the Portsmouth experience

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Purpose
To investigate the correlation of biopsy proven temporal arteritis with clinical symptoms and inflammatory markers.
Methods
Retrospective study of all patients (n=89) referred for temporal artery biopsy (TAB) over a 30-month period. Ten patients were excluded due to inconclusive biopsy or insufficient data. Correlation of presenting symptom (localised headache LH, jaw claudication JC, pain over temporal artery PTA, constitutional symptoms CS) and inflammatory marker level (ESR, CRP) with histological outcome (presence of giant cells) were assessed using a two-tailed unpaired t-test.
Results
50 cases had a negative (-ve) biopsy result and 29 positive (+ve). Mean age (SD) for each group was 71yrs (10) and 77yrs (6) respectively. No significant correlation was found between presenting symptom and biopsy result (-ve:+ve LH 88%:79%, PTA 46%:62%, CS 40%:59%) except for jaw claudication (36%:62%, $p<0.05$). Inflammatory marker result was found to significantly correlate with biopsy outcome. Mean ESR (SD) was 23 (21) in the –ve and 34 (24) in the +ve ($p<0.05$) and mean CRP (SD) was 33 (40) in the -ve and 98 (81) in the +ve group, ($p<0.001$). Mean ESR+CRP (SD) was 55 (52) in the –ve and 132 (87) in the +ve ($p<0.0001$). There were no significant differences in duration of steroid treatment prior to TAB or time to TAB between the two groups. One patient had normal ESR and CRP with a positive biopsy result.Treatment with steroids was continued for 48% of patients with –ve biopsy on clinical grounds.
Conclusions
Elevated ESR and CRP are strongly predictive of positive TAB outcome. Combining ESR+CRP increases the significance of the correlation. Further studies with larger patient numbers may identify an appropriate cut-off level which, combined with age and clinical features, may provide a clinical score to aid decision making regarding which patients require TAB.

• T071

Panton-Valentine leukocidin enhances glial reaction and microglial apoptosis through retinal ganglion and amacrine cell binding

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Purpose
Panton-Valentine Leukocidin (PVL) may be a critical virulence factor of S. aureus during endophthalmitis. This study aimed to identify the retinal cell targets for PVL, and to analyze early retinal changes during infection
Methods
After intravitreous PVL injection, adult rabbits were put down at different time points (30 min, 1, 2 and 4 h). PVL location in retina, its binding receptor C5aR, changes of Müller cells and microglial cells were analyzed using immunohistochemistry in the vertical sections or whole mounted retinas.
Results
In rabbit retina, only ganglion cells clearly were shown to express C5aR. PVL increasingly bound retinal ganglion cells (RGCs) with time, reaching 98% of labeled cells after 2 h of PVL presence. Displaced amacrine cells (DACs) did not express C5aR, but transiently bound PVL from 68 % to 5% between 30 min to 4 h. Müller cells abnormally expressed Glial Fibrillary Acid Protein in external retina compared with controls. Microglial cells body and dendrites were enlarged and dendritic processes sensibly decreased at 2 h and even disappeared at 4h. At 4 h following PVL injection, both immunohistochemistry and Western blot showed that some microglial cells underwent apoptosis and nitrotyrosine accumulated in retina.
Conclusions
In this model of PVL eye infection, PVL rapidly binds two kinds of retinal neural cells: RGCs possibly through C5aR interaction, DACs through an unknown mechanism. Müller cells and microglial cells were activated very early during the PVL binding process, suggesting an inflammatory cross-talk between retinal neural cells and glial cells. Some microglial cells underwent apoptosis after 4 h PVL infection, at least associated to an abnormal production of nitrotyrosine in the retina.

• T073

The effect of autoimmune retinopathy on retinal vessel oxygen saturation in patients with and without clinical features of retinitis pigmentosa

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Purpose
To study the retinal vessel oxygen saturation alterations in patients with autoimmune retinopathy (AIR) and patients with autoimmune retinopathy associated with retinitis pigmentosa (AIR-RP) in comparison to healthy controls and patients with isolated retinitis pigmentosa (RP).
Methods
Retinal vessel oximetry (RO) was performed on a total of 139 eyes: 6 eyes suffering from AIR and 4 eyes with AIR-RP were compared to 59 heathy control eyes and to 70 eyes with RP. The oxygen saturation in the first and second branch retinal arterioles (A-SO2) and venules (V-SO2) were measured and their difference (A-V SO2) was calculated. In addition, we measured the diameter of the retinal arterioles (D-A) and venules (D-V).
Results
Both, AIR and AIR-RP groups, differed from healthy controls showing significantly higher V-SO2 values and significantly lower A-V SO2 values ($p<0.025$). In addition, the AIR-RP group could be differentiated from eyes suffering from isolated RP by means of significantly higher V-SO2 values. Comparing retinal vessel diameters, both, the AIR and AIR-RP groups, presented with significant arterial ($p=0.05$) and venular ($p<0.03$) vessel attenuation than the healthy control group.
Conclusions
Based on our preliminary results, in analogy to patients suffering from RP, oxygen metabolism seems to be altered in AIR patients.

• T074

Unilateral retinal vasculopathy in systemic lupus erythematosus

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Purpose
Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder affecting multiple organ systems frequently with a relapsing and remitting clinical course. It may have ocular manifestations at posterior pole, cornea, conjunctiva, sclera, uveal tract and optic nerve.
SLE is a complex disease with dysregulation of the immune system with defects in the innate and adaptive immune systems.
Methods
A 40-year-old Spanish woman was diagnosed with SLE 5 years before. At the time she underwent treatment with a tapering dose of oral prednisone (currently 10 mg/day) and hydroxychloroquine because of a relapse only with cutaneous involvement. She came to the emergency department because she noticed a nasal visual field defect and flashes in her right eye. Her best corrected visual acuity (BCVA) was 20/20 in both eyes and slit-lamp anterior segment examination was unremarkable. Right fundus showed multiple cotton wool spots along the vessels, and some intraretinal haemorrhages in the inferior temporal branch retinal.Right fundus fluorescein angiography revealed an active vasculitis with abnormal vessel permeability and leakage of the dye together with a branch retinal artery occlusion along the inferotemporal arcade without ischemic areas. Her left eye was normal. She was treated with high-dose steroid (intravenous methylprednisolone 500mg/day during 3 days). Then, she completed 2 doses of intravenous cyclophosphamide 400 mg and oral prednisone (45mg/day) and hydroxychloroquine 400mg/day.
Results
The following week the fundus examination demonstrated resolution of haemorrhages without neovascularization or cotton wool spots. BCVA remained 20/20 and visual field exam slightly improved.
Conclusions
SLE may lead to severe unilateral vasculitis. However, an early diagnosis and aggressive treatment allow the resolution of the disease without many sequelae.

• T075

Fuchs' uveitis masquerading as a Behçet related anterior uveitis

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Purpose
To report a case of a Turkish patient with Behçet disease and a recurrent unilateral uveitis.
Methods
Observational report of a case of Behçet disease with unilateral anterior uveitis in the left eye (LE). The anterior inflammation was considered as part of the clinical spectrum of Behçet disease. The patient underwent an extensive ophthalmological work-up.
Results
A 37-years-old male Turkish patient presented with an unilateral panuveitis. The Behçet's diagnosis was based on the criteria published by the international study group for Behçet's disease. At presentation the patient reported fatigue, recurrent oral ulcerations and arthralgia. Ophthalmolgical work-up revealed a visual acuity of 4/10 in the LE. Slit lamp study showed cells in the anterior chamber (AC), vitritis and periflebitis. The panuveitis, refractory to local therapy, was treated with systemic corticosteroids and azathioprine. The posterior inflammation responded well. The anterior segment (AS) showed a chronic, recurrent low-grade inflammation refractory to conventional immunomodulatory therapy during 8 months. Based upon the therapy-resistant AS inflammation, the typical diffuse fine stellate keratic participates and the absence of posterior synechiae, the diagnosis of fuchs' uveitis was suspected. Fundoscopy of the right eye showed hyperpigmented chorioretinal scars, previously related to toxoplasmosis. The clinical picture was highly suggestive for a congenital rubella infection.
Conclusions
To our knowledge this is the first case of a patient with Behçet's disease associated to Fuchs' uveitis. The refractory anterior inflammation mimicking a Behçet's related AS uveitis is a diagnostic challenge. Ophthalmological work-up should include an AC punction with Polymerase Chain Reaction to rule out a possible viral genome. As in Hickam's Dictum, one pathology can masque another.

• T076

Towards a new therapy concept for acute microbial karatides, including Acanthamoebae

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Purpose
The purpose of this study was to develop novel therapeutic approaches for the management and treatment of microbial keratitides, especially pathologies resulting from Acantamoeba castellanii inoculations.
Methods
Growth inhibitory effects of plasma-induced reactive species on cultures of Staphylococcus aureus, Pseudomonas aeruginosa, Acantamoeba castellanii, and MRSA were assayed for in in an in-vitro setting. Human donor corneas were inoculated and cultured with cultures of above pathogens, followed by staining of cells and microscopic analysis.
Results
Our results show a substantial inhibitory effect of plasma-induced reactive species on the growth and migration of the pathogens tested.
Conclusions
The effects observed provide foundation for the development of new avenues for the management and therapy of microbial keratitides.

• T077

Efficacy of tumour necrosis factor inhibitors in peripheral ulcerative keratitis in Granulomatosis with polyangiitis

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Purpose
To report the efficacy of TNFi (tumour necrosis factor inhibitor), as a treatment of therapy-resistant peripheral ulcerative keratitis (PUK) in granulomatosis with polyangiitis (GPA), formerly known as Wegener granulomatosis.
Methods
Observational report about 2 cases, known with the diagnosis of GPA, presenting with therapy-resistant PUK.
Results
2 middle-aged females, known with GPA were referred to our department with a history of chronic redness resistant to local corticosteroids. Both patients showed a unilateral limbal vasculitis with necrotizing keratitis on slit lamp examination. In the first case, the diagnosis of GPA was confirmed by positive anti-neutrophil cytoplasmic antibodies (ANCA) and nasal septum biopsy. In the second case, the clinical presentation was considered as a viral keratitis due to recurrent unilateral inflammation. Polymerase chain reaction (PCR) could not confirm the viral aetiology. Extensive systemic evaluation revealed a cervical lymphadenopathy on PET-CT scan. Serology was positive for ANCA. In both cases, the PUK was nonresponsive to systemic corticosteroids. In the first case, cyclophosphamide failed to control the inflammation. Because the risk of corneal perforation, a treatment with TNFi, respectively Infliximab and Adalimumab, were successfully initiated.
Conclusions
Potentially lethal, it is important to diagnose and treat GPA urgently. Recently, TNFi were reported to be effective in the treatment of therapy-resistant GPA. Both patients were refractory to conventional immunomodulatory therapy. Infliximab and adalimumab successfully controlled the inflammation with disappearance of necrotic foci. In our experience, TNFi are a safe and effective therapeutic strategy.

• T078

Orbital lymphoma presenting as a recurrence of posterior scleritis after treatment with adalimumab

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Purpose
To report a case of recurrent therapy-resistant posterior scleritis in a patient with seronegative rheumatoid arthritis (RA). Following treatment with a tumor necrosis factor inhibitor (TNFi), an orbital lymphoma masquerading as a recurrence of posterior scleritis occurred.
Methods
Retrospective chart review.
Results
A 62-year-old woman was diagnosed with a unilateral posterior scleritis in 2008. Ophthalmological workup, including orbital imaging, confirmed the diagnosis. Complete systemic workup revealed a seronegative RA. Due to limited responsiveness to corticosteroids and conventional immunosuppressive therapy, adalimumab, a TNFi, was successfully initiated. Despite a recurrence-free period of 27 months, a relapse of posterior scleritis occurred. Systemic evaluation and orbital imaging showed a small orbital mass. Orbital biopsy confirmed the diagnosis of an extranodal marginal zone lymphoma or MALT.
Conclusions
Adalimumab is effective as a second-line anti-inflammatory drug in posterior scleritis. Studying the link between lymphoma and RA, several reports confirm an increased risk of lymphomas in RA with high disease activity. Although TNFi increases the risk of melanoma, there appears to be no increased risk of lymphoma. Whether it may be related to the underlying disease rather than to the treatment, ophthalmologists should be aware of the risk of a lymphoma.

• T079

Adalimumab as an alternative treatment in Serpiginous Choroiditis

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Purpose
Serpiginous Choroiditis is a type of chronic bilateral posterior uveitis, with a geographical pattern that begins in the juxtapapillary zone and spreads in an intermittent and centrifugal manner. The purpose is to describe an alternative treatment for SC based on Adalimumab monotherapy.
Methods
A female patient with decreased visual acuity in the last 6 months of the left eye and characteristic lesions in the ocular fundus of SC with juxtapapillary and paramacular involvement. The disease continued its course despite treatment with Prednisone at high doses, and affected the contralateral eye with small foci. Disease control was achieved by triple therapy of Prednisone, Azatriopine and Cyclosporin but the patient started with side effects derived from the treatment. Due to the immunological basis and supported on the literature, treatment with Adalimumab and decreasing doses of Prednisone was instituted.
Results
After 8 months of follow up, the patient presents a good control of the disease, besides the improvement of the secondary effects derived from the previous treatment.
Conclusions
Adalimumab may be a good alternative in cases of CS that are not controlled despite the maximum treatment with triple therapy, or in which the treatment can not be continued due to side effects or poor compliance.

• T080

INFLIXIMAB and ADALIMUMAB in uveitic macular edema

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Purpose
To compare the efficacy of infliximab versus adalimumab for the treatment of uveitis related refractory macular edema (ME).
Methods
We included in this retrospective case series patients diagnosed with uveitis related refractory ME and treated with infliximab (IFX) or adalimumab (ADA) at Pitie Salpetriere hospital between 2006 and 2016. All patients were assessed including best corrected visual acuity (BCVA), clinical inflammatory parameters, multimodality imaging, fluorescein angiography, ICG and SD-OCT. Central foveal thickness (CFT) and retinochoroidal architecture were analysed with SD-OCT at baseline, 6 and 24 months after treatment initiation. Findings of patients treated with IFX were compared with those of patients treated with ADA. Success was defined as a decrease of more than 50 microns of CMT.
Results
Twelve patients with a mean age of 40 years and 13 patients with a mean age of 46 years were respectively treated with ADA and IFX. At baseline, the mean BCVA of ADA patients was 0.59 logMar ((0; 1,3); median=0,54; SD=0,41) and the mean BCVA of IFX patients was 1,01 logMar ((0,52; 1,3) mediane=1; SD=0,31). The mean CFT of ADA patients was 417µ ((247; 732); median=350; SD=171) and the mean CFT of IFX patients was 450.4µ ((202; 617); median=521; SD=145). Six of the 12 patients (50%) were sucessfully treated by ADA at 6 months, and 8 of the 13 patients (61%) treated by IFX were successful at 6 months. At 6 months, CFT median decreasing from baseline was 61 microns for ADA groupe [range : 17; 136] showing no significant difference vs 92 microns for IFX [9; 165] showing no significant difference (p=0,32).
Conclusions
Anti TNF alpha therapy seems to be an efficient treatment at 6 month for uveitis related refractory macular edema. No difference in efficacy was observed between IFX and ADA.

• T081

Immunosuppression for uveal effusion syndrome – a report of two cases

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Purpose
Uveal effusion syndrome (UES) is a rare inflammatory disease characterised by massive choroidal detachment due to accumulation of fluid in the suprachoroidal space. There may also be an associated exudative retinal detachment (ERD). The cause of UES is not known but can be primary due to connective tissue disease (1) or secondary to inflammatory disease. We report two cases of secondary UES cases which were refractory to treatment and discuss further management.
Methods
A case series of two patients presenting to a hospital in United Kingdom with ocular symptoms secondary to UES.
Results
Case 1 presented with reduced vision and photopsia in one eye without obvious signs of inflammation while case 2 presented with a painful red eye associated with epiphora and increased intraocular pressure. Large uveal effusions and ERD were clinically apparent on fundoscopy in both patients and an inflammatory etiology was presumed. Both patients suffered a severe relapsing course requiring repeated adjustments to their immunosuppressive therapies - several pulses of intravenous methylprednisolone for exacerbations of the disease plus mycophenolate mofetil (MMF) (case 1) and azathioprine (case 2). Failure to respond required a cycle of cyclophosphamide (pulse 15mg/kg/infusion) which settled the disease in case 2. However, case 1 failed to respond and is treated with 8-weekly course of Remsima infusions (anti-TNFa, 5mg/kg/infusion) which led to essentially complete resolution of the effusion while maintaining patient's vision.
Conclusions
UES is a rare condition which is difficult to manage. In cases of secondary inflammatory UES a range of immunosuppressants may be required to achieve resolution of the disease.
1. Forrester et.al (1990) The uveal effusion syndrome and trans-scleral flow. Eye 4: 354-65.

• T082

A case of recurrent bilateral optic oedema in tubulo-interstitial nephritis and uveitis syndrome treated with plasmapheresis

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Purpose
To present a case of recurrent bilateral optic oedema in a patient with tubulo-interstitial nephritis and uveitis syndrome (TINU) with a limited response to corticosteroids, immunosuppressive drugs and tumor necrosis factor inhibitor (TNFi). Plasmapheresis was added as rescue therapy.
Methods
Observational case report about a 13-year-old boy diagnosed with TINU and bilateral optic oedema. An extensive general and ophthalmological work-up confirmed the diagnosis of TINU.
Results
At referral the patient presented with bilateral anterior uveitis and nephritis. Biomicroscopy showed a trace of anterior chamber cells. Funduscopy revealed bilateral optic oedema with neither haemorrhages nor exudates. Initially the patient responded well to systemic corticosteroids but he relapsed while tapering. Consecutive treatment consisted of azathioprine, tacrolimus and methotrexate. Due to limited response, infliximab, a TNFi, was associated. After 7 months disease-free, the TNFi treatment failed. Finally, he responded well to plasmapheresis.
Conclusions
TINU may rarely manifest with optic oedema. Although nephritis typically resolves, ocular inflammation often becomes chronic and can be therapy-resistant. This case suggests that plasmapheresis can be an alternative in case of a therapy-resistant TINU. A multidisciplinary approach is essential to confirm the diagnosis and initiate appropriate treatment.

• T083

Post-marketing surveillance study of the safety of dexamethasone intravitreal implant (DEX) in patients with retinal vein occlusion (RVO) or noninfectious posterior segment uveitis (NIPSU)

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Purpose
To evaluate the long-term safety of DEX in patients treated for RVO-related macular edema (ME) or NIPSU in clinical practice.
Methods
Multicenter (102 sites in France, Germany, Spain, United Kingdom), prospective, observational, post-authorization safety study in adult patients treated with DEX. Treatment and follow-up were at physicians' discretion. Data collected up to 2 years after enrollment included serious adverse events (SAEs) and adverse events of special interest (AESIs; adverse drug reactions with DEX as listed in the Summary of Product Characteristics).
Results
Overall, 753 patients (610 RVO, 143 NIPSU) received on-study DEX treatment and 73.0% completed 24 months follow-up; 74.0% had not used DEX previously. Median number of on-study injections per treated eye was 2 (range, 1–7) with median re-injection interval of 27 weeks; 36.4% of patients received >2 injections. Non-ocular SAEs affected 8.9% of patients; none were considered related to DEX. Ocular SAEs (most common: cataract progression) were reported in 3.4% of treated eyes. Non-ocular and ocular SAEs were similar in eyes stratified by previous DEX use and number of on-study DEX injections (≤2 or >2), regardless of indication (RVO or NIPSU). The most common AESIs reported were increased intraocular pressure (IOP) in 19.3% of treated eyes, cataract progression and cataract formation in 19.5% and 19.3% of treated phakic eyes (n=528), and vitreous hemorrhage in 3.2% of treated eyes. Cataract progression and vitreous hemorrhage were more frequent in eyes that received >2 DEX injections. Among eyes with RVO, cataract progression was more frequent in eyes previously treated with DEX.
Conclusions
The long-term safety profile of DEX was acceptable. The 2-year incidence of cataract and increased IOP was lower than previously reported (LOUVRE study). No new safety concerns were identified.
Conflict of interest
Any financial support like travel accomodation hospitality etc provided to you or a member of your staff or an accompanying person?:
I have received support from companies including Allergan, Bausch & Lomb, Bayer, and Novartis to attend a congress or symposium.

• T084

Portuguese prescription patterns of topical antibiotics in Ophthalmology: a yearlong analysis

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Purpose
Scarce data is available regarding topical antibiotics prescribing patterns in Ophthalmology. We aimed to describe and analyze the nationwide prescription of these antimicrobials during the year of 2016.
Methods
Cross-sectional study. A common electronic drug prescription system is used by all public or private hospitals and clinics in Portugal. We used this national database and included all the 2016 prescriptions of topical antibiotics used prophylactically or therapeutically in ophthalmology. Patients' demographic data and medications prescribed were provided in an encrypted form and anonymously extracted. Results were stratified by region, physician specialty (ophthalmology vs. general practitioner) and public/private sector. Statistical analysis was performed using STATA v14.1.
Results
During 2016 in Portugal, a total of 458,638 topical antibiotic medications were prescribed to 324,683 different patients (47% male), corresponding to approximately 3.2% of the country population. Mean age was 46.4 ± 29.9 years. Of all prescriptions, 46.6% were from ophthalmologists, 31.9% from general practitioners and 11.3% from pediatricians. The most prescribed drugs were chloramphenicol (24.2%), ofloxacin (14.0%) and fusidic acid (9.0%). A similar rank was found in the public sector, but in private practice moxifloxacin was the third most prescribed. The prescription pattern was markedly different among the different country regions. Lastly, a seasonal effect is suggested, since more than 35% of the prescriptions were made from October to December.
Conclusions
This nationwide study revealed prescription's trends of topical antibiotic drugs in Portugal. These results might contribute for the development of a wiser use of antimicrobial drugs, thus promoting the best patient care and the whole system sustainability.

• T085

Intravitreal ranibizumab treatment in choroidal neovascularization secondary to ocular toxoplasmosis in children

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Purpose
Choroidal neovascularization associated to ocular toxoplasmosis is a known complication of the disease. The important role that the intravitreal anti-VEGF therapy plays on the CNV has been well-established. Also, the efficacy of the treatment in CNV secondary to ocular toxoplasmosis in adult patients it has been long described, however there are not cases reported in young patients. The purpose is to describe the efficacy of intravitreal ranibizumab in CNV secondary to ocular toxoplasmosis in children.
Methods
We present the case of an 8-year-old patient with history of ocular toxoplasmosis comes to the hospital with a sudden loss of visual acuity in the right eye (BCVA: 20/200). The fundoscopy shows an old toxoplasmosis scar associated with new perilesional hemorrhages and macular edema. We confirmed these lesions with a SS-OCT which demonstrated the subretinal fluid associated with a RPE disruption and foveal fibrosis. CNV presence was suggested due to these retinal changes and we decided to treat with intravitreal injections of ranibizumab and anti-parasitic treatment.
Results
After three injections of ranibizumab and 6 months of follow up, all the CNV signs have disapeared and the patient has a good recovery of the visual acuity (BCVA: 20/25).
Conclusions
Intravitreal ranibizumab may be an effective treatment in CNV secondary to ocular toxoplasmosis also in children. In our case, three injections of ranibizumab controlled the secondary CNV, however it is necessary long-term studies to determinate the effectivity and frequency of the treatment in these patients.

• T086

Inflammatory choroidal neovascularization imaged by optical coherence tomography – angiography

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Purpose
To describe the optical coherence tomography - angiography (OCT- A) findings in patients with uveitis related neovascularization.
Methods
We included all patients diagnosed with inflammatory neovascularization (CNV) at the Pitie Salpetriere hospital between 2016/09/01 and 2016/11/15. All patients were assessed including best corrected visual acuity, clinical inflammatory parameters, multimodality imaging, fluorescein angiography, ICG and SD-OCT or SS-OCT. All patients underwent OCT angiography with SS-OCT DRI Triton (Topcon, Japan) or/ and Spectralis Angiography OCT (HRA, Heidelberg, Germany). OCT-A images were analyzed and compared with en face and B-OCT.
Results
Six patients (7 eyes), 3 women and 3 men, with a mean age of 55 years, were included. Three patients were diagnosed with ocular sarcoidosis and the rest of the patients with Birdshot chorioretinopathy, HSV-2 uveitis and ocular tuberculosis. OCT-A revealed inflammatory pre retinal pigment epithelial CNV in all cases. Three lesions were localized in the papillo-macular region and four close to the vascular arcades. The main length of the major axis was 2.806 microns. All lesions presented a sea fan pattern with an anastomotic network and a thin capillaries network surrounded by a dark halo. They were attached to a single or to multiple thick branches. Two patients had a follow-up of one month after the anti-VEGF therapy confirming the rapid fibrosis of these vessels. The characteristics of inflammatory CNV seem to differ from those of CNV in neovascular age related macular degeneration scanned with OCT-A. The branching seems to be less important, and capillaries thinner and pedicles thicker.
Conclusions
OCT-A is a new complementary imaging method for the diagnosis of inflammatory CNV. The features and the evolution of these lesions need to be investigated in further studies.

• T087

Superficial and deep retinal foveal avascular zone OCT-A findings of non-infectious anterior and posterior uveitis compared to healthy controls

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Purpose
To compare the superficial (FAZ-S) and deep retinal foveal avascular zones (FAZ-D) of non-infectious anterior and posterior uveitis and healthy controls, using optical coherence tomography angiography (OCTA).
Methods
OCTA was performed on a total of 74 eyes, 34 eyes suffering from non-infectious posterior uveitis (26 eyes without macular edema (post-CME), 8 eyes with macular edema (post+CME)), 11 eyes with non-infectious anterior uveitis (6 eyes without macular edema (ant-CME) and 5 eyes with macular edema (ant+CME). The control group included a group of 29 healthy eyes. The foveal avascular zones of the superficial (FAZ-S) and deep (FAZ-D) retinal vascular plexus were measured in mm2 via the software's ruler tool on a Heidelberg HRA2 Spectralis OCTA device (Germany). For statistical evaluation ANOVA-based linear mixed-effects models were performed with SPSS®.
Results
Eyes suffering from non-infectious posterior uveitis presented with significantly higher FAZ-D values when compared to healthy controls both, in the presence or absence of macular edema ($p<0.001$, post-CME subgroup and post+CME subgroups). In the presence of macular edema eyes presenting with anterior uveitis (ant+CME) also showed significantly higher FAZ-S ($p=0.03$) and FAZ-D ($p<0.001$) values when compared to healthy controls. Meanwhile, in the absence of macular edema eyes with anterior uveitis cannot be distinguished from controls ($p>0.6$).
Conclusions
Based on our preliminary results, the deep retinal foveal avascular zone seems to be enlarged in eyes presenting with non-infectious posterior uveitis, both in the presence or absence of macular edema. This finding could be used as a clinical marker in the future.

• T088

Macular study on SD-OCT in sarcoidosis uveitis at active and sequelae phases

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Purpose
To study macular involvement on SD-OCT in sarcoidosis uveitis at active and sequelae phases.
Methods
Twenty-nine eyes of 16 patients with sarcoidosis uveitis were retrospectively reviewed. All patients underwent complete ophthalmic examination completed with fluorescein angiography and SD-OCT to assess macular involvement at active and sequelae phases of the disease.
Results
The mean age was 44,6 ± 12,4 years. There were 8 men and 8 women. 19 eyes were assessed by SD-OCT at the active phase and 10 eyes at the sequelae phase. At the active phase, SD-OCT showed macular involvement in 9 (47,3%) eyes which consisted in cystoid macular edema in 5 eyes with serous retinal detachement in 3 eyes, epiretinal memebrane in 2 eyes and macular thinning in 2 eyes. At the sequelae phase, macular involvement was observed in 5 (50%) eyes which consisted in cystoid macular edema in 2 eyes, epiretinal membrane in 2 eyes and macular thinning in one eye.
Conclusions
Macular involvement in sarcoidosis uveitis is common. Cystoid macular edema was the most frequent macular complication. Epiretinal membrane can be seen either in the initial presentation or during follow-up as a sequelae of the disease. Macular atrophy may be a complication of sarcoidosis uveitis at the active and squelae phases. Macular thinning and, more importantly, photoreceptor degeneration are serious sequelae of this process. OCT can help identify abnormality of the ellipsoid zone.

• T089

Use of wide-field fluorescein angiography in the diagnosis and management of sarcoidosis uveitis

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Purpose
To assess the utility of wide field (WF) fluorescein angiography versus conventional angiography in the diagnosis and management of Sarcoidosis posterior uveitis.
Methods
Twenty-three eyes of 12 patients diagnosed with Sarcoidosis disease who underwent WF fluorescein angiography imaging with the Heidelberg scanning laser ophthalmoscope HRA2 using the Staurenghi SLO contact lens between January 2016 and March 2017 were included in our study. Complete clinical and imaging records (WF fluorescein angiography and SD-OCT) of the patients were retrospectively reviewed. A circle simulating the central 75-degree field was drawn on WF fluorescein angiography images. We compared the WF fluorescein angiography findings within the circle and the complete image and assessed its impact on patient management.
Results
Fourteen eyes of 23 (60.9%) were diagnosed with Sarcoidosis retinal vasculitis. WF fluorescein angiography revealed vasculitis not clinically evident in 9 of 14 eyes (64.3%). Predominant angiographic findings were diffuse vascular leakage in 6 eyes (26.1%), peripheral ischemia in 5 eyes (21.7%), vein sheathing in 12 eyes (52.2%) and multifocal hyperfluorescent spots in 8 eyes (34.8%). Ten eyes (43.5%) had no apparent retinal vasculitis but WF images have shown peripheral changes outside the circle. In four eyes (13%), WF fluorescein angiography showed the vasculitis to be much more extensive than usually seen by simulated conventional FA. WF fluorescein angiography influenced treatment decision in 9 eyes (39.1%).
Conclusions
Retinal vasculitis (RV) may be difficult to detect either clinically or with conventional retinal imaging in Sarcoidosis disease. Wide-field imaging is a useful tool in the diagnosis of RV associated to Sarcoidosis disease even in the absence of clinical retinal vasculitis and may influence management decisions.

• T090

A new model of fundus autofluorescence time evolution in multiple evanescent white dot syndrome

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Purpose

Fundus Autofluorescence proved to be a valuable non-invasive tool for Multiple Evanescent White Dot Syndrome evaluation. Until now several models describing time evolution of the Fundus Autofluorescence in MEWDS have been proposed.

The aim of our study is to present a new model of the Fundus Autofluorescence evaluation based on four examinations in a 56-year-old patient during a 3 months follow-up period.

Methods

Fundus Autofluorescence images were captured by HRA Spectralis Heidelberg Engineering Imaging System. The ImageJ image analysis software was used for image denoising by median filtering. We have applied Otsu's multilevel tresholding method for image segmentation to distinguish and differentiate autofluorescent areas from normal fundus.

Results

We have observed two levels of fluorescence intensity in the analyzed images. Bright fluorescence areas changed significantly with recovery time. Overall fluorescence areas changed to a lesser extent - the areas were shrinking centripetally with functional improvement.

Conclusions

Combination of Fundus Autofluorescence with image analysis methods brings us quantitative data, facilitating the trend analysis.

• F001
Falls re-audit

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Purpose
The economic burden and health consequences of falls are underestimated. Forty per cent of over 65 year olds will fall at least once each year, with half of these having multiple episodes. Visual impairment is common in the elderly and is associated with a higher falls risk. NICE recommends visual testing as part of a 'multifactorial falls risk assessment.' However, during a recent audit on three elderly care wards at a central London teaching hospital, only 11% of patients who presented with a fall had visual assessment during their admission.
Methods
A series of interventions were delivered in December 2016 to 'Educate, Equip, and Emphasise' clinicians. These included displaying posters on the wards, checking whether bedside equipment e.g. Snellen charts were available and facilitating replacement if missing, and a teaching presentation delivered to the elderly care team. A re-audit was performed in February 2017 to 'close the audit loop'
Results
In this cross-sectional re-audit, 9/64 of patients on the three wards (14%) originally presented with a fall (mean age 85.9 years; 6 were female; 3 were aided (i.e. used spectacles). 9/9 (100%) were visually impaired (best corrected visual acuity ≤ 6/12), most to a significant degree, however 0/9 (0%) had an assessment of vision during their admission. None of these patients were known to ophthalmic services previously.
Conclusions
The interventions were shown to be unsuccessful in improving adherence to guidelines. This highlights the need for awareness of the association between visual impairment and falls, and suggests education in training programmes may be necessary. The small sample size is a limitation to extrapolating the results on a national scale. Visual assessment and prompt referral to the eye clinic when necessary may prevent patients having future falls and readmissions to hospital.

• F002
Ocular traumas in the Finnish elderly- Helsinki Ocular Trauma (HOT) Study

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Purpose
To describe epidemiology, causes, treatments, and outcomes of all ocular injuries in southern Finland among people aged 61 and older.
Methods
All new ocular trauma patients, admitted to the Helsinki University Eye Hospital, during one year in 2011-2012. The data was from hospital records and prospectively from patient questionnaires. The follow-up time was three months.
Results
The incidence for ocular injuries among the elderly was 38/100,000/year. From 118 patients 69% were men. The mean age was 70.9 years old (median 67). Hospitalization rate was 14%. Injury types were minor traumas (48%), contusions (22%), chemical injuries (10%), eyelid wounds (8%), open globe injuries (OGI) (7%), and orbital fractures (5%). The injuries occurred at home (58%), in institutions (12%), and in other public places (12%). The main causes of ocular injury were falls (22%), sticks (19%), superficial foreign bodies (18%), and chemicals (12%). All OGI and 88% of contusions needed a life-long follow-up. A permanent visual or functional impairment occurred in 15 (13%) patients. Of these 53% were OGI, 40% contusions, and 7% chemical injuries. The causes of permanent injuries were falls (7 cases, 47%), work tools, sports equipment, sticks, chemicals, and eyeglasses.
Conclusions
Minor trauma was the most frequent type, and home was the most common place of eye injuries. Falls were the most frequent and serious cause, but behavioral causes (alcohol consumption and assaults) were not significant. Preventive measures should be directed towards the main identified causes and risk factors of the eye injuries in the elderly.

• F003
The effect of caffeine on retinal vessel diameters in the Inter99 eye study

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Purpose
To examine the effect of caffeine on retinal vessel diameters in the Inter99 Study.
Methods
The Inter99 Study comprised a population-based age-and sex-stratified sample of 13,016 residents of a suburban section of Greater Copenhagen, Denmark. From 6784 participants aged 30-60 years who volunteered to participate in the main study, a subgroup of 970 participated in the eye study. Vessel diameters were measured using a semi-automatic computer program. Exclusion of participants without images of acceptable quality (n=71) left 899 participants for analysis. Coffee and tea intake assessed using a food frequency questionnaire (FFQ) ranged from 0 to 35 cups. One cup of tea or coffee was assumed to contain 100 mg of caffeine.
Results
Of 899 eligible participants, 861 were daily coffee or tea drinkers, a mean of 5 cups per day. Thirty eight did not drink tea or coffee. The central retinal artery diameter was 214 µm in participants who did not drink tea or coffee and 209 µm in participants who drank tea or coffee (B = -5.7 CI 95%: -10.5 to -1.0, p = 0.019, adjusted for age, gender, systolic blood pressure, HDL cholesterol, BMI, diabetes mellitus status and smoking status). The central retinal vein diameter was 261 µm in participants who did not drink tea or coffee and 252 µm in participants who drank tea or coffee (B = -8.6 CI 95%: -15.2 to -2.0, p = 0.011, adjusted for age, gender, systolic blood pressure, HDL cholesterol, BMI, diabetes mellitus status and smoking status).
Conclusions
This cross-sectional study found that participants who drank tea or coffee on a daily basis had narrower central retinal arteries and veins than participants who did not drink tea or coffee. This is consistent with previous observations that caffeine induces cerebral vasoconstriction by antagonizing adenosine receptors.

• F004
Genetic evidence for the role of ultraviolet radiation in the pathogenesis of uveal melanoma

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Purpose
Recent advances in the understanding and treatments of metastatic cutaneous melanoma (CM) have not led to parallel improvements in the care of metastatic uveal melanoma (UM), and consequently, the two conditions are now often viewed as separate entities. One possible difference is the aetiological role of ultraviolet (UV) radiation, which although well-established in CM, remains uncertain in UM. This study hypothesised that UV radiation is a pathogenic factor in UM development, evidenced by genetic changes consistent with UV-related damage in UM.
Methods
We analysed data from 993 UM patient samples and 11803 CM patient samples available from the Catalogue of Somatic Mutations in Cancer (COSMIC) as well as 80 UM patient samples and 343 CM patient samples from the Broad Institute GDAC FireBrowse. UM samples were probed to identify the most frequently mutated genes, mutation types and specific nucleotide substitutions. Somatic mutation data was then cross-correlated with CM samples from COSMIC and Broad Institute GDAC FireBrowse.
Results
The most common overlapping mutated genes were BRAF, PTEN, CDKN2A, TERT, NRAS, TP53 and ARID2, with four shared point mutations in BRAF (V600E (1799T>A)), NRAS (Q61R (182A>G)) and TP53 (R273C (817C>T)), R248Q (743G>A)). These gene mutations were found to be strongly associated with UV-related damage in previous scientific reports. The proportion of samples with C>T substitutions (a marker of UV-related damage) were similar between UM and CM on both DNA strands (20.35% vs 20.05%) and coding strand (11.3% vs 15.7%).
Conclusions
These findings support the hypothesis that the pathogenesis of UM is more dependent on UV radiation than previously thought.

• F005

Directed migration of retinal astrocytes by PDGF signaling

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Purpose
Proper patterning of astrocytes is crucial for retinal angiogenesis in both rodents and human. Platelet-derived growth factor (PDGF) is one of the key regulators of cell migration, but distinctive downstream pathways have been implicated in a variety of cell types. Herein we investigated the detailed mechanism of PDGFA-directed astrocyte migration in early postnatal mouse retina.
Methods
Transgenic mice with glia-specific deletion of PDGFRα and multiple potential downstream effectors of PDGF signaling pathway are generated. Perinatal astrocytes and retinal vasculature are evaluated by whole mount IHC.
Results
Astrocyte migration and retinal angiogenesis are severely impaired in knockout mice of PDGFRα. This is phenocopied by mutations in PI3K catalytic subunits p110αβ, as well as in mutations of PI3K binding site in PDGFRα. Rac/Rap mediated cytoskeleton rearrangement is also imperative for the patterning of astrocytic network. On the other hand, disruption of mTOR signaling by knocking out binding partner Raptor or Rictor had no effect on astrocyte motility. PLCγ pathway, which is essential for PDGF chemotaxis in mesenchymal cells, is also dispensable for astrocyte migration.
Conclusions
This study demonstrated that PDGFA-directed astrocyte migration is mediated through PI3K and Rac/Rap signaling, but not PLCγ or Akt/mTOR pathway. These findings add mechanistic insight into cell type-specific regulation of migration by PDGF.

• F006

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency and age-related macular degeneration in a Sardinian male population, Italy

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Purpose
The reported prevalence of G6PD deficiency in Sardina, Italy, ranges from 8% to 15%. Hemizygous males have totally deficient erythrocytes. Evidence indicates that patients with G6PD deficiency are protected against ischemic heart and cerebrovascular disease, retinal vein occlusion, and nonarteritic anterior ischemic optic neuropathy. The purpose of this study was to assess the prevalence of G6PD deficiency in Sardinian men with age-related macular degeneration (AMD) and ascertain whether G6PD deficiency may have a protective effect against AMD.
Methods
G6PD blood levels were measured in 81 men with AMD. 119 men without AMD undergoing cataract surgery served as controls. The Z test was used to assess differences in G6PD deficiency prevalence rates between groups. The odds ratio (OR) was used to evaluate the association between G6PD deficiency and AMD.
Results
G6PD deficiency was found in 7 (8.6%) out of 81 patients with AMD and in 10 (8.3%) out of 121 controls. Differences between AMD patients and controls were not statistically significant (Z = 0.095, P = 0.9). G6PD deficiency showed no association with AMD (OR: 1.05; 95% Confidence Interval: 0.38-2.88).
Conclusions
Results suggest that G6PD deficiency has no protective effect against AMD and is not a risk factor for this degenerative macular condition.

• F007

Prevalence of refractive errors and visual impairment in university students

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Purpose
To determine the prevalence of refractive errors and visual impairment in a population of university students in Kazerun, south of Iran
Methods
Using multi-stage sampling in all universities located in Kazerun, a number of university majors were selected as clusters. Then, proportional to the size, a number of students in each major were randomly selected to participate in the study. All participants underwent the measurement of visual acuity , non-cycloplegic and subjective refraction, and corrected visual acuity. A spherical equivalent equal to or worse than -0.5 D and + 0.5 D was considered myopia and hyperopia, respectively. Astigmatism was defined as a cylinder power worse than -0.5 D. Visual impairment was defined as visual acuity worse than 20/60 in the better eye.
Results
Of 1595 students that were invited, 1462 participated in the study (response rate=91.66%). The prevalence of visual impairment was 2.19% (95% CI:1.48 – 3.23), of whom 1.92% (95% CI: 1.27 – 2.88) had low vision and 0.27% (95% CI: 0.12 – 0.62) were blind. Refractive erros comprised 75% of the causes of visual impairment. The prevalence (95% CI) of myopia, hyperopia and astigmatism was 42.71% (39.71 – 45.77), 3.75% (2.85 – 4.51) and 29.46% (27.50- 31.50), respectively. Totally, 49.03% (95% CI:46.39 – 51.68) of the participants had at least one refractive error. Myopia and hyperopia were not correlated with age and gender. The odds of astigmatism in participants aged 26-27 years (OR=1.64; 95% CI: 1.03 – 2.61) was higher than subjects aged 18-19 years.
Conclusions
The prevalence of refractive errors, especially myopia is low in university students. Since refractive errors constitute a major part of visual impairment, university students should receive optical sevices to reduce their burden.

• F008

The prevalence of asthenopia and its determinants in a population of university students

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Purpose
To determine the prevalence of asthenopia and some of its determinants in a population of Iranian university students
Methods
In this cross-sectional study, multi-stage cluster sampling was applied in students of Kazerun's universities in south of Iran. After selecting the subjects, ophthalmic examinations and interview was conducted with each student. In line with previous studies, any person with at least one of the symptoms of eye pain, dry eyes, eye swelling, blurred vision, diplopia, foreign body sensation, photophobia, tearing and low visual acuity was considered to have asthenopia.
Results
Of 1462 selected subjects with a mean age of 22.8±3.1 years, 73% of them were females. The prevalence of asthenopia was 71.2%, 40.6%, and 19.7% based on having 1, 2, and 3 symptoms, respectively. The prevalence of asthenopia was 73.3% in females and 65.5% in males (P= 0.004). The highest (81.5%) and lowest (58.4%) prevalence of asthenopia was seen in the age group 28-29 years and 30 years and above, respectively. The prevalence of asthenopia was higher in hyperopic subjects than myopic and emmetropic subjects (P<0.001). The prevalence of asthenopia was 77.7% in astigmatic and 79.2% in anisometropic participants. The mean amplitude of accommodation was 9.7 ±2.6D and 10.28 ± 4.3D in asthenopic and healthy subjects, respectively (P=0.008). The mean near point of convergence was 7.2±2.8cm and 7.7±3.9cm in asthenopic and healthy subjects, respectively (P0<0.001).
Conclusions
The prevalence of asthenopia is markedly high in university students, may causes difficulty in reading and is important to address this condition in this age group.

• F009

Genetic causes of deaf-blindness in sixteen Czech families

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Purpose
Usher syndrome (USH) is the most common cause of hereditary deaf-blindness in humans with an estimated prevalence of 3-6 per 100,000 inhabitants. USH is inherited as an autosomal recessive trait and is clinically divided into three types based on audiological profile and vestibular symptoms. The aim of the project was to phenotype the first cohort of Czech patients with USH (16 families, 21 affected individuals) and to perform investigation into the molecular genetic cause of their disease.
Methods
Sanger sequencing of 6 frequently mutated USH2A exons was performed as an initial step in probands suspected to suffer from USH type II. Unsolved cases were then investigated by a range of techniques including whole-exome sequencing, targeted gene panel next generation sequencing and single-nucleotide polymorphism (SNP) array for copy number variation analysis. Detected missense mutations were evaluated for pathogenicity by six in silico tools. Mutations were verified and their segregation within the families was performed by Sanger sequencing.
Results
In total 17 different mutations evaluated as pathogenic were identified in 20 individuals (95%) from 15 families, of these c.1256G>A, c.13342_13347del, deletion of exons 33 and 34 in USH2A, c.871G>A in CDH23 and c.937C>T in USH1C were novel. A known c.11864G>A in USH2A was the most prevalent mutation observed, found either in a homozygous or compound heterozygous state in 9 families. SNP haplotype analysis supported the hypothesis of a founder effect. Investigation into the geographic origin suggested regional clustering of the c.11864G>A allele in Southeastern part of the Czech Republic.
Conclusions
The proposed research will help to elucidate factors involved in the etiopathogenesis of USH, which is important for prognosis, patient counseling, management, development and introduction of novel therapies.

• F010

Motile activity and cytoskeleton changes in uveal melanoma after proton beam radiation

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Purpose
Proton beam irradiation is known to invoke different biological response than photons. We compared the effect of proton beam irradiation and X-rays on the survival and migratory properties of melanoma cells.**Methods**
Mel270, human uveal melanoma cell line was treated with physical doses of 1-5 Gy of proton beam (58 MeV) from Proteus C-235 cyclotron or X-rays (300 kV Phillips) at the dose rate of 1 Gy/min were given to suspended cells.
Results
Invasive potential of cells was slightly diminished after both types of radiation at 20 days post-radiation and then returned to normal at 40 days. Wound healing ability was decreased after X-rays. The beta-1-integrin level was decreased after both types of radiation in Mel270 cells, and vimentin, a marker of EMT was not changed. Less stress fibers were seen in cytoskeleton of Mel270 cells after radiation.
Conclusions
Low doses of both types of radiation influenced the motile activity and cytoskeleton in Mel270 cells.

• F011

SS - OCT angiography in retinal dystrophies with macular edema or cysts

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Purpose
To analyze swept source optical coherence tomography angiography (SS - OCT-A) findings in retinal dystrophies with macular edema or cysts.
Methods
Optical coherence tomography angiography and structural OCT were performed using a Swept-source DRI OCT Triton (Topcon, Corporation, Japan) for 3 patients with retinitis pigmentosa and macular edema, 3 patients with enhanced S-cone syndrome and 1 patient with X-linked retinoschisis.
Results
In all patients, changes were more pronounced in the deep plexus where macular edema was more evident. Also, there was focal dislocation of the vascular network in correspondence with the serous intraretinal cysts. In patients with retinitis pigmentosa, capillary were visible at the top of the cysts. On the other hand, in case of X-linked retinoschisis, we found wheel-like cystoids cavities separated by apparently well-vascularized walls with a good correspondence with structural en face OCT.
Conclusions
OCT-A may provide information of great interest in inherited retinal dystrophies with macular edema or cysts.
It reveals particular alterations above all located at the level of the deep capillary plexus and the choriocapillaris. Such information may be useful for phenotyping each case and understanding pathogenesis of cysts development in each dystrophy helping their future therapeutic management.

• F012

SS - OCT angiography in macular dystrophies

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Purpose
To assess the ability of swept source optical coherence tomography angiography (SS - OCT-A) to identify abnormalities of the retinal and choroidal vascular network in macular dystrophies.
Methods
Optical coherence tomography angiography and structural OCT were performed using a Swept-source DRI OCT Triton (Topcon, Corporation, Japan) for patients with Stargardt disease, Best maculopathy, pseudo-vitelliform dystrophy and progressive cone dystrophy. In our series, for every patient the clinical diagnosis was confirmed by the results of molecular genetic study.
Results
In Stargardt patients, we found alterations especially located at the level of the deep capillary plexus and choriocapillaris. There were different degrees of choriocapillaris impairment, with no residual choriocapillaris inside area of retinal epithelium pigment atrophy in advanced stages. Large choroidal vessels and borders of the atrophy were well visualized. In patients with Best maculopathy and pseudo-vitelliform dystrophy, OCT-A revealed neovascularisation in the outer retina and the choriocapillaris while traditional multimodal imaging wasn't conclusive. In progressive cone dystrophy, there was a retinal vasculature signal reduction in both superficial and deep plexus associated with window effect in the outer retina and the choriocapillaris due to the retinal and RPE atrophy.
Conclusions
In inherited macular distrophies, OCT-A may provide information of great interest. In stargardt disease, OCT-A findings were in agreement with the results suggesting primitive severe involvement of choriocapillaris. In Best maculopathy and pseudo-witelliform dystrophies, OCT-A helps diagnose choroidal neovascularization. In Progressive cone dystrophies, it could be useful for gaining deeper Knowledge of both the pathogenesis and therapeutic implications.

• F013

Clinical and genetic study of a new mutation in the choroideremia gene

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Purpose
To describe retinal findings as well as spectral domain OCT and fundus autofluorescence in a new genetic mutation in a choroideremia family.
Methods
An 11 year old boy was diagnosed with choroideremia by his fundus changes. In his mother´s family there was another cousin with the same symptoms and his grandfather and great grandfather had an impaired vision. The family was studied.
Results
The boy has a reduced visual acuity of 20/40 in both eyes with -6D, reduced sensibility in his perimetry, and important retinal pigment changes in his fundus. SD-OCT findings include changes in the external hyperreflective layers and hypofluorescence and hyperfluorescence changes in his fundus autofluorescence. His mother showed a normal OCT with hypofluorescence changes. His cousin, who was 13 years old, showed similar changes with a 20/20 vision and no myopic defect. The boys were hemizygous for a novel mutation c.1083_1084dupT of the CHM gene. The mutation was confirmed in heterozygosity in both carriers. The sister was not affected.
Conclusions
Clinical diagnosis and molecular analysis showed the new mutation leading to loss of function of the REP-1 protein. Autofluorescence changes were presented in both patients and carriers. Myopia could increases the visual loss and pigment changes in choroideremia.

• F014

High resolution imaging analysis of female carriers and patients of Choroideremia with CHM gene mutation

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Purpose
To report the high resolution imaging features of Japanese patient and female carriers of choroideremia using adaptive optics(AO) and other imaging modalities.
Methods
Three carriers and one patient underwent comprehensive examinations including AO fundus camera (rtx1™ Imagine eyes, France), spectral domain optical coherence topography (SD-OCT)and fundus autofluoresence (FAF). Cone density was measured by peak density method and compared with the data of 34 normal controls. The mutation analysis of the CHM gene was performed by Sanger sequencing. The protocol conformed to the tenets of the Declaration of Helsinki and was approved by the IRB of The Jikei University and Nippon Medical School.
Results
Three female carriers 1, 2, 3 (sister 9 y.o, mother 37 y.o and grandmother 65 y.o) and one patient (6 y.o, male). They had same CHM mutation, c.646delA, p.T216LfsX16. All carriers did not complain any symptoms, the BCVA of all were over 20/20. Fundus examination of carrier 2 showed mild generation in only periphery, the other carriers showed diffuse degeneration. AF showed mottled hypo-autofluoresence in degeneration area. SD-OCT of the carriers showed nearly normal,although peripheral SD-OCT and patient showed diffuse disruptions of interdigitation and ellipsoid zones. Cone density was measured at 2 to 8 degree temporal from the fovea in every 1 degree, using 50 x 50 micron images. Cone counting was performed by AO detect (Imagine eyes) with manual correction. Patient showed lower cone density more than 2 SD of normal control. The carriers showed lower cone density only at 7 and 8 degrees.
Conclusions
AO cone counting showed reduction of photoreceptors in carriers mainly at peripheral region. To elucidate the mechanism of peripheral degeneration and foveal sparing of female carriers may help preventing the disease progression of choroideremia patients.
Conflict of interest
Any Stocks or shares held by you or an immediate relative?:
spouse, Imagine eyes

• F015

Optical coherence tomography angiography in retinitis pigmentosa

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Purpose
The aim of this study is to describe macular vascular abnormalities in patients affected by retinitis pigmentosa using Optical coherence tomography angiography (OCT-A).
Methods
Patients with a clinical diagnosis of retinitis pigmentosa underwent 3×3 Swept Source OCT-A scans using a Swept-Source DRI OCT Triton (Topcon Corporation, Japan). Scans with artifacts were excluded. Retinal vascular supply was estimated at the level of the superficial (SCP) and deep (DCP) capillary plexus, choriocapillaris and choroid.
Results
Six patients (12 eyes) were included in this study. Five were females (83.33 %) and the mean age was 28.66 years. Mean best corrected visual acuity was 0.5±0.3 LogMAR. Two patients presented bilateral macular edema on Swept Source-OCT and showed focal dislocations in the vascular network at the level of the DCP on the OCT-A, corresponding to the serous intraretinal cysts displacing the vascular plexus and the neural tissue. Qualitative analysis of OCT-A at the macular area revealed a reduction of vessel density in the SCP and DCP. The DCP and especially the temporal area are more affected. Three patients (50%) showed an enlarged foveal avascular zone at the DCP level.
Conclusions
Using OCT-A, we have demonstrated reduction of vessel densities especially located in the DCP. This vascular depletion could be an early event in the disease, which eventually causes ischemia, tissue loss and affects the macular function. Morphological vascular evaluation in patients affected by retinitis pigmentosa allows better understanding the pathogenesis of this disease and can have direct therapeutic implications for the future practical management of retinal dystrophies.

• F016

The important role of OCT in the diagnosis of Oculocutaneous albinism

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Purpose
Oculocutaneous albinism (OCA) is a group of genetic diseases with an autosomal dominant pattern. It affects skin, hair and eyes, leading in an hypopigmentation of all these organs. In ophthalmology we can observe a low visual acuity, photophobia, nystagmus, foveal hypoplasia and retinal hypopigmentation. The hypopigmentation may also affect the iris with a characteristic iridian translucence. The disease is also associated with chiasm alterations.
Methods
We present the case of a 40 year old patient that was referred to our service to confirm the diagnosis of oculocutaneous albinism. The patient presents a severe hypopigmentation of the skin and hair. She also referred a low visual acuity since birth. She didn't presented family antecedents, or personal ophthalmologic history.
Results
The best corrected visual acuity (BCVA) was 0.1 in both eyes. The patient presented horizontal nystagmus and iridian translucence. The fundus examination revealed an important retinal atrophy that showed the choroidal circulation.The optical coherence tomography (OCT) revealed a foveal hypoplasia, atrophy in the epithelial retinal epithelium.
Conclusions
In the patients that the diagnosis of oculocutaneous albinism is not clear, the use of an objective complementary test may be determinant before the genetic diagnosis. This case shows the utility of macular OCT to guide the molecular diagnosis.

• F017

X-linked juvenile retinoschisis: different mutations – same phenotype

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Purpose
To describe the phenotype-genotype correlation of three X-linked retinoschisis (XLRS) cases in juveniles with different novel mutations from Lithuanian population.
Methods
Based on clinical symptoms and family history, a preliminary diagnosis of XLRS was established in three adolescent male patients. Comprehensive ophthalmological examinations, including best-corrected visual acuity (BCVA), slit-lamp, fundus examination, spectral domain optical coherent tomography (SD-OCT) and full-field electroretinography, were performed. RS1 (NM_000330.3) gene coding exons Sanger sequencing was performed.
Results
At the time of ophtalmic and genetic counselling the patients were 9, 12 and 17 years old. The patients demonstrated macular retinoschisis and typical cyst-like cavities on SD-OCT images with logMAR BCVA ranging from 0.5 to 0.2. The mean central foveal thickness was 569.7 µm. Two of the three patients presented with peripheral retinoschisis. Flash-ERG demonstrated a reduced b/a ratio (<1.0) in all patients. RS1 c.599G>T (p.R200L) mutation was detected in one case, in silico analysis showing to be pathogenic. HGMD involves three other different mutations at the same position supporting the pathogenicity of the identified variant. c.(92_97)insC (p.W33fs) mutation was identified for another proband, in silico analysis indicating the variant is possibly damaging. The third case was identified with a pathogenic mutation c.422C>G (p.R141H), HGMD CM981753.
Conclusions
These are the first cases of XLRS in the Lithuanian population confirmed by molecular genotyping. Although clinical expression of XLRS is highly variable presented patients had a different genotype but similar phenotypic traits. Functional analysis would be of benefit to characterise the identified variants on the effect of retinoschisin expression.

• F018

Adaptive optics retinal imaging in patients with GNAT2 mutations

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Purpose
To investigate the retinal structure in three subjects, from two pedigrees, with molecularly confirmed GNAT2 gene mutations with heterogeneous phenotype.
Methods
Spectral Domain OCT (SD-OCT) scans and custom-built Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) sequences were acquired after full ophthalmological examination, ERG and colour vision testing twice, 1-2 years apart. The foveal outer nuclear layer (ONL) retinal thickness was measured using Bioptigen SD-OCT; 120 B-scans were acquired with a 7mm nominal scan width, aligned, registered and averaged in ImageJ. A 5-pixel wide longitudinal reflectivity profile provided the distance between the internal and external limiting membrane. Peak cone density and inter-cone spacing were measured at 0.5 degree from the fovea using confocal AOSLO images. Voronoi analysis was also performed.
Results
Hardy-Rittler-Rand plates suggested normal colour vision in one of our subjects. Conversely, the colour vision test for the other two subjects (from the other pedigree) suggested colour blindness. All three subjects had non-detectable cone ERG. The peak para-foveal density varied from 30 543 to 50 943 cones/mm2 and was significantly lower than previously reported values for unaffected subjects at 168 162 ± 23 529 cones/mm2 (mean ± SD). Voronoi diagrams revealed the heterogeneity of the cone mosaic with only 44% - 53% of photoreceptors having six neighbouring cells. The ONL thickness was variable and due to the small sample size no conclusion could be drawn.
Conclusions
Microscopic retinal imaging allowed photoreceptor visualisation and quantification. It can play a significant role in a multimodal investigation, including functional and structural measurements for an in depth phenotyping of GNAT2 gene, implicated in achromatopsia and other inherited retinal diseases.

• F019

Recurrent corneal erosions dystrophy (ERED) in a Finnish family is caused by a COL17A1 splice-altering mutation

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Purpose
The epithelial recurrent erosion dystrophy (ERED) is a rare autosomal dominant corneal disease. Recently, mutations in collagen type XVII, alpha 1 (COL17A1) gene have been identified as the cause of ERED. Here we report a Finnish family with recurrent erosions with dominant inheritance pattern. We performed COL17A1 candidate gene sequencing.
Methods
Five affected and five unaffected family members underwent standard ophthalmological examination, corneal topography, anterior segment optical coherence tomography and in vivo confocal microscopy. Next-generation exome sequencing of peripheral blood was made in two of the affected individuals to identify mutations in the large COL17A1 gene. Sanger sequencing was used to verify the presence of the identified variant in the other family members.
Results
Affected patients reported recurrent corneal erosions beginning at the age of 4-6 years. The frequency of erosions decreased in adult age. Corneal scarring and anterior stromal opacities were observed. The visual acuity slowly deteriorated. Exome-sequencing revealed a synonymous splice-altering variant c.3156C>T in COL17A1 in two affected patients. Sanger sequencing confirmed the presence of the same variant in four affected family members and its absence from two unaffected ones. The variant was not present in the Sequencing Initiative Suomi (SISu) database consisting of 10,490 Finns.
Conclusions
The variant c.3156C>T in COL17A1 is reported recently in five English, American, New Zealand, and Tasmanian families with ERED. Our finding of the same synonymous variant in yet another population strengthens the evidence this variant is a frequent cause of ERED.

• F020

CTG18.1 trinucleotide repeat expansion in Polish patients with Fuchs endothelial corneal dystrophy

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Purpose
To genotype the CTG18.1 repeat expansion in TCF4 gene and determine an association between genetic variant and Fuchs endothelial corneal dystrophy (FECD) development in Polish patients.
To analyze possible reationship between the different CTG18.1 genotypes and clinical picture of the patients.
Methods
Clinical evaluation was based on slit-lamp examination, in vivo confocal microscopy (IVCM) and anterior segment optical coherence tomography (AS-OCT). Genomic DNA was isolated from peripheral blood samples of unrelated FECD patients (n=236) and control subjects (n=58). We genotype the CTG18.1 repeat expansion to determine an association between the genetic variant and FECD development and to analyse possible relationships between the different CTG18.1 genotypes and clinical picture of the patients. For this purpose a combination of methods, i.e. analysis of short tandem repeats (STR), triplet repeat primed PCR (TP-PCR) and statistical analysis were performed.
Results
The results showed that the repeat expansion CTG18.1 is currently the strongest predisposing factor for the development of FECD in a group of Polish patients (OR=43,72; CI:13,20-144,83; $\chi 2$=80,77; p<0,0001). There were no significant associations between the CTG18.1 genotype and the best corrected visual acuity (BCVA), central corneal thickness (CCT) or the density of the corneal endothelium.
Conclusions
Our study confirms association of CTG18.1 repeat expansion with FECD by testing a novel previously not analysed population. This genetic determinant has an important predictive value and may be beneficial in clinical practice.

• FO21

Familial foveal aplasia

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Purpose
Foveal aplasia, or hypoplasia, refers to the lack of foveal depression with continuity of all neurosensory layers in the presumed location of the fovea. Whilst it is has been reported in cases of aniridia, albinism, microphthalmia and achromatopsia, foveal hypoplasia as an isolated entity is a rare phenomenon. We describe the presentation of a child and her mother with subsequent discussion on the spectrum of the disease.
Methods
Case report and literary synthesis.
Results
A frustrated 16 year old girl was brought in by her mother for review following several attendances to opticians with best-corrected visual acuity of 6/9 both eyes. Ophthalmic examination revealed bilateral subtle spoke like cataracts with a featureless macula. There was no nystagmus present. Optical coherence tomography demonstrated lack of a foveal pit without extrusion of the plexiform layers. There was appropriate outer segment lengthening with a widened outer nuclear layer. Although asymptomatic, examination of her mother demonstrated best corrected visual acuity of 6/7.5 both eyes, with foveal tomography confirming foveal aplasia.
Conclusions
Although foveal aplasia typically presents with other ocular pathology, and most often exhibits nystagmus with decreased visual acuity, the entity can exist in isolation and without nystagmus. Familial cases, and those with pre senile cataracts, have been associated with PAX6 gene mutations and subsequent alterations in ocular morphogenesis.

• F022

Popper associated maculopathy – Case report and literary synthesis

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Purpose
Prevalence of Alkyl Nitrate, or 'Poppers' abuse has remained high since its putative birth in the urban disco scene of the 1970's, with UK figures from 2014 suggesting a 9.1% adult lifetime use rate. However, an associated retinal toxicity is a new and emerging phenomenon due to the recent change of its main compound and continued popular recreational use. Here, we describe a case of Alkyl Nitrate associated maculopathy.
Methods
Case report with literary synthesis.
Results
A 44-year-old Caucasian male with no previous ophthalmic history presented to our eye casualty department with bilateral central vision blurring following repeated inhalation of Alkyl nitrates. Drug use was believed to have occurred twice daily by inhalation over an interrupted 6-week period. Best-corrected visual acuity at presentation was 6/6-1 in the right eye and 6/9+1 in the left. Fundal photography reveals subtle yellow foveal spots bilaterally with an otherwise normal peripheral retina and optic disc. Optical coherence topography demonstrates marked disruption of the photoreceptor inner segment / outer segment junction. Fundus Fluorescein Angiography exhibits a subtle foveal hyper-fluorescence bilaterally. Multifocal ERG displayed attenuated responses from the foveal and parafoveal segments of the left eye with blunting of the foveal peak. A synthesis of current literature and various hypotheses to date is subsequently discussed.
Conclusions
The rarity of this phenomenon, along with tendencies of reluctant disclosure of substance abuse behaviours, can lead to diagnostic difficulties. When faced with bilateral painless central blurring, in otherwise healthy, young individuals, physicians should obtain a detailed history of possible substance abuse.

• F024

Is the age a prognostic factor for the outcome after treatment of myopic CNV?

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Purpose
Choroidal neovascularization (CNV) can develop in eyes with pathologic myopia. The study investigates the role of age as a prognostic factor for the outcome of eyes with myopic CNV after treatment with intravitreal ranibizumab injections.
Methods
Retrospective review of charts of 21 eyes with myopic CNV treated with ranibizumab injections. Diagnosis was confirmed with fundus examination, fluorescein angiography, SD-OCT, refraction and axial length measurement in all cases. Two age subgroups were created, putting the limit to 40 years of age. The correlation of age with the change in visual acuity and the number of injections was evaluated.
Results
The follow-up period was for at least 30 months. Age of the patients was significantly correlated with the number of injections, as well as with the improvement in the LogMAR corrected distance visual acuity. All patients in the younger aged subgroup were stable or improved in comparison to the initial CDVA, versus 57% of patients in the older aged subgroup (p=0.04, chi square test). In the younger aged subgroup 86% of patients had final CDVA equal to or better than 20/40 and in the older aged subgroup 14% of patients (p=0.001, chi square test).
Conclusions
Younger than 40 years old patients found to need fewer intravitreal injections and to obtain a more prominent visual improvement. Age seems to be a critical prognostic factor for the outcome in cases of myopic CNV treated with reanibizumab.

• F025

Intravitreal bevacizumab administration for complicated retinal arterial macroaneurysm in a young male patient

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Purpose
Retinal arterial macro aneurysms (RAM) represent aquired retinal vascular disorders encountered predominantly in elderly, with marked female predominance, and most often associated with hypertension, arteriosclerosis and cardiovascular disease.
In this poster we try to assess functional and anatomical results after bevacizumab (Avastin) injection in a young male with complicated RAM.
Methods
A 27 years old male presented in our clinic with decreased visual acuity into the right eye with the debut 10 days before. The patient underwent a comprehensive ophthalmologic and OCT examination. The diagnosis of retinal arterial macroaneurysm complicated with macular edema associated with lipoprotein exsudation was established. The patient underwent intravitreal injection of bevacizumab (Avastin) 1.25 mg/0.05 ml; two follow-up visits were planned at 1 and 4 weeks after bevacizumab intravitreal administration.
Results
At 4 weeks after intravitreal bevacizumab, right eye BCVA improved from 0.17 logMAR to 0.1 logMAR; the retinal hemorrhage reduced considerable, retinophotography demonstrated resolution of the exsudative changes and OCT examination showed physiologic appearance of the fovea. The patient underwent thorough investigations in cardiovascular area, including cerebral MRI. He was also proposed for retinal angiofluorography.
Conclusions
Although many patients are asymptomatic, decreased visual acuity is the most frequent symptom, and it is determined by hemorrhage and/or macular edema with macular star formation. The differential diagnosis of RAM includes retinal and systemic diseases that require thorough investigation.

• F026

Long-term outcome following ranibizumab treatment for CNV related to ND: YAG-Laser macular injury

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Purpose
To present a case of a macular injury caused by Nd: YAG laser, the early clinical findings, the late complications and the anatomic and functional status after treatment with intravitreal ranibizumab in a five year follow-up period.
Methods
A 32-year-old man working on the physics laboratory, suffered a macula injury in his right eye after accidental exposure of a 800nm wave length Nd: YAG laser pulse. His measured best corrected visual acuity on the day of the accident was 0.70 logMAR. One month later the formation of a full-thickness macular hole was observed. Any surgical intervention was postponed and a close monitor was proposed. A spontaneous closure of the hole was observed within the next month and the vision improved to 0.18 logMAR. Six months later the patient presented with sudden deterioration of his visual acuity again measured 0.70 logMAR. OCT and FA performed, which revealed macular oedema and hemorrhage due to choroidal neovascularisation. A single intravitreal injection of ranibizumab was applied to the affected eye.
Results
The oedema resolved within 45 days after the injection and the visual acuity improved to 0.48 logMAR. No regression was noticed and the BCVA and the macula area remain stable for a period of four and a-half years after the resolution of the oedema,
Conclusions
All personnel working with laser products should take the necessary precautions and use protective goggles. In the event of a macular hole formation, spontaneous closure can occur and a close observation can be an alternative to the early surgical treatment. Choroidal neovascularization can occur and treatment with anti-VEGF therapy may help to maintain a stable anatomic and functional outcome for a long period.

• F027

Dexamethasone intravitreal implant combined with anti-VEGF in patients with neovascular age related macular degeneration resistant to anti-VEGF alone

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Purpose

To evaluate the efficacy and safety of a single intravitreal Dexamethasone implant (DXI) combined with anti-vascular endothelial growth factor (anti-VEGF) therapy, in patients with neovascular age related macular degeneration (wet-AMD) resistant to the conventional treatment.

Methods

In this prospective, randomized, controlled pilot study 16 eyes of 15 patients, unresponsive to previous anti-VEGF therapy, were enrolled. Patients were randomly assigned to three groups: DXI + Pro Re Nata (PRN) anti-VEGF, DXI + monthly anti-VEGF, and monthly anti-VEGF alone. Each patient was treated at baseline, according to the assigned treatment, and followed up to 180 days. Primary outcomes were: complete regression of retinal fluid and best corrected visual acuity (BCVA) change. Secondary outcomes were: safety of the treatment, the change of median central foveal thickness (CFT) and macular volume. Correlations between anatomical features and visual function were also assessed.

Results

Eyes distribution was: 5 in DXI + anti VEGF PRN; 6 in DXI + monthly anti-VEGF (treatment group), and 5 in monthly anti-VEGF. BCVA showed no significant change from baseline in both the treatment and control group. Eight eyes (72.7%) in the treatment group showed complete retinal fluid resorption versus 2 eyes (40%) in the control group (P=0.049). Both median CFT and macular volume showed a greater reduction from baseline in the treatment group. BCVA significantly correlated with the outer retinal layers status (rho=0.82; P=0.0001) and pattern of retinal fluid (rho=-0.59, P=0.02). Several eyes in the treatment group experienced a transient increase of the intraocular pressure.

Conclusions

A combined approach with DXI and intravitreal anti-VEGF may be a feasible option for those wet-AMD patients with an incomplete response to anti-VEGF therapy.

• F029

Bevacizumab-treated diabetic macular edema: a pilot yearlong analysis of anatomic and functional outcomes from a referral center in Portugal

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Purpose

There is high quality evidence that antiangiogenic drugs are a valuable option on diabetic macular edema (DME) treatment. However, evidence under real-world conditions is lacking. This paradigmatic pilot study aims to characterize and discuss the 1-year functional and anatomic response of intravitreal bevacizumab in DME.

Methods

Observational retrospective study. Clinical charts from consecutive patients referred from the Lisbon and Tagus valley region (Portugal) between Jan-2014 and Dec-2015 were reviewed. All patients who underwent intravitreal injection of bevacizumab for DME were analyzed. Efficacy outcomes were i) visual acuity (VA) improvement (i.e. halving the visual angle or doubling the decimal value), and ii) a 10% or higher decrease in central macular thickness (CMT), both after a 12-months follow-up period. Statistical analysis were performed using STATA.

Results

A total of 107 eyes of 84 patients, with a mean age of 66.0 ± 8.8 years were studied. Mean time elapsed since diabetes diagnosis was 19.1 ± 7.9 years, and mean HbA1c levels were 8.1 ± 1.2 %. Baseline VA improved from 0.35 ± 0.22 at baseline to 0.39 ± 0.25 after 12 months ($p < 0.05$). Also CMT significantly decreased from 464 ± 144 to 379 ± 144 µm one year after injection. The rate of VA and CMT improvement was 31% and 48%, respectively. A non-statistically significant trend was observed for better outcomes in patients who were concomitantly treated with either focal laser or intravitreal triancinolone. No differences were noted considering the loading dose. No major complications were observed.

Conclusions

This pilot study suggests intravitreal bevacizumab was effective in the DME treatment of our cohort, with a good safety profile. A longer follow-up and larger sample will help building better evidence to DME management.

• F028

The development and performance of a new patient derived tool to measure Dimensions in Treatment of Age-related Macular Degeneration (DITAMD)

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Purpose

A growing aging population increases the number of patients treated for neovascular Age related Macular Degeneration (nAMD). Studies reporting the patient's perspective during treatment are limited. Our aim was to develop and test a tool for monitoring treatment burden and satisfaction among nAMD patients.

Methods

Development: Patients (n=44), mean (SD) age 80.4 (8.2), 62.8% females, diagnosed with nAMD selected dimensions mattering most during treatment. Reported dimensions were analysed according to similar content, then coded. Test: Recently diagnosed patients (n=178), with logMAR visual acuity in treated eye 0.43 (0.42), completed DITAMD after 3 months treatment on a Likert scale (1-5). A weight based on the identified importance in the development phase, had a sum score, range 0-10.

Results

Development: Dimensions reported most frequently were included in DITAMD; receive treatment , information, waiting time, confidence, accommodating staff, follow up, planning, continuity, pain relief, injection technique, transportation, hygiene, early treatment access, involvement and visual aids. Test: Patients (n=178) reported DITAMD score of 8.1 (0.9) suggesting satisfaction with treatment. The score was not significantly associated to age or gender. A subgroup of patients (n=70) considered relevance (0-10) of the questionnaire; mean (SD) 8.3 (1.3), indicating high level of face validity. Satisfaction during treatment and perceived importance of the dimensions were compared with paired T-test for each item, for some dimensions, satisfaction was significantly higher than importance. However, information about visual aids had significantly lower satisfaction the importance.

Conclusions

DITAMD allows monitoring patient relevant experience during treatment of nAMD. The discrepancy between satisfaction and perceived importance should guide patient care.

• F030

Refractive changes after anti-VEGF injections for diabetic macular edema

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Purpose

To evaluate refractive changes after anti-vascular endothelial growth factor (anti-VEGF) injections for the treatment of diabetic macular edema (DME).

Methods

Participants in this retrospective study were 37 patients (37 eyes) with DME, who received intravitreal anti-VEGF injections with either ranibizumab or aflibercept. Spherical equivalent refractive power was evaluated before treatment and at least one month after the last injection where no fluid existed. Demographic characteristics, visual acuity, central retinal thickness and the number of injections were recorded and analyzed.

Results

Changes in visual acuity and central retinal thickness were statistically significant before and after injections. The spherical equivalent refractive power did not differ significantly pre- and post- injections.

Conclusions

Intravitreal anti-VEGF injections did not seem to affect the refractive power of patients with DME. Therefore, appropriate spectacle correction can be prescribed any time during ongoing treatment with anti-VEGF agents.

• F031

Treatment of diabetic macular edema with micropulse laser therapy

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Purpose
The aim of the present study is to investigate the effect of Micropulse Laser Therapy (MP) in the treatment of diabetic macular edema (DME).
Methods
Forty eyes from 25 patients with clinically significant DME were included in the study. We used MP as first-line therapy in cases of diffuse DME if central macular thickness (CMT) was < 300 µm.
However, if DME was diffuse and CMT was > 400 µm, we began anti-VEGF therapy to reduce CMT and improve vision as quickly as possible.
We started with MP also in patients who refused intravitreal anti-VEGF injections, whom compromised systemically or those for whom they are not effective.
Best corrected visual acuity (BCVA) and central macular thickness (CMT) were measured before, 3, 6 and 12 months after intervention, and the results were compared.
Results
Mean age of our patients was 60,1 years. Mean BCVA was 0,67+/- 0,37 Logmar before treatment.
After three months of MP, it improved to de 0,55+/-0,4, p=0,024. CMT was 511,79 um, and improved to 481,8um (p: 0.055) at 3 month after treatment and to 410 um at 6 months (p: 0.004) and 257,21 un at 12 months (p=0,002).
OCT detected early retinal reflectivity changes after treatment. All patients reported subjective improvement. No adverse events were observed during follow-up
Conclusions
In this study, MP laser seems to be an effective laser to treat DME.
Its attractive safety profile allows clinicians to offer earlier treatment to prevent tissue damage and the development of visual disability.

• F032

Changes in retinal vessel diameters after intravitreal aflibercept in patients with diabetic macular edema.

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Purpose
To evaluate changes in retinal vessel diameters after loading doses with intravitreal aflibercept in patients with diabetic macular edema (DME).
Methods
This was a three months prospective, interventional study. We included 17 patients with DME, central retinal thickness >300 µm and no active proliferative diabetic retinopathy. Previous treatment with any intravitreal vascular endothelial growth factor inhibitor was not allowed within 4 months prior to inclusion. All patients received 3 monthly intravitreal injections of aflibercept, and vessel diameters were evaluated at baseline and four weeks after the last injection. Retinal arterial and venous diameters were measured in 50-degree disc-centered images using the Oxymap model T1 (Oxymap, Reykjavik, Iceland) as the average diameter of the four major arterioles and venules from the four quadrants. Paired t-test was used to test for differences in mean oxygen saturations from baseline to follow-up.
Results
Median age and duration of diabetes were 59.5 and 2.6 years at baseline. Median HbA1c and CRT were 65 mmol/mol and 336 µm, respectively, and 23.5% were women. Venous diameter decreased from baseline to follow-up (157.9 µm vs. 153.2 µm, p=0.03), whereas arterial diameter was unchanged (115.4 µm vs. 116.1, p=0.70).
Conclusions
Retinal venous diameter decreased after treatment with 3 monthly intravitreal injections of aflibercept in patients with DME, whereas no difference was found in the retinal arterial diameter. As previous studies have demonstrated that retinal venules dilate with increasing severity of diabetic retinopathy, our results suggest that treatment with intravitreal aflibercept causes positive changes to retinal vessel geometry.

• F033

Vascular macular capillary plexus in patient with Type 1 diabetes with no retinopathy are correlated with OCT volume changes

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Purpose
Diabetic retina undergoes neurodegenerative changes at the neuronal level in addition to vascular changes. Neuronal changes can be study indirectly using spectral domain OCT thickness and volumen. OCT angiography (OCTA) allows studying the macular vascular plexus in a non-invasive way. The purpose of our study was to evaluate changes in the macular vascular density changes using OCTA, and to examine its correlation with OCT macular thickness diminution over 8 year follow-up in patients with type 1 diabetes and no signs of diabetic retinopathy. To quantify foveal avascular zona (FAZ) area and to correlate with vascular modifications.
Methods
18 eyes of 9 diabetic patients with no retinopathy were studied by SD-OCT at 2009. The patients were reexamined by SD-OCT looking for changes in macular thickness and volumen; all eyes underwent angio OCT. FAZ was manually measured. Macular thickness and volume changes over these 8 years were correlated with finding at the OCTA and FAZ area.
Results
Mean age of the patients was 35.32±14.23 years (range 23-54). Mean time of diabetes evolution was 15.96±11.46 years. Best corrected visual acuity (BCVA) was between 0 and -0.3 logMAR. 16 eyes showed no signs of diabetic retinopathy. One patient had mild-moderate diabetic retinopathy with macular edema in his LE. Eyes with OCTA changes showed modification in both superficial and deep plexus. Vascular changes included reduced capillary density, regions of capillary dropout and foveal avascular enlargement. Patients with OCTA changes displayed a diminished macular volume over the 8 years of follow up (excluding the one with diabetic retinopathy).
Conclusions
Despite we are not able to find signs of diabetic retinopathy, type 1 diabetic patients develop changes at the vascular level that are related to a diminution of the OCT macular volume.

• F034

Types of diabetic retinopathy studied by wide field angiography

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Purpose
To evaluate the types of diabetic retinopathy (DR) using a wide field fluorescein angiography and to identify the associated factors.
Methods
In a retrospective study, consecutive wide-field angiographs obtained using the Heidelberg Retina Angiograph 2 with a contact lens system Staurenghi were graded in: anterior, posterior or diffuse diabetic retinopathy. Anterior DR was defined if diabetic retinal changes were noted only at the location anterior to the imaginary circle bordered by the Early Treatment Diabetic Retinopathy Study seven-standard fields. In all patients central foveal thickness was measured on Spectral-domain optical coherence tomography using Topcon 2000.
Results
A total of 69 eyes of diabetic patients were included. Diabetic retinopathy was anterior in 12 eyes (17.4%), posterior in 24 eyes (34.8%) and was diffuse in 33 eyes (47.8%). Retinal non perfusion was associated with anterior DR in 17.5%, posterior DR in 2.5% and diffuse DR in 80% of eyes (p<0.001). Peripheral vessel leakage was present in 14.3% of anterior DR, and in 85.7% of diffuse DR, and none eye in posterior DR (p<0.001). The average of central foveal thickness was 232 µm in anterior DR, 303µm in posterior DR and 459µm in diffuse DR (p=0.01). No correlation was found between types of DR and age (p=0.22), sex (p=0.2), arterial hypertension (p=0.12), cardiopathy (p=0.16), nephropathy (p=0.16) and dyslipidemia (p=0.07).
Conclusions
This study highlighted that diffuse DR was significantly associated with retinal non perfusion and macular edema. Posterior DR was less associated with retinal non perfusion and peripheral vessel leakage. Eyes with anterior and diffuse DR are at greater risk of ocular complications, needing more clinical monitoring.

• F035

Cost-effectiveness of intravitreal therapy with both anti-VEGF and Dexamethasone implant in patients with Diabetic Macular Edema

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Purpose
The aim of this study was to evaluate the cost-effectiveness of intravitreal therapy (IVT) with both anti-VEGF and Dexamethasone implant in patients with Diabetic Macular Edema (DME) during two years' follow-up.
Methods
A retrospective review of 191 patients (382 eyes) with type I and II diabetes and DME was performed. Pre-IVT and final best correct visual acuity (BCVA), central macular thickness (CMT), intraocular pressure (IOP), number and type of IVT,number of examinations, and fluorescein angiography were assessed. Based on surgery procedure other than IVT, patients were divided into 5 groups. To avoid bias, we analysed only patients who had undergone cataract surgery before (group 1) or during enrolment (group 2).
Results
41 eyes from Group 1 and 48 eyes from group 2 were evaluated. Median BCVA ranged between 20/80 and 20/63 Snellen (P=0.008) in Group 1 and from 20/63 to 20/40 Snellen (P=0.0035) in Group 2, while improvement up to 1 Snellen line was observed in 58.5 and 68.75% of eyes in Group 1 and 2, respectively.In terms of median CMT, a statistically reduction (P=0.0007) was found in Group 2 (-85 µm), whereas no statistical differences were found in Group 1. The two groups showed no statistically significant difference in median IOP. The estimated cost per eye was €7803 in Group 1 and €8988 Group 2, whereas the mean cost per patient was €15190 and €16580 in Group 1 and 2, respectively. Analysis between groups did not show any statistical difference in the considered parameters.
Conclusions
In this study, despite the high treatment cost, vision improvement in DME patients undergoing IVT was disappointing. Our results emphasise the need for a better understanding of the cost-effectiveness of DME treatment

• F036

Topical betamethasone sodium phosphate, tetracycline hydrochloride and nonsteroidal anti-inflammatory drugs in the treatment of diabetic macular edema: a case report

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Purpose
To report a case of clinically significant diabetic macula edema (DME) cured only with topical Betamethasone Sodium Phosphate, Tetracycline Hydrochloride and nonsteroidal anti-inflammatory drugs.
Methods
A 44-year-old type I diabetic woman was referred to our Unit after a partial tarsorrhaphy procedure for exposure keratopathy in her left eye. OCT examination of her right eye revealed a clinically significant DME with important visual loss (Central Macular Thickness [CMT] 716 µm, Best Correct Visual Acuity [BCVA] 20/100 Snellen). The patient refused the suggested intravitreal therapy (Ranibizumab injections with PRN protocol). Topical treatment with Betamethasone Sodium Phosphate, Naphazoline Nitrate, Tetracycline Hydrochloride (Alfaflor®, Alfa Intest, Italy) and Diclofenac (Voltaren Oftabak®, Thea, France) eye-drops 4 times/day was started.
Results
In the following 10 months, right CMT decreased to 335 µm and right BCVA increased to 20/25 Snellen. However, OCT scans still showed some intraretinal cysts. Topical Diclofenac was then replaced with Bromfenac (Yellox®, Bausch & Lomb, Italy) eye-drops 2 times/day. After 4 months' treatment, right BCVA was 20/20 Snellen and OCT scans showed a normal CMT. This treatment was continued and there was no recurrence of DME in the next 11 months of follow-up. No adverse events were noted.
Conclusions
Topical Betamethasone Sodium Phosphate and Tetracycline Hydrochloride, together with nonsteroidal anti-inflammatory eye-drops, might be an effective alternative for the treatment of newly diagnosed DME in patients not suitable for intravitreal therapy. Future case-control studies are necessary to confirm these results.

• F037

OCT Angiography in angioid streaks without neovascular complications

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Purpose
To describe the features of angioid streaks (AS) without neovascular complications using swept source optical coherence tomography.
Methods
This is a retrospective observational study.
All patients underwent slit-lamp and fundus examination, fundus photos, swept source optic coherence tomography (SS-OCT) and OCT angiography (OCT-A).
Comparisons were made between en face OCT and OCT-A images.
Results
Seven eyes had AS without neovascular complications, foveola was involved by the streak in 3 eyes of them.
In en face OCT, we found hyper-reflective points in 5 eyes in the deep plexus (DP), and in 2 eyes in the choriocapillaris (CC) giving a shadow in the level of the choriocapillaris in the corresponding OCT-A.
In the outer retina (OR), Streaks were detectable in patients having macular involving AS as hyposignal in the OR and the CC.
Also, 5 eyes had CC diffuse rarefaction (CR) that seems more extensive than the masking from the hyper-reflective material visible in the DP on en face-OCT.
An irregular vascular network (IVN), different from choroidal neovascularisation (CNV), was detected in 3 eyes with AS involving the macula in the level of the OR and CC. This IVN fills spaces between streaks. On structural OCT, it corresponds to flat elevation of the retinal pigmentary epithelium (RPE) with hyper reflective accumulations between the RPE and the Bruch membrane (BM).
Conclusions
This imaging tool provides new information about AS.
We illustrate different findings including hyper reflective deposits, CR and IVN.
CR suggests early and severe involvement of all the CC.

• F038

Cross-sectional static retinal vessel analysis in routine optometric practice

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Purpose
Do retinal vessel calibres provide the same conclusions regardless of which eye was assessed?
Methods
A cross-sectional sample of patients seen in routine optometric practice [n=225] underwent a standard eye examination including subjective refraction and slit-lamp biomicroscopy. Undilated optic nerve-centred fundus photographs were obtained (camera angle: 50 degrees). Red-free photographs were analysed using iFlexis software (Vito, Belgium) to give objective retinal vessel calibre measurements (central retinal artery/vein equivalents; CRAE/CRVE), as described by Knudtson et al.
Results
The mean age of the cohort was 59 years (range: 16-90 years ±15) and comprised of 137 women and 88 men. BMI ranged between 17.6 – 37.3 kg/m2. Average systolic blood pressure (BP) was 131mmHg ±20 and diastolic BP was 82mmHg ±12. Refractive error (MSE) ranged from -10.00 to +7.00D. CRAE was found to be 142AU ±16 (RE) and 143AU ±18 (LE). CRVE was 210AU ±23 (RE) and 209AU ±22 (LE). Paired t-test showed no difference between RE and LE calibres. There was good agreement of both vessel calibres in both eyes, as shown by Bland-Altman plots. (CRAE: bias: -0.88; upper/lower limits: 27.81/-29.57; CRVE: bias: 0.08; upper/lower limits: 33.43/-33.26). Stepwise forward multiple regression analysis found a significant (all $p<0.001$) decrease in both CRAE and CRVE with increasing myopia and age; CRVE also increased with increasing BMI. Analysis was run on all RE, all LE and randomly selected eyes to test if the same conclusion could be drawn regardless of eye selected.
Conclusions
Established associations between age, refractive error and BMI with retinal calibres were in agreement with the sample used. The impact of refractive error on retinal vessel calibre measurements highlights its importance as a co-variate in larger studies, especially when assessing systemic vascular disease.

• F039

Ophthalmoscopic and video OCT methods to detect spontaneous venous pulsation in individuals with apparently normal intracranial pressure: the rebirth of the SVP?

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Purpose
Purpose: To compare the efficiency of high magnification binocular indirect ophthalmoscopy and direct ophthalmoscopy in detecting the spontaneous venous pulsation (SVP) at the optic nerve head, and to demonstrate the utility of video optical coherence in detecting the phenomenon in patients with normal intracranial pressure.
Methods
Methods: The SVP of the right eye of 54 consecutive clinic patients presenting without neuro-ophthalmic symptoms and with BMIs under 30 were dilated and examined by one ophthalmologist using a 66D handheld Volk lens, then examined by a second blinded ophthalmologist using direct ophthalmoscopy. Immediately the patient was assessed by a third blinded ophthalmologist via vOCT for the presence or absence of SVP.
Results
Results: The population included 20 males and 34 females and were corrected for VA (M 0.127 LogMAR, SD 0.22, SE 0.036), IOP(M 16.5 SD 4.02 SE 0.558), phakia, age (M 68.3, SD 15.15, SE 2.062), C:D ratio (M 0.48 V 0.58 H, SD 0.19 V 0.18 H, SE 0.035 V and 0.033 H), BP (M 136/79, SD 17.71 Sys 12.04 Dia, SE 2.410 Sys, 1.639 Dia) and weight (M 75.48, SD 15.92, SE 2.486). SVPs were detected in 32 of 54 patients using direct ophthalmoscopy, and in 33 of 54 patients using a 66D lens and slit lamp. The ophthalmologists using direct ophthalmoscope and the 66D lens agreed in 49 of 54 cases, giving an inter-rater reliability of 91%. All patients were found to have SVP on vOCT.
Conclusions
Conclusions: Ophthalmoscopically-assessed SVP has a high inter-observer agreement in normal subjects. However, 26% of patients with apparently normal ICP had no ophthalmoscopically detectable SVP. Conversely, SVP was detectable in all patients with apparently normal ICP by vOCT, suggesting it may be a more useful clinical assessment than ophthalmoscopically assessed SVP-detection.

• F040

Inner retina changes in hydroxychloroquine patients

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Purpose
To study if hydroxychloroquine (HCQ) patients with apparent no retinal toxicity will show lower retinal thickness in inner layers as compared to healthy controls.
Methods
Retrospective study of 43 patients (86 eyes) evaluated for HCQ macular toxicity with spectral-domain OCT (SD-OCT) and with no OCT signs of maculopathy were subdivided into two groups: 1) no blunting of the foveal contour (foveal splaying), 2) with foveal splaying. Age and sex-matched controls were used for comparison. Automated retinal layer segmentation at the center of fovea and at a radius of 3 (parafoveal) to 6mm (perifoveal) from the superior, inferior, temporal and nasal sectors was performed. Statistical analysis using two sample t-test was made to calculate significant results between groups.
Results
Center macular and internal retinal layers thickness in all parafoveal sectors, particularly in the retinal nerve fibre (RNFL) and ganglion cell layer (GCL), was statistically reduced when compared to control group ($p<0.05$) and differed between group 1 and 2. RNFL thickness was also reduced in all perifoveal sectors but temporal sector ($p<0.05$) and inner plexiform layer and inner nuclear layer thickness showed only significant reduction in foveal and nasal parafoveal sector ($p<0.05$) in HCQ eyes. No significant differences in outer layers was observed between groups.
Conclusions
Small changes in inner retinal layers thickness have been described with HCQ use and conflicting correlation with HCQ toxicity is present in the literature. This study supports that inner retina at the fovea and parafovea is thinner in patients with no outer retinal OCT signs of HCQ toxicity. Further investigation is needed to assess if an inner retinal thickness reduction threshold could serve as valuable tool for identifying patients with increased risk of HCQ maculopathy.

• F041

Idiopathic retinal vasculitis, arteriolar macroaneurysms and neuroretinitis (IRVAN): Case series of three patients with multimodal imaging

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Purpose
To describe the clinical presentation, disease progression, treatment and complications of IRVAN.
Methods
Retrospective review of three patients with a diagnosis of IRVAN seen at the Birmingham and Midland Eye Centre between 2010 and 2017. Multimodal imaging investigations included wide-field fluorescein angiography, optical coherence tomography, and indocyanine green angiography.
Results
A total of 6 eyes from 3 patients with bilateral disease were included. All six eyes were treated with panretinal photocoagulation (PRP). One eye received a dexamethasone implant for refractory macular oedema and exudation. One eye was treated with Avastin injections for persistent optic disc neovascularization. All 3 patients were treated with oral steroids at some point in the course of their disease and one was subsequently immunosuppressed with mycophenolate mofetil.
Visual outcomes varied. One patient maintained excellent visual acuity of 6/6 in both eyes at 72-months follow-up.
The second patient experienced progressive visual loss from 6/9 right eye, 6/6 left eye at presentation; to 6/18 right eye, 6/60 left eye at 12 months follow-up due to macular exudation despite aggressive PRP and intravitreal Ozurdex.
The third patient deteriorated from 6/5 right eye, 6/4 left eye at presentation to 6/60 right eye at 6 months, despite aggressive PRP. He had recurrent vitreous haemorrhages in the right eye secondary to NVD despite further interventions with Avastin injections; seven years after presentation, vision remained at 6/60 right eye and 6/18 left eye.
Conclusions
The cadence of progression of IRVAN can vary greatly, despite aggressive treatment with PRP, intravitreal steroids, and anti-VEGF agents. We observed variation in disease progression both among patients as well as within the same individual, supporting an individualized approach to therapy.

• F042

Choroidal vascular abnormalities by UWF ICGA in central serous chorioretinopathy

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Purpose
To evaluate vortex vein engorgement and choroidal vascular hyperpermeability in patients with central serous chorioretinopathy (CSC) using ultra-widefield indocyanine green angiography (UWF ICGA).
Methods
Twenty two patients with unilateral (19 patients) or bilateral (3 patients) CSC were consecutively included and imaged by UWF autofluorescence, fluorescein angiography and ICGA, and spectral domain optical coherence tomography (OCT). The number of quadrant of vortex vein engorgement was evaluated in the early phase of ICGA, which was classified as effective if the dilated choroidal vessels affect the macula. The area of choroidal vascular hyperpermeability was quantified in the late phase using by stereographic projection method. And they were correlated with clinical findings and OCT features.
Results
In all affected eyes, choroidal hyperpermeability from dilated choroidal vessels was observed in association with 1 or more engorged vortex vein. Affected eyes showed significantly greater choroidal hyperpermeability area ($P < 0.001$) and thicker subfoveal choroidal thickness ($P = 0.022$) compared with unaffected eyes although both eyes in the patients with unilateral CSC demonstrated symmetry of vortex congestion (78.1%). The choroidal vascular hyperpermeability was significantly correlated with subfoveal choroidal thickness (P=0.012, rho=0.493) and the height of subretinal fluid (P=0.012, rho=0.514). The number of quadrant of the effective vortex vein engorgement was correlated with subfoveal choroidal thickness (P=0.010, rho=0.505).
Conclusions
UWF ICGA could demonstrate vortex vein engorgement and choroidal vascular hyperpermeability, suggesting outflow congestion as a potential contributor to the pathogenesis of CSC. And they may serve as diagnostic clues or even predictors of disease course.

• F043

Clinical significance of subretinal hyper-reflective material in retinal angiomatous proliferation patients

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Purpose
To evaluate the association of subretinal hyper-reflective material(SHRM) with visual acuity(VA) in Retinal angiomatous proliferation(RAP) patients treated with anti-VEGF.
Methods
38 Patients(38 eyes) diagnosed with RAP were included in the study and retrospective chart review was done. Optical coherence tomography(OCT) and VA measurement was conducted at initial diagnosis, 6 months follow up and 12 months follow up. Measurement of SHRM height and width were obtained on each OCT image. Comparison of SHRM existence, height and width with VA was done.
Results
VA after anti-VEGF treatment was associated with initial VA(p=0.024) and existence of SHRM(p=0.045) at baseline, while SHRM height and width were not statistically significant.
Conclusions
Existence of SHRM at baseline and initial VA in RAP patients could be a prediction factor of the final VA treated with anti-VEGF.

• F044

Long-term reproducibility of axial length in eyes undergoing combined phacovitrectomy for macular-sparing rhegmatogenous retinal detachment

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Purpose
To evaluate the change of axial length (AL) and the long-term reproducibility measured by optical biometry and ultrasound A-scan (US) after combined phacovitrectomy for macular-on retinal detachment (RD).
Methods
Thirty-seven eyes that underwent combined phacovitrectomy with intraocular lens implantation were analyzed, prospectively. The ALs were measured before surgery, after 1 year and 2 years, using optical biometry (IOL Master®, Carl Zeiss, Jena, Germany) and US. Intraclass correlation coefficient (ICC), coefficient of variation (CV), and test–retest standard deviation (TRTSD) were assessed.
Results
The mean age of patients was 56.5 ± 6.2 years, and 20 (54.1%) of the 37 were men. The mean preoperative AL measured by optical biometry was 25.03 ± 1.69 mm in vitrectomized eyes and 24.96 ± 1.70 mm in fellow eyes. The ICC, CV, and TRTSD were 0.97, 0.45 and 0.114 in vitrectomized eyes and 0.98, 0.66, 0.167 in fellow eyes, respectively. These parameters exhibit excellent long-term reproducibility. Refractive prediction error by optical biometry and US were -0.41 ± 0.67 D (p = 0.001), and -0.49 ± 0.68 D (p = 0.000) respectively, which shows myopic shift. Correlation analysis showed significant relationships between myopic shift with shallow anterior chamber and thick lens.
Conclusions
After combined phacovitrectomy for macular on RD, the AL showed excellent long-term intervisit reproducibility for two years. Regardless of AL, combined phacovitrectomy and gas tamponade resulted in significant myopic shift of postoperative refraction, for both optical biometry and US.

• F045

Acute macular neuroretinopathy type 2: an unusual case

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Purpose
Acute Macular Neuroretinopathy (AMN) is a rare retinal disease distinguished in two different types. In type 1 the lesion occurs above the outer plexiform layer (OPL) interesting the inner nuclear layer (INL), differently in type 2 the lesion occurs below the OPL interesting the outer nuclear layer (ONL). Type 1 is more common among elderly, males, and associated with cardiovascular risk factors while type 2 is more usual in young and females.
Methods
A 68 years-old white man presented to Ophthalmic Emergency Room complaining the acute-onset of a paracentral superonasal scotoma in his left eye. His medical history was significant for systemic arterial hypertension in good control with diuretics and sartans. He also refers primary open angle glaucoma in treatment with prostaglandin analogous in both eyes. We performed fluorescein and indocyanine green angiographies, spectral domain-Optical Coherence Tomography (SD-OCT), OCT angiography (OCTA), standard automated perimetry (SAP), microperimetry, and multifocal electroretinogram (mfERG).
Results
Fluorescein and indocyanine green angiographies were unremarkable. SD-OCT revealed a focal hyperreflective band that involved the OPL and ONL localized in the parafoveal inferior region. The SAP showed a superonasal scotoma that was confirmed by the mfERG trace decrease and the inferotemporal reduced retinal sensibility at microperimetry. OCTA revealed a deep retinal capillary plexus perfusion defect area inferotemporally to the fovea.
Conclusions
Our case describes an unusual AMN type 2 that occurs in an elderly male patient affected by systemic arterial hypertension typical for type 1. These evidences suggest a closer pathogenic relationship between the two forms of AMN. Further studies will be able to determine whether AMN type 1 and AMN type 2 rapresent single or multiple entities.

• F046

The impact of epiretinal membrane on neovascular age-related macular degeneration treatment: A spectral-domain optical coherence tomography study

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Purpose
The purpose of this prospective study was to evaluate the impact of epiretinal membrane (ERM) on anatomical and functional results in patients with wet age-related macular degeneration (AMD) treated with intravitreal anti-vascular endothelial growth (anti-VEGF) injections.
Methods
Participants in the study were 48 patients with either wet AMD alone (n=27) or AMD and ERM (n=21). All patients received intravitreal anti-VEGF injections (3 monthly injections and PRN thereafter) and were followed-up for at least 12 months. All participants had best corrected visual acuity (BCVA) measurement and optical coherence tomography (OCT) at each visit, while fluorescein angiography was performed at baseline and then at the discretion of the physician. The main outcomes were the change in BCVA and central retinal thickness (CRT) along with the presence of fluid in the two groups.
Results
There was a statistically significant improvement in BCVA in both groups, while the two groups did not differ significantly regarding BCVA at the end of the follow-up. Accordingly, there was a statistically significant reduction in CRT in both groups, which did not have any difference in between. Patients with AMD alone presented subretinal fluid in a lower percentage than patients with AMD/ERM at the end of the follow-up. In addition, patients with coexistence of AMD and ERM needed more injections than patients with AMD alone.
Conclusions
Patients with AMD combined with ERM seemed to need more injections for the treatment of AMD, while they presented higher percentage of subretinal fluid at the 12-month follow-up, although there was no significant difference in BCVA and CRT in comparison with patients having AMD alone.

• F047

Intra- and inter-grader agreement in grading of coverage of panretinal photocoagulation by ultra-wide field color fundus images

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Purpose
Panretinal photocoagulation (PRP) is the gold-standard treatment for proliferative diabetic retinopathy (PDR), but evaluation of the coverage of PRP after treatment can be difficult and is not standardized. Ultra-wide field (UWF) color fundus images may offer an objective alternative to subjective evaluation of PRP-coverage. We propose a new model to quantify the coverage of PRP treatment in each retinal quadrant by UWF images. The purpose of the study was to evaluate the intra- and inter-grader reliability of the model.
Methods
The retinal coverage of PRP in each quadrant of the retina on 20 UWF color fundus images in patients treated for PDR was quantified by two independent graders (grader A and B), and intra- and inter-grader association (Kappa) were calculated. In each retinal quadrant, OPTOS UWF color fundus images (Optomap, Optos PLC., Dunfermline, Scotland, UK) were used, and each grader evaluated the total retinal area covered by laser. The graders categorized the amount of laser visible on the retina into four categories (no visible laser spots, <50%, 51-75%, 76-100%).
Results
The total retinal area covered by laser was 76-100% (for both graders). Intra-grader association was 0.715 and 0.464 for Grader A and Grader B, respectively, and inter-grader association was substantial at 0.627.
Conclusions
Using Optos UWF images, we were able to achieve high intra- and inter-grader reliability for the quantification of the retinal area covered with PRP in patients with PDR. This might aid clinicians when comparing PRP coverage between patients.

• F048

Multimodal imaging of combined harmatoma of the retina and retinal pigment epithelium

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Purpose
To describe the use of multimodal imaging in defining the anatomical features of combined harmatoma of the retina and retinal pigment epithelium (CHRRPE) and assess its role in the diagnosis and management of CHRRPE.
Methods
Retrospective case series of three patients with unilateral, juxta-papillary CHRRPE, who underwent Spectralis Enhanced Depth Imaging Optical Coherence Tomography (EDI-OCT), MultiColor (MC) and autofluorescence (AF) in addition to a complete ophthalmic examination.
Results
EDI-OCT demonstrated thickening and disorganisation of retinal architecture, with intraretinal cysts disrupting the retinal layers and a loss of photoreceptors. An overlying epiretinal membrane was shown to be causing 'mini-peaks' of the inner retinal surface in all cases and vitreoretinal traction in two cases. Details of the retinal pigment epithelium (RPE) were revealed, including RPE thickening and sectoral atrophy. MC revealed areas of red-shifting, demonstrating partial pigmentation. On green reflectance (GR) the degree of inner retinal distortion and extent of macular involvement could be visualised. Near infra-red (NIRR) reflectance displayed the lesions as areas of hyporeflectance and allowed delineation of the tumour borders. On AF, the lesions were represented by areas of hypo-autofluorescence that obscured the normal blood vessel hypo-autofluorescence.
Conclusions
In this case series, multimodal imaging enabled the anatomical characteristics of CHRRPE to be defined in greater detail. NIRR enabled better visualisation of tumour boundaries and the extent of macular involvement, which may be useful in assessing the impact on visual function. GR better defined the degree of inner retinal distortion, which may be useful in surgical management decisions. We believe that multimodal imaging is a valuable adjunct in correctly diagnosing and managing CHRRPE.

• F049

Changes in axial length before and after recovery in patients with idiopathic central serous chorioretinopathy with serous retinal detachment

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Purpose
To evaluate the changes of axial length (AXL) in eyes with unilateral idiopathic central serous chorioretinopathy (CSC) after subretinal fluid absorption.
Methods
We studied 31 consecutive patients with unilateral resolved central serous chorioretinopathy. The keratometric value and AXL were measured by partial coherence interferometry (IOL Master®). Presence of subretinal fluid and central macular thickness (CMT) were measured by spectral domain optical coherence tomography (Cirrus HD OCT®).
Results
The mean age of 31 CSC patients was 42.7 years, and 19 males were included. The AXL was statistically significant difference from 23.41 mm to 23.58 mm after subretinal fluid absorption ($p<0.001$). The differences in AXL correlated with CMT differences ($r=-0.616$, $p<0.001$). Best corrected visual acuity and CMT were statistically significant difference after subretinal fluid absorption ($p<0.001$).
Conclusions
In unilateral idiopathic CSC, the AXL was increased after subretinal fluid absorption. Therefore, the impact of serous retinal detachment should be considered in AXL measurement.

• F050

Relationship between macular thickness and mesopic visual acuity in older subjects without retinal disease

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Purpose
Impaired mesopic visual acuity (VA) is a risk factor for incident early age-related macular degeneration 3 years later. However, there is a lack of data on the retina structure-function relationship in healthy eyes. In this study, the correlations of macular thicknesses with photopic and mesopic VA were analyzed in young and older subjects without retinal disease.
Methods
Retinal thickness was measured by spectral-domain optical coherence tomography in one eye of 40 young and 41 older healthy subjects with best corrected VA of 20/20. Macular thicknesses measurements from complete and inner and outer retinal-segmentation (IRS and ORS) of the central fovea, inner ring, outer ring, and ganglion cell complex were used in analyses. Best-corrected distance VA was measured using HC and LC logMAR charts under photopic and mesopic (1 cd/m2) luminance conditions. The decrease in mesopic VA when compared to photopic VA (low luminance VA deficit) was registered. Pearson correlation followed by multiple forward stepwise regression analyses were performed in each age group.
Results
In the older group, the macula was thicker in the ORS of the central fovea and inner ring, and thinner in the IRS of inner ring and outer ring (all, $P<0.01$). Mean photopic and mesopic HC-VA and LC-VA, and mean HC-low luminance VA defict were significantly worse in the older group (all, $P<0.01$). Significant correlations were detected only in the older group. Multiple regression analysis showed that ORS thickness of inner ring was independent contributor to mesopic LC-VA ($r=0.40$, $p=0.01$) and the complete thickness of central fovea was independent contributor to HC- and LC-low luminance VA deficit ($r=0.45$, $p=0.003$; $r=0.32$, $p=0.04$ respectively).
Conclusions
A thickening of central fovea was associated with greater increase in the low luminance visual acuity deficit in healthy older eyes.

• F051

Clinical application of enhanced retinal vasculature visualization using hemoglobin absorbance

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Purpose
To develop a digital filter for better visualization of retinal blood vessels and verify its clinical usefulness
Methods
. Four-hundred 24-bit color fundus images were analyzed and properties of red, green, and blue channels were extracted. Then, using hemoglobin absorption coefficients, the relevant weights for gray-scale conversion that emphasizes retinal vessels were calculated. To evaluate images, edges were detected via convolutional 2D Laplacian kernel from the processed images, and the number of edges, number of effective edges, and sum of intensities of edges were evaluated. The values of weights for red, green, and blue channels were calculated to be -0.0572, 0.7335, and 2.2079, respectively. The number of edges, effective edges, and sum of intensities of edges were all found to be significantly higher in the images processed with the new filter ($P < 10\text{-}16$). To evaluate the clinical usefulness of the digital filter, 2 individual observers graded 100 photographs from subjects with diabetes mellitus before and after application of newly developed digital filter. Grading was compared with FA findings.
Results
Correspondence of diabetic retinopathy grading from 2 independent observers were 0.36 and 0.29 before application of digital filter and 0.61 and 0.65 after application of digital filter(kappa value, respectively). Correspondence of presence of diabetic retinopathy from 2 independent observers were 0.69 and 0.69 before application of digital filter and 0.86 and 0.84 after application of digital filter(kappa value, respectively).
Conclusions
The hemoglobin absorbance reinforced the edges of retinal blood vessels, verifying that the new RGB filter can enhance the visualization of retinal vasculature and increase the accuracy of diagnosis.

• F052

Ocular manifestations associated with takayasu arteritis: a multimodal imaging study

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Purpose
The goal of this study was to describe ophtalmological features of Takayasu disease on fundus exam, in fluorescein angiography and OCT angiography.
Methods
All patients diagnosed with Takayasu disease and followed in la pitié salpétrière hospital from 2004 to 2016 were restrospectively included. They underwent a complete ophtalmological exam including best correct visual acuity, slit-lamp biomicroscopy, fundoscopy and multimodality imaging including fluorescein angiography and SD OCT. Most patients underwent OCT angiography.The images were analyzed to evaluate perifoveal anastomotic capillary arcade disruption, capillary perifoveolar density, mivroaneurysms. The foveal avascular zone (FAZ) was measured for superficial (SCP) and deep (DCP) capillary plexus.
Results
26 eyes were included. Most frequent anomalies were retinal microaneurisms (6 patients). Stage I retinopathy was seen in 5 eyes; stage II in 10, stage III in 2 and stage IV in 3 eyes. 14 eyes underwent OCT Angiography. 11 eyes of 6 patients presented with ruptures of the perifoveal anastomotic capillary arcade in SCP. 5 eyes had microaneurysms. 11 eyes of 6 patients had rarefaction of the perifoveolar vascular density in SCP. The average measure of the SCP FAZ was increased to 0.34 mm2 (0.19 – 0.74) in takayasu patients compared to 0.27 mm2 (0.18-0.33) in the patients with no maculopathy.
Conclusions
Macular abnormalities are uncommon in patients with Takayasu disease as the retinopathy signs are most likely located in the peripheric retina. This study reveals that most of our patients present an enlargement of the FAZ, even in the earliest stages of retinopathy with no macular abnormality on fluorescein angiography. The study finally highlights the relevance of using OCT A to evaluate the macular ischemia as a complement to usual retina global study in fluorescein angiography.

• F053

Associations between individual retinal layer thicknesses and diabetic peripheral neuropathy using retinal layer segmentation analysis

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Purpose
To evaluate clinical correlations between the thicknesses of individual retinal layers in the foveal area of diabetic patients and the presence of diabetic peripheral neuropathy (DPN).
Methods
This retrospective, observational cross-sectional study enrolled a total of 120 eyes from 120 patients. The eyes were divided into three groups: normal controls(n=42 eyes), patients with diabetes mellitus (DM)(n=42 eyes) but no DPN, and DM patients with DPN(n=36 eyes). The primary outcome measures were the thickness of all retinal layers in the central 1mm zone measured by using the segmentation analysis of spectral domain optical coherence tomography (SD-OCT). Correlations between the thicknesses of the individual retinal layers and the presence of DPN were also analyzed. Logistic regression analyses were used to determine which change of layer thickness had the most significant association with the presence of DPN.
Results
The mean thicknesses and the ratios of retinal nerve fiber layers (RNFLs) to total retina thicknesses in the DPN group were 10.77 ± 1.79 μm and 4.10 ± 0.55 percent (%), significantly lower than those in normal controls and the DM with no DPN group ($p=0.014$ and $p=0.001$, respectively). Logistic regression analyses also showed the decrease in thicknesses of the RNFLs and the INL are significant factors for predicting a higher risk for DPN development (odds ratio = 7.407 and 1.757; $p<0.001$ and $p=0.001$, respectively).
Conclusions
A decrease in the RNFL and the INL thickness was significantly associated with presence of DPN. Using SD-OCT segmentation method, these structural changes could be used as a potential biomarker for early detection of DPN.

• F054

Relation between cardiovascular conditions and macular and retinal nerve fiber layer thickness evaluated with Spectral-Domain OCT

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Purpose
To detect changes in the macular and Retinal Nerve fiber Layer (RNFL) thickness in subjects with cardiovascular risk factors or subclinical ischemia
Methods
152 healthy men were evaluated. They underwent cardiovascular examination (including quantification of classic major risk factors, blood analysis and quantification of subclinical atheroma plaques by ultrasound scans) and a complete ophthalmic evaluation including evaluation with spectral-domain optical coherence tomography (SD- OCT) registering macular and RNFL thickness
Results
Subjects without cardiovascular risk factors did not show higher macular or RNFL thicknesses than subjects with at least one risk factor. Subjects with subclinical atheroma plaques in the carotid artery showed significantly lower central macular thickness in the left eye compared to the right eye ($p=0.016$). Subjects with atheroma plaques showed significantly reduced RNFL thickness in the superior quadrant ($p=0.044$) and in the 2 o'clock sector ($p=0.014$) compared to subjects without atheroma plaques. Smokers showed significant thinning in central macular thickness ($p= 0.034$), and also in the nasal RNFL quadrant ($p=0.006$) and the 3 and 5 o'clock RNFL sectors ($p=0.016$ and 0.009), compared to non-smokers
Conclusions
Subjects with subclinical atherosclerosis assessed by ultrasound scans showed reduced RNFL thickness in the superior quadrant. Smokers showed reduced central macular thickness and reduced RNFL thickness in the nasal quadrant. Macular and RNFL analysis with SD-OCT could be a good biomarker of early axonal damage in subjects with cardiovascular conditions

• F055

Photostimulation with subthreshold yellow micropulsed laser for chronic residual subfoveal rhegmatogenous retinal detachment after surgery

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Purpose
The aim of this pilot study, the first of this kind, was to evaluate the safety and efficacy of Subthreshold Yellow Micropulsed Laser (SML) to treat eleven patients with chronic residual subfoveal Retinal Detachment (RD) after surgery to repair Rhegmatogenous Retinal Detachment (RRD).
Methods
Eleven eyes with residual subfoveal RD after surgery, dating from eight to sixteen months before treatment have been evaluated. Evaluation included visual acuity, Amsler test, ophthalmoscopy, Autofluorescence (AF) and Spectral-Domain Optical Coherence Tomography (SD-OCT).
Results
After treatment we recorded improved visual acuity and Amsler test, disappearance of subfoveal detachment by ophthalmoscopy, reduced retinal pigment epithelial distress by AF and restored macular retinal profile without neuroretinal alterations by SD-OCT evaluation in nine eyes.
Conclusions
Photostimulation with SML, selective for the Retinal Pigment Epithelium (RPE), is proved to be painless, effective and safe. The possibility to reabsorb subretinal liquid by foveal and parafoveal RPE photostimulation, without neuroretinal damage, opens new prospects for the therapy of this pathology. If further studies confirm the results of the present pilot study, SML treatment can be considered the first and only non invasive option for chronic residual RD after retinal surgery to repair RRD.

• F056

Evaluation of efficacy and safety of dexamethasone intravitreal implants between vitrectomized and non-vitrectomized eyes in a real-life study

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Purpose
To compare the efficacy and safety of dexamethasone intravitreal implant (Ozurdex) between vitrectomized and non-vitrectomized eyes in real-life conditions and to evaluate the change in intravitreal DEX-implant efficacy before and after pars-plana vitrectomy (PPV) in patients vitrectomized during follow-up
Methods
This was a bicentric, retrospective, observational study. Four hundred and one eyes in 361 patients were enrolled between October 2010 and February 2015. Sixty-seven eyes were vitrectomized at baseline, 301 had no vitrectomy at the last visit. Fifteen eyes were vitrectomized during follow-up and had at least one DEX-implant intravitreal injection before and after PPV. Eighteen eyes vitrectomized during the follow-up were excluded because these eyes did not have at least one intravitreal injection of DEX-Implant after pars-plana vitrectomy. Three hundred eighty-three eyes in 343 patients were studied. We evaluated the efficacy and safety of OzurdexÓ between vitrectomized and non-vitrectomized eyes and before and after PPV in patients vitrectomized during follow-up. Main outcome measures included changes in best-corrected visual acuity, central macular thickness and incidence of adverse effects.
Results
Variations of BCVA and CMT were not significantly different neither between non-vitrectomized eyes and baseline-vitrectomized eyes nor before and after PPV in patients vitrectomized during follow-up. The IOP profile was the same between non-vitrectomized eyes versus baseline-vitrectomized eyes and before versus after PPV in patients vitrectomized during the follow-up.
Conclusions
This large cohort shows that vitrectomy seems not to influence the efficacy and safety profile of DEXimplant regardless of the indication.

• F057

Enzymatic vitreolysis with ocriplasmin for symptomatic vitreomacular traction syndrome

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Purpose
To evaluate the anatomical and functional outcomes of patients treated with ocriplasmin for vitreomacular traction syndrome (VMT) or macular holes (MH) combined with VMT in a tertiary retina center.
Methods
Eleven eyes of ten patients (8 females, 2 males) with VMT (8 with VMT alone and 3 with MH combined with VMT) were included in the study. The patients were treated with a single ocriplasmin injection and examined at day 1, 7 and 28 post-injection. Age, gender, phakic lens status, vitreomacular adhesion diameter, presence of epiretinal membrane, macular hole size, cystoid macular oedema and the status of the ellipsoid zone were recorded. Best-corrected visual acuity (BCVA) and spectral-domain-optical coherence tomography (SD-OCT) were performed at baseline and at each examination during the follow up period. Adverse effects were also recorded.
Results
Six eyes (54,5%) presented VMT resolution, while one out of three patients presented MH closure. All patients experienced VMT release by 7 days. Patients with VMT resolution had an increase in BCVA of +0.5 logMAR. .
Conclusions
Ocriplasmin may be considered as an effective treatment option for VMT and macular holes with VMT.

• F058

Efficacy and safety of primary posterior capsulotomy in combined phaco-vitrectomy in patients with rhegmatogenous retinal detachment

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Purpose
To evaluate the efficacy and safety of posterior capsulotomy by analyzing the visual outcomes in patients with rhegmatogenous retinal detachment (RRD), who underwent combined phaco-vitrectomy.
Methods
A retrospective longitudinal cohort analysis was performed by using data of RRD patients undergoing combined phaco-vitrectomy. Patients were divided into two groups; Group A (69 patients) with capsulotomy, and Group B (39 patients) without capsulotomy. We reviewed the best-corrected visual acuity (BCVA), incidence of posterior capsule opacification (PCO), clinical features of RRD, and complications.
Results
The BCVA measured by the LogMAR at initial diagnosis was 0.67 in Group A versus 0.78 in Group B ($p = 0.246$). The BCVA of Group A was only significantly higher at 12 months (0.21 versus 0.28 [$p = 0.013$]) after surgery, respectively. In subgroup with macula-on RRD, Group A exhibited better visual outcomes compared to Group B at 6 (0.17 versus 0.40 [$p = 0.037$]) and at 12 months (0.17 versus 0.40 [$p = 0.030$]). The incidence of PCO in Group B was higher than A (28.2% versus 5.8% ($p = 0.000$)). There were no complications associated with capsulotomy.
Conclusions
A primary posterior capsulotomy during combined phaco-vitrectomy is the safe and effective procedure in patients with RRD for preventing postoperative PCO.

• F059

Eccentric macular hole after pars plana vitrectomy for epiretinal membrane without internal limiting membrane peeling

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Purpose
Postoperative eccentric macular hole formation is an uncommon complication after pars plana vitrectomy (PPV) without internal limiting membrane (ILM) peeling for epiretinal membrane (ERM). Herein, we present a case of eccentric macular hole formation after PPV for ERM without ILM peeling.
Methods
A 68-year-old male patient presented with ERM and visual acuity of 6/24 in his left eye. He underwent 23-gauge PPV without ILM peeling for ERM treatment.
Results
One week postoperatively the retina was attached and the epiretinal membrane was successfully removed, while visual acuity was 6/9. One month after PPV, there was a single eccentric retinal hole below the macula, which was detected at the fundoscopy and was confirmed by optical coherence tomography (OCT). The visual acuity was 6/9 and the patient referred no symptoms. No further intervention was attempted and at the 6-month follow-up, the visual acuity and the size of the eccentric macular hole remained stable.
Conclusions
Eccentric macular holes can be developed after PPV even without ILM peeling and are usually managed conservatively by observation.

• F060

The effect of internal limiting membrane peeling in surgical treatment of combined hamartoma and epiretinal membrane

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Purpose
This study was designed to evaluate the effect of internal limiting membrane (ILM) peeling in the surgical management of combined hamartoma of the retina and retinal pigment epithelium and epiretinal membrane (ERM).
Methods
The records of 11 patients (11 eyes) with ERM of combined hamartoma of the retina and retinal pigment epithelium, 22 patients (22 eyes) with ERM who had undergone pars plana vitrectomy with removal of the ERM were retrospectively reviewed. The patients were divided into four groups: eyes without (6 eyes) or with (5 eyes) ILM peeling in ERM of combined hamartoma of the retina and retinal pigment epithelium and eyes without (12 eyes) or with (10 eyes) ILM peeling in ERM. Anatomical outcomes, functional outcomes, complications and recurrences were compared between the eyes without and with ILM peeling. Anatomical outcome included the central retinal thickness and subfoveal choroidal thickness from optical coherence tomography (OCT). Functional outcomes included the change in best-corrected visual acuity (BCVA).
Results
Central retinal thickness and subfoveal choroidal thickness decreased and postoperative BCVA improved in without and with ILM peeling in ERM of combined hamartoma and ERM. But there were no statistically significant differences in central retinal thickness, subfoveal choroidal thickness, BCVA between without and with ILM peeling in ERM of combined hamartoma and ERM. There was no complicated and recurred case in four groups.
Conclusions
The additional ILM peeling in patients with ERM of combined hamartoma of the retina and retinal pigment epithelium, ERM doesn't affect the postoperative results in central retinal thickness, subfoveal choroidal thickness and visual acuity.

• F061

Retinal diseases of patients without discomfort associated with retinal abnormalities

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Purpose
To identify the retinal diseases in patients who did not complain discomfort of retinal abnormalities.
Methods
A retrospective chart review of 1516 eyes, 765 patients who visited for cataract operation, glaucoma evaluation, refractive surgery was performed. We evaluated fundus abnormalities by fundus examination using slit lamp and systemic risk factors.
Results
The mean age of the 765 patients was 63.2 ± 14.6 years (18-93 years), and 34.2% were men. Four hundred ninety seven eyes (32.8%) were diagnosed as retinal diseases. Peripheral retinal degeneration that does not need treatment in 119 eyes (include atypical retinitis pigmentosa in 2 eyes), peripheral retinal degeneration that does need barrier laser in 65 eyes, epiretinal membrane in 97 eyes, diabetic retinopathy in 57 eyes, vitreous hemorrhage in 4 eyes, retinal hemorrhage in 23 eyes, retinal vascular occlusion diseases in 16 eyes, degeneration at posterior pole (pp) in 36 eyes (include central serous chorioretinopathy in 1 eye), exudation at pp in 103 eyes, age related macular degeneration (AMD) in 47 eyes were identified. Treatment performed in 104 patients (13.6%), 146 eyes (9.6%) – medication in 53 eyes, laser photocoagulation in 71 eyes, intravitreal injection in 7 eyes, vitrectomy in 15 eyes. Peripheral retinal degeneration showed significant positive correlations with higher degree myopia ($p < 0.001$). AMD, vascular occlusion disease, degeneration at pp, exudation at pp showed significant positive correlations with increased age ($p < 0.001$, $= 0.008$, < 0.001, < 0.001).
Conclusions
The retinal examination, including the peripheral retina, should be carried out in patients without discomfort of retinal abnormalities.

• F062

Evolution of foveal detachment in dome-shaped macula after treatment by mineralocorticoids: report of three cases

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Purpose
To analyze three cases of visual acuity improvement after treatment with spironolactone in patients with dome-shaped macular and related serous retinal detachment.
Methods
We evaluated four eyes of three patients of 38, 49 and 64 years old with serous retinal detachment associated with dome-shaped macula. The patients were treated daily with oral spironolactone 50mg. Ophthalmic examination included best-corrected visual acuity (BCVA) and central retinal thickness (CRT), determines by optical coherence tomography (OCT). They were evaluated on their first visit and on monthly follow-up visits.
Results
The first patient's pretreatment BCVA was 20/80 in both eyes; after treatment BCVA improved to 20/50 in the right eye and 20/40 in left eye. Second patient's pretreatment right eye's BCVA was 20/100, and one month after treatment improved to 20/63. The patient stopped the treatment due to a secondary effect (asthenia) and two month later visual acuity declined to 20/80. The last patient's pretreatment BCVA in his right eye was 20/200 and four months after treatment was 20/63.
Conclusions
We evaluated a mineralocorticoid antagonist treatment for serous retinal detachment associated with dome-shaped macula in myopic patients. One to six months after treatment with the mineralocorticoid antagonist spironolactone, the subretinal fluid and CRT were significantly reduced and there was an improvement in BCVA.

• F063

Effects of dexamethasone implant on macular morphology and visual function in patients with different diseases

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Purpose
To evaluate the effects of dexamethasone implant in patients with different retina diseases.
Methods
In the study 194 eyes of patients treated with Dexamethasone implant were included restrospectively in the study. Best-corrected visual acuity (BCVA) measurement, complete ophthalmic evaluation with Intraocular pressure (IOP), and spectral-domain optical coherence tomography (OCT) were performed at baseline and 30 days after treatment.
Results
We have analyzed the results of the administration of dexamethasone implant in 194 eyes, during the years 2015 and 2016. The main indications for the treatment with dexamethasone implant were central retinal oclusion (54,20%), diabetic macular edema (35,35%), Irvine Gass syndrome (4,71%), uveitis (3,03%), macular degeneration (2,02%), vitreous- macular traction syndromes (0,33%) and neovascularization of the anterior segment (0,33%). The best visual acuity and the IOP before the administration of dexamethasone implant were respectively 0.21(+/- 0.15) and 16 mmHg. After the treatment the best visual acuity improves to 0,27 (+/- 0,2) and the IOP was 18,9 mmHg (+/-6,28). The macular thickness has been reduced to 519.72 micron (+/- 157.86) to 429.96 microns (+/-153.98) after the dexamethasone implant.
Conclusions
Intravitreal dexamethasone implant showed an early and fast effect in reducing CRT and moderatly improving BCVA. There are IOP variations, but it rarely exceeds normal limits.

• F064

Neural degeneration mechanisms in diabetic retinopathy: The role of apoptosis and autophagy

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Purpose
That neuronal injury plays a major role in diabetic retinopathy (DR) is gaining increasing recognition. In particular, we have recently shown, using an ex vivo model of early DR, that neuroprotection may also reduce the expression of proangiogenic factors. Given the importance of neuronal health in DR, we chose to better analyze the mechanisms of cell death involved in this disease. Our hypothesis was that the balance between neuronal death and survival may depend on a similar equilibrium between apoptosis and autophagy: in this context, a neuroprotective treatment would act by influencing this equilibrium.
Methods
Ex vivo mouse retinal explants were treated with high glucose (HG, 75 mM) for 10 days and the somatostatin analog octreotide (OCT, 1μM) was used as a neuroprotectant. Chloroquine (CQ, 10μM) was used as an autophagy inhibitor. Apoptotic and autophagic markers were evaluated using Western blot and immunohistochemistry.
Results
Consistent with our previous observations, HG-treated retinal explants displayed a significant increase of apoptosis. Concurrently, HG treatment caused a significant decrease of the autophagic flux, which was likely to be due to increased activity of the autophagy regulator mTOR. Treatment with OCT rescued HG-treated retinal explants from apoptosis and determined an increase of autophagic activity with concomitant mTOR inhibition. Blocking the autophagic flux with CQ completely abolished the anti-apoptotic effect of OCT.
Conclusions
Apoptosis and autophagy seem to play opposite roles and a delicate balance between apoptotic and autophagic fluxes is responsible for the death or survival of retinal neurons in stressing conditions like HG. Consistently, the data obtained with CQ suggest that the anti-apoptotic effect of OCT in HG-treated retinas is mediated by an increase of the autophagic flux.

• F065

Functionalized magnetic nanoparticles as a novel strategy for the treatment of diabetic retinopathy

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Purpose
Neuroprotection-based strategies may be exploited to treat diabetic retinopathy (DR). Our aim is to establish a method for magnetic nanoparticle (MNP)-mediated delivery of neuroprotectants to the retina, expecting a prolonged therapeutic action. In the first phase of this project, we assessed the bioavailability and bioactivity of the neuroprotectant octreotide (OCT), a somatostatin analog, delivered as OCT-MNP.
Methods
The effects of OCT-MNP and those of free OCT (fOCT) were evaluated in in vitro assays using human retinal endothelial cells (HRECs), in H2O2-treated ex vivo retinal explants, and in vivo in untreated or in kainate-injected mouse eyes. In the in vitro assays, vascular endothelial growth factor (VEGF)-induced HREC proliferation, migration and tube formation were assessed. In the ex vivo and in vivo models, qPCR, histochemical and immunohistochemical techniques were used.
Results
In HRECs, 1μM OCT-MNP displayed the same efficacy of 1μM fOCT in inhibiting VEGF-induced changes. In H2O2-treated explants, both 1μM OCT-MNP and 1μM fOCT inhibited apoptosis. In particular, the efficacy of OCT-MNP was detected at concentrations as low as 0.001μM. After intraocular injection in mouse eyes, OCT-MNP were localized to the retinal pigment epithelium and they did not induce any apoptotic sign in the retina. 1μM OCT-MNP or fOCT co-delivered via intraocular injection with 100μM kainate similarly protected the retina from apoptosis.
Conclusions
OCT-MNP maintain the functional properties of fOCT, in particular its neuroprotective capabilities. Intraocularly injected OCT-MNP are not toxic. They penetrate the retina, where they may release OCT in a sustained manner. Although needing confirmatory observations, these preliminary data are encouraging for a possible use of MNP-mediated drug delivery to treat DR.

• F066

The SRPK1 inhibitor SPHINX31 prevents increased retinal permeability in a rodent model of diabetes

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Purpose
In diabetic retinopathy (DR) microvascular damage results from ischaemia driven production of pro-angiogenic vascular endothelial growth factor (VEGF) inducing angiogenesis and increased permeability in the retina. Small molecule inhibitors of serine-rich protein kinase-1 (SRPK1), with good penetration properties to the retina, have been shown to inhibit choroidal neovascularisation in mice as eye drops by decreasing pro-angiogenic and increasing anti-angiogenic VEGF isoforms. SRPK1 inhibitors such as SPHINX31 may therefore switch splicing in DR and prevent increased vascular permeability.
Methods
FFA was performed in Norway Brown rats on day 0 and 7, using the Micron IV retinal microscope (Phoenix Research). Animals received twice daily topical eye drops with eye formulation only control buffer (n=5) or SPHINX31 (200μg/ml, n=6). On day 1 animals received a single dose of streptozotocin (50mg/kg, i.p.) to induce type I diabetes and maintained for one week without insulin. The ratio of interstitial to vascular fluorescence was calculated and plotted against time to determine an estimate of permeability.
Results
Retinal permeability (12.67 ± 1.09 x10-4 cms-1) was shown to significantly increase ($p < 0.01$) in diabetics compared to before diabetes (8.85 ± 1.29 x10-4 cms-1) in the eye formulation control group. Following a weekly regimen of twice daily topical eye drop treatment with SPHINX31 retinal permeability was no greater in the diabetics than (7.92 ± 1.65 x10-4 cms-1) than before induction of diabetes, (8.15 ± 2.33 x10-4 cms-1) and in the control group.
Conclusions
SPHINX31 protected the retinal endothelial permeability barrier from diabetes-associated loss of integrity. SPHINX31 may therefore be a potential alternative and more specific topical therapeutic for DR.

• F067

Resveratrol diminishes oxidative stress in lenses of rats with streptozotocin-induced type 1 diabetes

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Purpose
Nowadays, the plant-derived antioxidants, that may be useful in the prevention or treatment of oxidative stress-associated diabetes and cataract are sought. A common compound of plant origin with a well-proven antioxidant and antidiabetic properties is resveratrol.
The aim of this study was to investigate the effect of resveratrol on oxidative stress markers in lenses of rats with streptozotocin-induced type 1 diabetes.
Methods
The study was conducted on rats divided into experimental groups: C – non-diabetic rats; D – diabetic rats; D+R10 – diabetic rats + resveratrol (10 mg/kg); D+R20 – diabetic rats + resveratrol (20 mg/kg). Resveratrol was administered orally for 4 weeks. The effects of resveratrol on oxidative stress markers in the lenses was evaluated based on analysis of activity of the superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), level of the glutathione (GSH), malonyldialdehyde (MDA), advanced oxidation protein products (AOPP), vitamin C (VC) and calcium (Ca2+).
Results
Induction of experimental type 1 diabetes caused changes in oxidative stress markers in the lenses in rats. An increase of SOD, CAT and GPx activity was noted. There were also increases of the MDA, AOPP and Ca2+ levels, while decreases of GSH and VC were observed.
Administration of resveratrol at both doses resulted in the decrease of SOD, CAT and GPx activities as well as of MDA and AOPP levels. There were no significant changes noted in GSH, VC and Ca2+ levels after resveratrol administration.
Conclusions
Resveratrol shows antioxidative effect in the lenses of the rats with streptozotocin-induced type 1 diabetes.

• F069

Microelectrode penetration of the wall of porcine retinal arterioles in vitro results in recordings from several cell types

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Purpose
A novel population of perivascular cells (PVC) is located immediately external to the vascular smooth muscle cells of retinal arterioles, express immunoreactivity to the pericyte marker NG2 and give rise to processes that extend into the retina. This suggests that PVCs could play a role in neurovascular coupling. However, the anatomical basis for the connection of PVC processes to the surrounding retina has not been characterized in detail. The aim of the present study was to establish a method for electrophysiological characterization of cells in the perivascular retina for the study of neurovascular coupling.
Methods
First order porcine retinal arterioles with preserved perivascular retinal tissue were mounted in a wire myograph. A glass microelectrode (WPI, USA) with a tip resistance of 30 - 100 MOhm filled with 3M KCl solution was inserted into cells in the perivascular retina using an electronic micromanipulator. The microelectrode was connected to an amplifier (Electrometer 773 Duo, WPI, USA) and the intracellular membrane potential was recorded at resting conditions and after addition of 40mM KCl or solvent.
Results
Recordings from thirty perivascular retinal cells from eight arterioles showed membrane potentials ranging from -100 to -40 mV (mean -68± 3 mV). The most frequent membrane potential was -80 mV (30% of the cells). 40mM KCl produced a significant depolarization of the cells of 13 ± 3 mV (p=0.03, n=10), whereas solvent induced no significant change in the membrane potential (p=0.6, n=10).
Conclusions
Cells in the retinal arteriolar wall can be penetrated with microelectrodes for measurement of the membrane potential. The recordings suggest the existence of multiple cell types with distinct membrane potentials. The anatomical basis for these different cell types should be characterized further by intracellular dye injection.

• F068

Retinal vessel geometry and oxygen saturation in patients suffering from diabetes mellitus and/ or cardiovascular disease

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Purpose
To explore the association of retinal vessel parameters such as calibres, reactivity and complexity with vessel oxygen saturation in patients with Diabetes Mellitus and/ or cardiovascular disease.
Methods
All 123 patients underwent a full eye examination including IOP and dilated fundus photography. Retinal oxygen saturation of arteries and veins were measured from dual wavelength retinal photographs (IMEDOS Oxygen module). A-V saturation was calculated as an estimate of oxygen consumption. Retinal vessel calibre's, tortuosity and fractal dimension were measured using a semi-automated software to determine CRAE and CRVE (Visualis, IMEDOS and Iflexis, Vito).
Results
Patients mean ranged in age from 32 to 85 years (77 out of the 123 were diabetic). Principal component analysis was performed to establish if the cohort should be split into sub-groups for further analyses but showed a clear overlap of all patients with no distinct clustering. Subsequently a stepwise forward multiple regression analysis was conducted to explore the relationship between retinal vessel geometry and saturation parameters. Following adjustment for axial length (to account for magnification errors), diastolic blood pressure, retinal vessel fractal dimension and intraocular pressure were significantly associated with A-V saturation (all $p<0.05$) meaning a retinal vascular network with a lower fractal dimension (i.e. less vessel density and branching) showed a lower A-V saturation.
Conclusions
The current study shows that in patients suffering from Diabetes Mellitus and/ or cardiovascular disease, the amount of oxygen used is depending on the complexity of its vascular bed as well as on local and global pressure parameters. These findings could be useful to explore in patients over time or those diabetic retinopathy manifest in different retinal locations.

• F070

Involvement of peroxisome proliferator activator receptors in the photoprotective activity of the di-apo-carotenoid norbixin on RPE cells

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Purpose
There are increasing evidences for the involvement of peroxisome proliferator activator receptors (PPARs) in the development of ocular diseases, in particular AMD. PPAR receptors comprise three sub-types of nuclear receptors: PPARα, PPARβ/δ and PPARγ. The mechanism by which norbixin (NBX), a di-apo-carotenoid exerts in vitro and in vivo protective effects on RPE was studied.
Methods
The affinity of NBX for the 3 PPAR subtypes was determined by binding studies. The photo-protective properties of NBX were evaluated by an in vitro assay using primary cultures of porcine RPE cells challenged with A2E then blue light illumination. With the same assay, NBX protective activity was then characterized by a pharmacological approach employing different PPAR subtypes' selective agonists and antagonists. The expression level of the PPARs was assessed by western blot.
Results
NBX bound PPARα and PPARγ with Ki values of 16.5 and 1.15 µM, respectively. In a non-cellular PPARβ/δ receptor functional assay, NBX displayed a Kb value of 3.2 µM. Further, PPARγ (troglitazone) and PPARβ/δ (GW0742) agonists strongly and significantly protected RPE cells. NBX protective activity was partially reversed by PPARγ (T0070907) and PPARβ/δ (GSK3787) antagonists. We showed for the first time that PPARα protein expression was rapidly and strongly reduced upon A2E treatment. Most interestingly, its expression was maintained or restored when RPE cells were treated with NBX before or after A2E exposure, respectively. Interestingly, some PPARγ and β/δ agonists displayed similar patterns, and other compounds were unable to sustain PPARα protein expression.
Conclusions
Taken together, this study demonstrates that NBX photoprotective activity relies potentially on both PPARβ/δ and PPARγ activation and on a sustained expression level of PPARα.
Conflict of interest
Any research or educational support conditional or unconditional provided to you or your department in the past or present?:
Research was funded by Biophytis

• F071

Effects of plasma kallikrein inhibitors in an in vitro RPE oxidative stress model

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Purpose

Plasma Kallikrein (PK) Inhibitors (PKI) are a promising treatment for retinal diseases such as diabetic macular edema, where PK activity is implicated. Our aim was to set up an in vitro model of chronic oxidative stress in the retinal pigment epithelium cell line ARPE19 and use it to test the effect of 8 PKI on cell viability and proliferation.

Methods

ARPE19 cells were grown to a sub-confluence stage, synchronized, and exposed to different dilutions of glucose oxidase (GOx) from Aspergillus niger, culture medium (- control) and benzalkonium chloride (+ control) for 24h. Cell viability and apoptosis were analyzed (MTT assay and caspase-3/7 detection, respectively). The oxidative stressed cells were exposed to 8 different PKI developed by KalVista (Salisbury, UK) at 100nM and 1µM. Also, ARPE19 cells were exposed to PKI previously and simultaneously to GOx and cell viability and proliferation were assessed (alamarBlue® assays).

Results

Exposure of ARPE19 to GOx induced dose-dependent decreased cell viability and increased cell apoptosis. A sub-lethal GOx dose reducing viability by 30% and increasing apoptosis by 59% was chosen for PKI exposure experiments. Exposure of GOx stressed cells to PKI for 24h did not further reduce cell viability after 5 days. No effect on cell proliferation was observed when GOx stressed cells were either pre-treated or simultaneously exposed to PKI.

Conclusions

GOx oxidative sub-lethal stress model in ARPE19 cells may be used for screening new drugs with therapeutic potential for retinal diseases. The PKI did not reduce GOx-induced cytotoxic effects in RPE cells suggesting plasma kallikrein has no role in this stress mechanism. Support: FP7-PEOPLE-2013-IAPP (612218/3D-NET) and Regional Junta de Castilla y León Scholarship/European Social Fund Program (Va040-13).

• F072

Regenerative therapies with combined axoprotectants in AGE-exposed retinas

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Purpose

To examine the best effective combination of axoprotectants in AGE-exposed rat retinas in culture.

Methods

Seven SD rats were used in this study. Retinal explants were three-dimensionally cultured in collagen gel and incubated in serum free media, AGEs, AGEs+100 mM citicoline, AGEs+100 mM TUDCA, AGEs+10 ng/ml NT-4, AGEs+citicoline+TUDCA, and AGEs+citicoline+TUDCA+NT-4. The numbers of neurites were counted after 7 days of culture, followed by TUNEL staining and immunostaining of phosphorylated JNK and active-form of caspase-9.

Results

All of the axoprotectants decreased TUNEL-positive cells, p-JNK and caspase-9 immunopositive cells, and increased the numbers of neurites. However, the number of neurites was significantly higher in the retinas incubated with combined three agents.

Conclusions

Combination solutions containing citicoline, TUDCA, and NT-4 should be considered regenerative therapy for AGE-related retinal degeneration.

• F073

Melatonin and epigallocatechin gallate reduce the loss of visual function in an animal model of retinal degeneration, P23H rat

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Purpose

Retinitis Pigmentosa (RP) is a heterogeneous group of retinal degenerative disorders which represent a major cause of blindness in adult people with no effective therapy found.

Most RP cases are due to rhodopsin mutations, which cause retinal disorganization due to rod degeneration and oxidative stress. Melatonin and epigallocatechin gallate (EGCG) have been reported to exhibit anti-apoptosis, antioxidant and neuroprotective effects. The aim of this study was to evaluate the synergistic effects of these two natural antioxidants in the P23H rat.

Methods

20 P23H rats crossed with Long Evans (LE) rats, were used and compared to 20 SD (P23H background) crossed with LE rats. Vehicle, or 10 mg/kg/day of Melatonin and/or 10mg/kg/day of EGCG were orally administered for 6 months. Visual acuity and contrast sensitivity was evaluated by a monthly optomotor test.

Results

P23HxLE rats showed lower values than SDxLE rats in all optomotor parameters studied. SDxLE rats treated with melatonin or EGCG increased, after 60 days of treatment, visual function parameters even higher than young animals. P23HxLE rats treated with melatonin or EGCG showed better visual acuity and contrast sensitivity than those treated with vehicle in all measurements done after 30 days of treatment, slowing the disease progression. In all animal groups, treatment with melatonin and EGCG simultaneously obtained better visual acuity and contrast sensitivity values than treatment with any of those compounds alone.

Conclusions

In conclusion, oral treatment of melatonin or EGCG improved vision in wild type animals and delayed vision loss in P23H rats. Furthermore, combination of both compounds had a better effect than any of those treatments alone, suggesting different mechanisms of action.

• F074

Effect of AVS Retina in a rodent model of retinal ischemia-reperfusion

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Purpose
Anti-VEGF agents currently available for the treatment of Diabetic Retinopathy and Wet Age-Related Macular Degeneration do not possess a direct effect on inflammation. Our previous findings show that a nutritional supplement formula codenamed AVS is able to inhibit nitric oxide and prostaglandin E2 accumulation by modulating important pro-inflammatory genes in vitro. Here, we set out to test whether AVS may exert a protective effect in a model of retinal ischemia/reperfusion (IR) damage in rat.
Methods
Brown Norway rats were subjected to retinal IR injury by rising intraocular pressure to 130 mmHg for 60 minutes. Animals were treated once daily by oral gavage with AVS or vehicle (VHC) starting five days before insult and until sacrifice 6 hours (T6h) or 7 days (T7) after IR. Electroretinograms (ERG) were recorded in unconscious rats before IR (baseline), and then at T3 and T7. Total RNA was extracted from retinas at T6h to assess the expression of tumor necrosis factor alpha (TNFa) mRNA by Real-time RT-PCR.
Results
Retinal ischemia in VHC and AVS groups produced a significant reduction of a- and b-wave amplitudes at T3 when compared with baseline. Notably, a- and b-wave amplitudes reduction observed at T7 in the VHC group was significantly inhibited ($p \leq 0.05$) by treatment with AVS. Moreover, the a- and b-wave amplitudes in the AVS group were found not to differ from baseline ($p > 0.05$) while being markedly suppressed in the VHC-treated rats ($p \leq 0.05$). The expression of TNFa was strongly upregulated in the VHC group as assessed in retinas sampled at T6h. Most importantly, treatment with AVS significantly reduced TNFa expression compared to VHC ($p \leq 0.05$).
Conclusions
AVS was found to reduce retinal damage caused by IR favoring its functional recovery possibly by a mechanism involving inhibition of early pro-inflammatory mediators such as TNFa.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Manuela SANTONOCITO, Research Scientist, employed at S.I.F.I. S.p.A.
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• F076

FluoroGold-labeled organotypic retinal explant culture (FLOREC) for neurodegeneration and neurotoxicity screening studies

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Purpose
To create a fast and reproducible system for retinal drugs toxicity screening.
Methods
In this study, we used retinal explants culture from 4 weeks old Wistar rats (n=16). First, to determine the effect of FluoroGold (FG) on explants quality, we used 8 animals. FG was injected into midbrain of rats (n=4) 5 days before euthanasia. Each retina after isolation was divided into 2 parts. In this way, we prepared 16 retinal explants with FG labeling and 16 explants without FG. Explants were cultured in supplemented Neurobasal A medium in Millicell culture inserts. After 7 days of culture, the explants were fixed, stained with ß3-tubulin and processed for stereology. The culture medium was used to evaluate LDH release. The other group of 8 rats was processed in a similar way, but the culture medium was additionally supplemented with CNTF or toxic concentration of Gentamycin.
Results
We did not observe differences between FG and no-FG explants for ß3-tubulin-positive cell count and LDH release after 7 days of culture. The number of ß3-tubulin-positive cells was similar to FG-labelled cells (57±23; 58±17 cells respectively, $p > 0.5$). Gentamycin treatment resulted in retinal cell damage expressed in rapid LDH release to culture medium. After 7 days of culture, the levels of LDH in medium increased up to 157±57% and 144±27% when compared to the corresponding LDH levels before Gentamycin exposure in no-FG ($p < 0.05$) and FG ($p < 0.05$) explants respectively. CNTF supplementation minimized the cell damage and the release of LDH was 106±36% and 104±23% when compared to the corresponding LDH levels before Gentamycin exposure in no-FG ($p > 0.5$) and FG ($p > 0.05$) explants respectively.
Conclusions
The FLOREC protocol could be considered as a fast, reproducible and sensitive method to detect neurotoxicity and neuroprotection in the screening studies of the retinal drugs.

• F075

THR-687, a potent small molecule integrin antagonist, holds promise as a therapeutic approach for back-of-the-eye vascular pathologies

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Purpose
Pathologic neovascularization and vessel leakage are key drivers for vision loss in several back-of-the-eye diseases, such as diabetic retinopathy and age-related macular degeneration. In the eye, integrin receptors play an important role in (pathological) angiogenesis and vascular leakage. Blocking integrin receptors has the potential to inhibit these processes, independent of anti-VEGF responsiveness. In this study, we evaluated the integrin-blocking and anti-angiogenic properties of THR-687, a novel small molecule integrin antagonist.
Methods
Competition ELISA assays were used to assess the ability of THR-687 to compete with the binding of integrin receptors to their natural ligands. The inhibitory effect of THR-687 on the migration of human umbilical vein endothelial cells (HUVECs) was evaluated in the ORIS cell migration assay. The effect of THR-687 on blood vessel outgrowth was evaluated in an ex vivo mouse choroidal explant model. Cytotoxicity of THR-687 on human retinal microvascular endothelial cells (HRMVECs) was evaluated using the CellTox Green assay. The safety profile of THR-687 was further evaluated using hERG and genotoxicity assays.
Results
THR-687 was found to inhibit multiple integrin receptors belonging to the RGD class with IC50 values in the low nanomolar range, including, but not limited to, αvβ3, αvβ5 and α5β1. THR-687 potently inhibited the migration of HUVECs in the ORIS system (IC50 of 82 ± 11nM). Ex vivo choroidal vessel sprouting was dose-dependently inhibited by THR-687 (IC50 of 1.50 ± 0.27µM). No relevant cytotoxicity signal was observed on HRMVECs at concentrations ranging from 0.25nM to 20µM, and in vitro pharmacological profiling studies indicated a good safety profile.
Conclusions
THR-687 is a potent drug candidate for the treatment of diabetic eye disease.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Employee at ThromboGenics

• F077

Effect of intravitreal bevacizumab and aflibercept on retrobulbar blood flow in injected and uninjected sound eyes of patients with neovascular age-related macular degeneration

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Purpose
To evaluate early changes in retrobulbar blood flow following intravitreal injection of anti-vascular endothelial growth factor (VEGF) agents.
Methods
Ten patients affected by neovascular age-related macular degeneration in 1 eye were enrolled. Five eyes received intravitreal bevacizumab (1.25mg/0.05mL) and 5 eyes aflibercept (2mg/0.05mL). Retrobulbar blood flow was examined by color doppler ultrasonography (Aplio 500, Toshiba Medical System, Tokyo, Japan). Peak systolic velocity (PSV) and resistivity index (RI) was measured from ophthalmic artery (OA), central retinal artery (CRA) and posterior ciliary artery (PCA) in both injected and uninjected sound eyes, before and 21 days after treatment.
Results
Before and after intravitreal bevacizumab mean retrobulbar blood flow parameters significantly change in PCA: PSV 15.24±3.96 cm/sec vs 12.90±2.63 cm/sec ($p=0.0012$), RI 0.74±0.02 vs 0.77±0.07 ($p=0.009$) and in CRA: PSV 14.16±1.8 cm/sec vs 12.29±1.54 cm/sec ($p=0.005$), RI 0.77±0.03 vs 0.79±0.03 ($p=0.029$). In the sound fellow eyes, significant changes resulted in PCA: PSV 17.26±3.45 cm/sec vs 13.63±3.3 cm/sec ($p=0.003$), RI 0.74±0.05 vs 0.79±0.03 ($p=0.026$). Before and after intravitreal aflibercept measured data significantly change in PCA: PSV 12.8±3.09 cm/sec vs 7.20±0.62 cm/sec ($p=0.023$), RI 0.68±0.03 vs 0.77±0.03 ($p=0.007$) and in CRA: PSV 14.28±1.2 cm/sec vs 11.04±0.77 cm/sec ($p=0.037$), RI 0.73±0.03 vs 0.78±0.05 ($p=0.022$). In the sound fellow eyes, significant changes resulted in PCA: PSV 12.44±2.89 cm/sec vs 9.18±1.42 cm/sec ($p=0.044$), RI 0.69±0.05 vs 0.75±0.02 ($p=0.028$).
Conclusions
Intravitreal injections of bevacizumab and aflibercept significantly reduce ocular hemodynamic parameters both in treated and in untreated eyes. These evidences suggest a possible systemic effect.

• F078

Changes in retinal arteriolar oxygen saturation predict disease activity in patients treated with aflibercept for neovascular age-related macular degeneration

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Purpose
In order to individualize treatment, it is important to identify non-invasive markers for disease activity in patients with neovascular age-related macular degeneration (nAMD). In this prospective study we aimed to investigate changes in retinal oxygen saturation in patients with nAMD before and after initial aflibercept therapy.
Methods
Sixty-six eyes diagnosed with nAMD were included. All patients received three monthly injections with 2.0 mg aflibercept and were then divided into responders and non-responders according to post-treatment disease activity. Non-responders by definition had loss of ≥5 ETDRS letters or residual retinal edema (based on spectral domain-OCT) or macular hemorrhage. Retinal oximetry (Oxymap T1, Oxymap, Reykjavik, Iceland) was performed at baseline and follow-up, and images were graded by a trained grader.
Results
At baseline, mean age was 80.0 years and 62.1% were women. Thirty-six of 66 patients (54.5%) were non-responders, and these were younger (77.8 vs. 82.8 years, p=0.01) and trended towards a higher increase in retinal arteriolar oxygen saturation from baseline to follow-up (+1.0% vs. +0.1 %, p=0.06). In a multiple logistic regression model, adjusted for sex, age, diabetes and smoking, each 1%-point increment in retinal arteriolar oxygen saturation from baseline to follow-up was independently associated with a lower chance of full treatment response (odds ratio 0.78, 95% confidence interval 0.62-0.98, p=0.036). Retinal venular oxygen saturation did not associate with pre- or post-treatment disease activity.
Conclusions
Retinal oxygen saturation may be a promising marker for disease activity in nAMD. Increasing retinal arteriolar oxygen saturation in response to initial intravitreal aflibercept therapy associates with a 22% lower chance of full treatment response after initial aflibercept therapy.

• F080

Bilateral tacrolimus-associated optic neuropathy after kidney transplant

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Purpose
Tacrolimus is an immunosuppressant drug which is often used after allogenic transplant to prevent organ rejection. It blocks T-cell development and inhibits cytokine synthesis. We report the case of a patient who developed bilateral optic neuropathy as a suspected complication of tacrolimus therapy.
Methods
A 75 year-old man who underwent orthotopic kidney transplant in 2013 was treated with tacrolimus since that moment without toxic blood levels at any moment. He had a history of moderate hypertension but neither other atherosclerotic risk factors nor ophthalmological disease associated. He came to the Emergency department for the first time in 2015, when he noticed sudden blurred vision in his left. His best corrected visual acuity (BCVA) in his left eye was 20/30. Dilated fundus examination revealed hyperemia, haemorrhages and swelling of the disc with distended veins. Visual field analyser showed a superior altitudinal defect in the left eye. Complete blood count, erythrocyte sedimentation and C-reactive protein were normal. He underwent oral treatment with prednisone 60 mg in descendent pattern. In the follow-up the visual field worsened, with abolished visual field, BCVA was hand movement at one meter distance and a relative afferent pupillary defect in his right eye was demonstrated. Optic disc showed evidence of atrophy. The right eye examination was unremarkable.
Results
Two years later in 2017 the patient came back to the Emergency department complaining of severe painless visual loss in his left eye. Fundoscopy revealed an optic disc edema with splinter haemorrhages which was confirmed with the OCT where we could see a diffuse edema of the fibre layer.
Conclusions
We should be aware of ophthalmological symptoms in patients who have been receiving therapy with tacrolimus, even in the absence of toxic blood levels of that drug.

• F079

Intraocular expression of microfibrillar-associated protein 4 (MFAP4) in patients with neovascular age-related macular degeneration (nAMD)

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Purpose
Pharmacological inhibition of the constitutively expressed extracellular matrix integrin ligand MFAP4 is previously shown with efficacy in mouse model of choroidal neovascularization. To evaluate the intraocular expression of MFAP4 in the anterior chamber (CA) and vitreous body (VB) in patients with nAMD (cases) as compared to controls.
Methods
Aqueous humour from 29 patients and vitreous humour of 54 patients were collected during elective cataract surgery and pars plana vitrectomy, respectively. Samples from the CA consisted of three cases and 26 controls and from the VB of 42 cases and 12 controls. The 42 samples from the VB were further divided into four subgroups depending on the subtype of nAMD (CNV with retinal hemorrhage, CNV without retinal hemorrhage, fibrosis, PE-detachment)
Samples were analyzed by the AlphaLISA technique. Wilcoxon rank-sum test and Kruskall-Wallis test was used to test for differences between two and multiple groups, respectively.
Results
Median MFAP4 was significantly lower in the anterior chamber as compared to the VB (7.9 Units/ml vs. 17.9 Units/ml, p<0.0001). There was no difference in the median MFAP4 between cases and controls (CA: 8.1 Units/ml vs. 7.9 Units/ml, p=0.33) (VB: 17.9 Units/ml vs. 17.8, p=0.79). Neither were there any differences between nAMD-subgroups in the VB (18.7 Units/ml vs. 24.4 Unit/ml vs 15.1 Units/ml vs. 17.5 Units/ml, p=0.57).
Conclusions
These preliminary results demonstrated intraocular expression of MFAP4 in the human eye. Further, a higher expression of MFAP4 was demonstrated in the vitreous body as compared to the anterior chamber. Vitreal MFAP4 does not appear to be regulated with neovascular disease supporting that MFAP4 is constitutively expressed and permissive for integrin activation during neovascularization.

• F081

Optimisation of potent topical SRPK1 inhibitors with improved retinal pharmacokinetics through ex vivo trans-scleral permeability modelling

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Purpose
Development of non-invasive therapies for wAMD and DME has been unsuccessful to date. Delivery of potent small molecules to the retina as eye drops would be a treatment paradigm shift but remains an unmet need due to incomplete understanding of the physicochemical properties required. We hypothesised that trans-scleral permeability modelling could identify these features and enable optimisation of inhibitors of the VEGF-A splicing kinase SRPK1.
Methods
Porcine eye tissue was clamped into a scaffold with drug formulations for 24 h. Compound levels were analysed by LCMS. For PK, Hy79b pigmented rabbits received a single eye drop for successive timepoints or tri-daily eye drops for 6 days. Compound levels in eye tissues and plasma were analysed by LCMS. Efficacy was evaluated in vivo in C57/Bl6 mice.
Results
We identified potent and selective SRPK1 inhibitors with improved permeability ex vivo (ranging to 8.154x10-6 cm/s compared to 0.07x10-6 cm/s for pazopanib). Multiple regression analysis generated predicted permeability values which correlated with ex vivo permeability and in vivo retinal PK. SRPK1 inhibitors were equally distributed across the retina at 4 h at significantly higher concentrations than pazopanib and at significantly lower concentrations in plasma. SRPK1 inhibitors potently inhibited laser-CNV following eye drop administration in mice (EC50s<0.5 µM, n=6-8, P<0.05).
Conclusions
Ex vivo permeability screening enabled modelling and design of novel compounds with improved permeability and optimisation for in vivo retinal delivery. Increased potency and ocular permeability of the novel SRPK1 inhibitors show potential to reach therapeutic levels in the retina following eye drop administration and improve treatment for patients with wAMD and DME.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Employed by EXONATE Ltd

• F082

Aerobic exercise causes changes in choroidal thickness in young adults

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Purpose

In this study we evaluate the changes of choroidal thickness after doing physical aerobic exercise in healthy young adults using spectral-domain optical coherence tomography (SD-OCT), with Enhanced Depth Imaging (EDI) protocol, and manual segmentation. This is a modified technique which allows us to obtain an improved image of the choroidal layer.

Methods

Thirty eyes of 15 volunteers between 18 and 31 years old were prospectively and consecutively enrolled, with ±6.50 D maximum ametropia and 3.00 D of astigmatism, with neither systemic nor ocular pathology as inclusion criteria. All the subjects were examined in the same conditions and by the same investigator. Measures from autorefractometer, ocular biometry and SD-OCT were taken. The SD-OCT images were taken at basal measurement, after doing 10 minutes of physical exercise and then two more measures after the exercise (3 and 10 minutes after finalization). The choroidal layer was manually segmented, valuing thicknesses and volumes in the different areas from the ETDRS (Early Treatment Diabetic Retinopathy Study).

Results

In all the areas the average thickness increased 3 minutes after exercise compared to basal. We found significant differences ($p<0.05$) by means of the test of ranks with signs of Wilcoxon in the areas: 3 mm temporal, 3 mm nasal, 6 mm superior, 3 mm superior and in the subfoveal choroidal thickness. After 10 minutes, this value decreased, finding only statistical values ($p<0.05$) in the subfoveal choroidal thickness. Volumes measures showed the same pattern.

Conclusions

In healthy young people 3 minutes after finishing physical exercise the choroidal thickness increases. Ten minutes after the finish, the choroidal thickness decreases.

• F083

The changing sphingolipidome of retinal ganglion cells in response to stress

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Purpose

To capture dynamic sphingolipid profile of retinal ganglion cells (RGC) subjected to stress.

Methods

RGCs from P0-P8 C57BL/6 mice were purified using 2-step immunopanning method: after initial anti-macrophage depletion retinal suspension was enriched for Thy1.2+ cells. RGCs, cultured on poly-D-lysine and laminin substrate in defined serum-free medium with addition of BDNF, CNTF and forskolin, were subjected to 2 psi (~100 mmHg) hydrostatic pressure by addition of carbon dioxide, resulting in additional stress components of acidosis and mild hypoxia. Samples were spiked with internal standards and lipids extracted using Bligh&Dyer method. Untargeted profiling analysis was carried out using reverse phase liquid chromatography coupled to high-resolution mass spectrometer (Q Exactive). Subsequently, peak extraction, identification and alignment were performed in Lipid Search 4.1 software. Quantification is based on the ratio to respective internal standard and normalized to total DNA content.

Results

Based on MS/MS spectra we identified a total of 725/839 species at 4/24 h stress exposure, respectively, from 7 sphingolipid subclasses of which 76/174 (10.5%/20.7%): 31/81 ceramide, 14/35 hexosyl-ceramide, 2/20 dihexosyl-ceramide, 13/18 ceramide 1-phosphate, 6/13 sphingomyelin, 10/6 sphingoid base, 0/1 sphingoid base 1-phosphate species changed significantly when compared to time-matched controls (t.test $p<0.05$). We did not find changes in total levels of metabolites in any of the subclasses. 67% of the early (4 h) altered species displayed increase, while 71% of the late (24 h) ones - decrease.

Conclusions

Levels of particular RGC sphingolipid species change upon acute stress. It may suggest that individual sphingolipids have distinct roles in cell fate decisions. The great challenge now lies in understanding biological significance of these alterations.

• F084

Nebivolol acts as a beta3-adrenergic receptor agonist in a mouse model of oxygen-induced retinopathy

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Purpose

Nebivolol is a β1-adrenergic receptor (AR) antagonist with vasodilatory properties. Nebivolol, but not the β1-AR antagonist atenolol, has been found to ameliorate endothelial dysfunction. There is no clear evidence about the molecular target of the vasodilatory action of nebivolol, but several studies seem to indicate that the activation of β3-ARs may mediate such vasodilation. In the present study, we evaluated the possible activity of nebivolol as β3-AR agonist in a mouse model of oxygen-induced retinopathy (OIR) using β1/β2-AR knockout (KO) mice. These mice are quite resistant to retinal hypoxia, with reduced neovascularization in respect to their wild type (WT) controls.

Methods

The OIR model was established in KO and WT. Nebivolol was subcutaneously administered at 0.1, 1 or 10 mg/kg once daily between PD12 and PD16, before animal sacrifice at PD17. The effects of nebivolol on retinal neovascularization, VEGF levels and nitric oxide (NO) production were assessed by CD31 immunohistochemistry, real time RT-PCR and ELISA, and the Griess method, respectively.

Results

In OIR, nebivolol minimally affected retinal neovascularization in WT while dose-dependently induced pathologic angiogenesis in KO mice. In addition, nebivolol dose-dependently increased VEGF levels in KO. The NO pathway was likely to be involved in the angiogenic effects of nebivolol.

Conclusions

The weak effects of nebivolol in the WT retina indicate that β1- and/or β2-ARs play a pivotal role in retinal angiogenesis and that the angiogenic role of β3-ARs may be unraveled only in the absence of the two other subtypes and when adequately stimulated. The present study indicates that nebivolol may stimulate β3-ARs in the mouse retina suggesting this drug as a possible candidate as β3-AR agonist.

• F085

Modulation of iris sphincter and ciliary muscles by Urocortin 2

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Purpose

Urocortin 2 (UCN2) is a peptide related to corticotropin-releasing factor, capable of activating CRF-R2. Among its multisystemic effects, it has actions in all 3 muscle subtypes, either increasing or decreasing contractility.

This study's aim was to determine its potential role in two of the intrinsic eye muscle kinetics and to study the likely subcellular pathways involved.

Methods

Strips of iris sphincter (rabbit) and ciliary (bovine) muscles were dissected and mounted in isometric force-transducer systems filled with aerated-solutions, subjected to 0.5mN and 1.0mN preloads, respectively. Contraction was elicited using carbachol (10-6M for iris sphincter, 10-5M for ciliary muscle), prior to all testing substances.

Results

UCN2 induced relaxation in iris sphincter muscle, being the effect maximal at 10-7M concentrations (-12.2% variation, versus control, n=6). This effect was abolished with incubation of indomethacin (n=8), antisauvagine-30 (n=7), chelerytrine (n=6) and SQ22536 (n=8), but preserved with L-nitro-L-arginine (n=9). In carbachol pre-stimulated ciliary muscle, UCN2 (10-5M) enhanced contraction (maximal effect of 18.2% increase, versus control, n=10 pairs); pre-contraction studies were negative.

Conclusions

UCN2 is a new neurohumoral modulator of iris sphincter relaxation, dependent on CRF-R2 activation, synthesis of prostaglandins (COX pathway) and both adenylate cyclase and PKC signaling pathways, but independent of nitric oxide production. Regarding ciliary muscle, UCN2 enhances carbachol-induced contraction, in higher doses.

• F086

Alzheimer's disease: can the retina be a window to the brain?

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Purpose

The diagnosis of Alzheimer's disease (AD) is difficult. Since AD patients have visual problems, even before AD diagnosis, and retina is part of the CNS, we aim to understand whether retina could be used as a window to the brain, and for earlier and better diagnosis of AD.

Methods

To achieve this, we are performing a longitudinal study to evaluate potential changes in several molecular, cellular, structural and physiological parameters in the retina of a triple transgenic mouse model (3xTg-AD), comparing to age-matched wild-type (C57BL6/129S) mice, at 4, 8 and 12 months (M) of age, by Western blot, immunohistochemistry, TUNEL assay, ERG, PERG and OCT.

Results

In 3xTg-AD mice, at 8 and 12 M, the retinal thickness decreased significantly, and at 4, 8 and 12 M the scotopic b-wave and photopic flicker amplitude increased. No differences were detected in PERG recordings. Amyloid beta protein was not detected in the retina of 3xTg-AD at 4 and 8 M. The p-Tau protein levels increased at 4 M, but not at 8 M. At 4 and 8 M, amyloid precursor protein, beta-secretase 1, choline acetyltransferase, syntaxin and synaptophysin levels remained unchanged in the retina of 3xTg-AD. Apoptotic cells (TUNEL+ cells) were not detected. Also, no alterations were detected in the immunostaining of vimentin in 3xTg-AD, but GFAP immunostaining decreased at 8 M.

Conclusions

These results show that retinal thickness and function are early affected in a mouse model of AD. However, no molecular and cellular correlates were found in the majority of parameters evaluated in the retina, with the exception of p-Tau and GFAP, at least in early timepoints.

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• F088

Influence of metabolic control in patients with refractory diabetic macular edema treated with Ozurdex

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Purpose

To analyze the relationship between glycemic, lipid, and blood pressure control following the American Diabetes Association(ADA) goals, and the response of refractory diabetic macular edema (DME)in patients treated with Ozurdex.

Methods

A retrospective, descriptive and observational study was conducted on patients with refractory DME treated with Ozurdex® in the University Hospital of Burgos, Spain, between 2012 and 2015.

Results

21 patients were included. Almost all (95%) patients had type 2 diabetes mellitus (DM), and 81% were treated with insulin. The mean time of evolution of DM in this series was 16 years (± 12). The mean HbA1c was 7.22 ± 1.06. The mean initial best corrected visual acuity (BCVA) was 0.72 (log Mar ±0.33) and improved to 0.58 (log Mar ±0.31) after 6 months of follow up. The initial central macular thickness (CMT) was 506µ ±99, and a reduction to 384µ ±128 was observed after 6 months of follow up. Taking into account the overall metabolic control of the patient, a statistically significant difference was found in the improvement in BCVA after 3 months of follow up in patients with good metabolic control. A greater central macular thickness reduction was observed in patients with a better metabolic control at six months of follow up. This study also suggests that patients with an optimum HbA1c control have a tendency to achieve a better visual acuity after an Ozurdex implantation. No statistical differences were found between blood pressure and lipid parameters, and the anatomic or functional response to Ozurdex.

Conclusions

Ozurdex is an effective and safe treatment in the treatment of DME in patients that did not respond or poorly responded to other therapies. The overall metabolic control of the patient following the criteria of the ADA is related to the success of the treatment with Ozurdex.

• F087

Electrical direct current stimulation affects retinal vessel diameter and vasodilation in healthy subjects

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Purpose

Electrical stimulation (ES) of the human eye is an emerging technique in the treatment of ophthalmic diseases since several studies showed improvements of visual functions in patients. Neuroprotective effects are assumed to cause beneficial impacts of ES. We investigated the acute effects of ES on retinal vasculature in healthy subjects using dynamic vessel analysis (DVA). This method enables continuous measurements of vessel diameters and assessment of flicker-induced vasodilation.

Methods

DVA was performed in 7 healthy subjects (5 females, 25.7±1.7 years, one eye) to examine retinal vessel behavior. Two primary vessel segments were analyzed in each eye (temporal artery (tA) and vein (tV)) regarding baseline vessel diameter (BLD) and vasodilation provoked by flicker (VD). For non-invasive ES a ring-shaped rubber electrode surrounding the eye and a square rubber electrode at the occiput were used. Positive direct current (800µA) was applied for 20min at the eye. Each subject participated in two experimental trials in random order, applying real and sham ES (rES/sES) once. DVA was conducted before and immediately after rES/sES to observe changes in BLD and VD. Results were analyzed using paired t-test to check for changes in BLD and VD due to rES/sES on a level of p=0.05.

Results

All subjects showed retinal vessel reactions to flicker in DVA. BLD decreased significantly after rES for tA (-3.4±1.7%; p=0.003) but not for tV (-0.2±1.6%; p=0.814). In contrast, VD of tA showed an upward trend (+0.7±1.2%; p=0.162), while VD of tV was reduced after rES (-0.4±1.6%; p=0.547). For sES no significant changes of BLD and VD were observed.

Conclusions

Real ES affects both arterial BLD and VD by narrowing tA in resting state and enhancing vessel reaction to flicker provocation. These results provide evidences for beneficial effects of ES on circulatory processes.

• S001

In vivo evaluation of voriconazole eye drops efficacy in a rat Acanthamoeba polyphaga keratitis model

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Purpose
Acanthamoeba keratitis is a sight-threatening infectious disease. Its effective and safe medical therapy remains highly debated. The aim of this study is to test in vitro and in vivo voriconazole as a potential antiamoebic treatment for Acanthamoeba keratitis.
Methods
In vitro sensitivity of Acanthamoeba polyphaga to voriconazole was assessed using a commercially available viability assay. In vivo, Sprague-Dawley male rats were injected in the left cornea stromal layer with trophozoites. Forty rats were divided into 3 groups, topically treated with 1% voriconazole eyedrop (hourly administrations for 3 days followed by every two hours for 11 days and followed every four hours for 7 days), orally treated with voriconazole (60 mg/kg/day), and control. At day 28, cornea and blood samples were collected and corneal scrapings were performed for bacterial and parasitological cultures and real-time PCR analyses. Paraffin-embedded corneas were analyzed. The plasma and corneal concentration of voriconazole was determined by high-performance liquid chromatography.
Results
In vitro, voriconazole inhibited Acanthamoeba polyphaga trophozoites proliferation with IC90 value of 6 µg/ml, however no cystical activity was found. Mean intracorneal concentration of voriconazole eyedrops after three days treatment was 5.6 +/- 4.4 ng / mg; after seven days treatment was 2.38 + /1.6 ng/mg; and after twenty one days treatment was 0.32 +/- 0.15 ng / mg. Clinical infection worsened in fewer rats between the 7th and the14th day post infection in the voriconazole eye drops group (1/10 rats) and the control group (9/10 rats) (p = 0.001).
Conclusions
Our findings support the potential use of voriconazole as anti-amoebic agents.

• S002

Hydrops: Not that bad!

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Purpose
To demonstrate that hydrops is not a disaster and often evolves favorably especially under surgical treatment.
Methods
Prospective study of 30 eyes of 30 patients with corneal hydrops who underwent clinical examination with anterior segment photography, corneal topography, ultrasound corneal pachymetry and corneal OCT. All of them underwent in an outpatient setting and under topical anesthesia, anterior chamber air injection, peripheral iridotomy and deep corneal sutures perpendicular to Descemet membrane tear then kept under observation for 1 hour. Patients were asked to stay laying on their backs for 3 days. All patients were able to wear scleral lens after 1 week post surgery.
Results
Corneal edema decreased dramatically since the first day concomitantly with corneal thickness and average SimK reading. Mean LogMAR with scleral lens was 0.4.
Conclusions
Proper surgical approach of hydrops can provide a spectacular quick healing with visual improvement avoiding corneal graft.

• S003

Two photon microscopic findings of sonoporation-assisted enhancement of corneal penetration of fluoroquinolone antibiotics

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Purpose
To investigate the sonoporation-assisted enhancement of corneal penetration of fluoroquinolone antibiotics.
Methods
Enucleated mouse corneas were imaged by two-photon microscopy to observe normal corneal structure ex vivo. For estimation of the threshold of corneal epithelial damage, sonoporation was applied with different intensities (1.5, 2.0 and 3.0 W/cm2) for 5 minutes on each cornea. Gatifloxacin and besifloxacin were applied on each cornea and the depth of drug penetration was observed with two-photon microscopy. After sonoporation (1.5 and 1.7 W/cm2, respectively) was applied with fluoroquinolone eyedrops, we compared the aspects of drug penetration in sonoporated cornea with those in normal cornea. In vivo two photon microscopy imaging was conducted with gatifloxacin application.
Results
Normal cornea observed with two-photon microscopy showed regular arrangement of epithelial cells without any damaged cells. Threshold intensity of sonoporation that can damage some epithelial cells without significant structural destruction was determined as 1.5~2.0 W/cm2. When gatifloxacin was applied on normal cornea, gatifloxacin fluorescence was observed only on surface of corneal epithelium. After sonoporation, whole epithelium showed increased gatifloxacin and besifloxacin fluorescence. But the penetration depth and the extent of Besifloxacin were less than those of gatifloxacin, due to its own molecular structure. The threshold intensity was revealed as 1.3 W/cm2 in vivo. In vivo corneal penetration of gatifloxacin enhanced after sonoporation, and this result was comparable with that of ex vivo.
Conclusions
We observed the enhancement of corneal penetration of fluoroquinolone antibiotics after sonoporation was done on mouse cornea ex vivo as well as in vivo. Besifloxacin showed poor penetration compared with gatifloxacin even after sonoporation.

• S004

Efficacy of a RARγ selective agonist eye drop formulation on improvement of tear production and corneal fluorescein staining in the BTX-B mouse model of dry eye disease

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Purpose
Multiple studies have demonstrated the potential beneficial effects of retinoids on dry eye disease. Retinoic acid receptors (RAR) α, β and γ are widely distributed in ocular tissues. In vitro data suggest that the beneficial effects of retinoids on ocular health are mediated via RARγ (Kimura 2015). The purpose of this study was to evaluate the in vivo effects of palovarotene (PVO), a RARγ selective agonist, in a dry eye animal model.
Methods
The efficacy of a PVO ocular formulation was tested in the botulinum toxin type B (BTX-B) mouse model which involves injection of BTX-B into the lacrimal gland of the right eye with contralateral control. Eye drop formulations at 3 doses of PVO (low, mid, high) with vehicle, were administered by daily topical instillation for 28 consecutive days and compared to current standard of care, Restasis®. Endpoints included ophthalmic examinations, tear production measurement (TPM) by phenol red-impregnated cotton threads, corneal fluorescein staining (CFS) using a scoring system of 0 to 4, and histopathology.
Results
At Day 28 post BTX-B injection, the mean (SD) TPM and CFS score in the untreated group were 1.5 (0.3) mm and 2.0 (0.7), respectively. In comparison, PVO eye drop treatment significantly improved dry eye signs ($p<.0001$) at all doses tested – TPM was increased by 132, 166 and 188% at low, mid and high dose, respectively, while CFS score was decreased by 70, 85 and 85%, respectively. PVO treatment effects were greater than Restasis® (113% increase in TPM, 50% decrease in CFS). All PVO doses were tolerated for 28 days. Histopathology evaluation revealed no effects on the Meibomian glands.
Conclusions
These results indicate a beneficial therapeutic effect of PVO in the BTX-B animal model and support further development of a PVO ocular formulation for the treatment of human dry eye disease.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Presenter and co-authors are employees of Clementia
Any Stocks or shares held by you or an immediate relative?:
Presenter and co-authors have Clementia stock options

• S005

Graft blues: case report

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Purpose

To describe unusual inadvertent persistent staining of stromal structures by trypan blue (TB) after penetrating keratoplasty (PK) and Descemet membrane endothelial keratoplasty (DMEK) performed in patients suffering from lattice corneal dystrophy (LCD)

Methods

Case report of patients suffering from LCD and having received intracamerular TB. Series 1: retrospective study on 85 consecutive triple procedures (PK+cataract+IOL) performed by a single surgeon (PG) in a tertiary care university hospital during 7 years. 0.4% TB was systematically used. Series 2: case report of a DMEK (stained with TB) performed after a late endothelial failure of a previous PK realized 5 years before for advanced LCD. Six weeks after DMEK, the patient was hospitalized for acute rejection that appeared unusual

Results

Series 1: Only patients with LCD (n= 18 eyes in 17 patients) presented an isolated intense blue staining of the graft host interface (blue ring). It persisted during 18-24 months and had no consequence. Series 2: during the acute rejection, intense blue staining was observed in spindle shaped small structures located in the first third of the whole stroma. The DMEK was partially detached. Stromal edema almost completely resolved after intense steroid therapy but the stromal blue staining persisted (9 month follow-up) with impaired vision.

Conclusions

Abnormal amyloid protein characterizing LCD can be stained by TB in vivo. In PK it stains a ring in the recipient stroma and has no consequence. However, during DMEK performed after a PK, TB may also stain the protein accumulated in the graft stroma during slow recurrence of the disease. TB-stained DMEK should therefore be avoided in late endothelial failure of a PK initially performed for LCD.

• S006

Comparison between over-glasses patching and conventional patching for children with moderate amblyopia : a prospective randomized clinical trial

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Purpose

Objectives: To investigate the clinical effects of orthokeratology lens wear on inhibition of the myopic progression and axial length elongation in Korean children with myopia.

Methods

Methods:. The authors reviewed out-patient records of 37 eyes of 19 patients wearing orthokeratology lenses. The 46 eyes of 23 patients wearing spectacles were included into the control group. We evaluated the relationship between orthokeratology lens wear and control group according to age, initial myopia, initial astigmatism, axial length elongation.

Results

Results: There were no significant differences between two groups as for age, initial myopia, astigmatism, spherical equivalent, and axial length at baseline (t-test, $p > 0.05$). Significant reduction of refraction was shown in patients with wearing lenses after 1 year (t-test, $p < 0.001$). The mean axial length before and after 1 year was 24.62 ± 1.39 mm and 24.73 ± 1.28 mm respectively after lens wearing, and 24.59 ± 0.74mm and 24.80 ± 0.71 mm respectively after wearing glasses. The axial length elongation was 0.11 ± 0.12 mm, and 0.21 ± 0.07 mm in patients with wearing lenses and glasses, respectively, which showed statistically significant difference (t-test, $p < 0.0001$).

Conclusions

Conclusions: The orthokeratology lens was found to be effective in suppression of myopic progression through less axial length elongation, compared with the glasses.

• S007

Micro-instillation of fluorescein with an inoculation loop for ocular surface staining in dry eye syndrome.

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Purpose

To describe and validate the micro-instillation of fluorescein on the ocular surface by a disposable calibrated inoculation loop in order to improve corneal and conjunctival staining quality.

Methods

Prospective interventional non-randomized low risk study performed in the Department of Ophthalmology at Saint-Etienne University Hospital. Twenty patients (40 eyes) suffering from dry eye syndrome were enrolled. Accuracy and precision of 0.5% sodium fluorescein collected by a disposable 1µL-calibrated inoculation loop were measured using a precision balance. Fluorescein was instilled in patients' eyes with the loop, and slit lamp images were taken within 30 seconds using cobalt blue light with and without a yellow barrier filter. For comparison, after a washout period, the same images were retaken after instillation of one drop of fluorescein from a single-dose unit. The main outcome measure was the staining quality assessed by three experts, blind to the instillation method and to discomfort felt by patients.

Results

The mean amount collected by the loop was 1.18±0.12µL, compared with 33.70±6.10µL using the single-dose unit. Tolerance was excellent. The loop avoided excess dye responsible for unpleasant tearing, masking of lesions, and rapid diffusion into the stroma. Micro-instillation greatly improved image quality without losing information. The yellow filter further improved image contrast.

Conclusions

The 1µL-calibrated inoculation loop is a safe, convenient, inexpensive, disposable, sterile, well-tolerated tool for reproducible micro-instillation of commercial fluorescein. By greatly improving staining quality, it will help standardize assessment of dry eye severity.

Conflict of interest

Any post or position you hold or held paid or unpaid?:

Employee of Laboratoires Thea and BiiGC PhD Student.

• S008

Does femtosecond laser assisted penetrating keratoplasty lead to less astigmatism in keratoconus patients, compared with conventional penetrating keratoplasy?

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Purpose

Visual impairing including high irregular astigmatism is a well-known problem after penetrating keratoplasty (PK). The femtosecond (FS) laser technique allows completely new trephination methods such as the zig-zag, top hat or the mushroom cutting profiles, which result in a more rapid and stable wound healing. In the present study we compare conventional PK and FS laser PK concerning astigmatism and visual outcome in keratoconus patients 2 years postoperatively

Methods

A total of 67 patients were operated with PK between September 2013 and June 2015 at Oslo University Hospital, Norway. All patients were examined 2 years after surgery. Ten keratoconus patients who were operated with FS laser-assisted PK (FS group) were included, using Alcon Wavelight FS200 Femtosecond Laser, and compared with a control group who underwent conventional PK (n=20). Controls were matched for diagnosis, age, gender and time of operation. Postoperative results regarding astigmatism and visual outcome were compared.

Results

At the 2 years follow-up, the mean logMAR BCVA was 0.17± 0.14 in the FS-group and 0.16 ± 0.19 in the control group (p=0.89). The mean spherical equivalent was -1.91 ± 4.58 in the FS-group, and -3.08 ± 2.81 in the control group (p=0.39). The mean subjective and corneal cylinder was -6.08 ±2.50 and 7.71±3.78 in the FS-group, compared to -4.89 ± 2.57 (p=0.24) and 5.73±3.84 in the control group (p=0.21), respectively. K-mean was 44.00 D ± 3.99 in the FS-group and 44.98 D ± 1.63 in the control group (p=0.50). ECD was 1456 cells/mm^2± 325 in the FS-group, and 1679 cells/mm^2± 475 in the control group (p=0.22).

Conclusions

Even though the study included relatively few eyes, the findings confirm previous studies. No significant difference in astigmatism or visual outcome was found between the two groups 2 years postoperatively.

• S009

Corneal confocal microscopy assessment in contact lens discomfort

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Purpose
The aim of this study was to analyze whether symptoms of discomfort in CL wearers were associated to changes in the nerve morphology and/or the density of dendritic cells in the corneal sub-basal nerve plexus.
Methods
Sixty subjects were included: 20 symptomatic CL wearers (SCLW), 20 asymptomatic CL wearers (ACLW), and 20 non wearers (NCLW). Ocular Surface Disease Index (OSDI), visual acuity, tear osmolarity, biomicroscopy findings, tear film break-up time, corneal and conjunctival staining, Schirmer test, and confocal microscopy were performed. In the confocal images number and density of nerves, density of nerve branches, grade of nerve tortuosity, and density of dendritic cells were analyzed.
Results
OSDI and lid roughness was higher in the SCLW group (p=0.009 and p=0.04, respectively), limbal hyperaemia was raised in the ACLW group (p=0.009), and tear osmolarity was increased in both CL wearers groups (p=0.000), in comparison with the NCLW group. Subjects were divided into low and high density of dendritic cells using a 75 cells/mm2 cut-off. This distribution was significantly different (p=0.04) between the CL wearers (21 and 19 subjects had low and high cell density, respectively) and the NCLW group (16 and 4, respectively). The CL type was significantly different (p=0.011) between CL wearers with low (4 and 17 subjects wear conventional and silicone hydrogel CLs, respectively) and high (11 and 8, respectively) cell density.
Conclusions
Symptoms of discomfort in CL wearers seem not to be related to changes in the nerve morphology or density of dendritic cells in the corneal sub-basal nerve plexus.

• S010

Effects of trypan blue on corneal endothelial cell viability ;Optimal time of Trypan Blue Dye Application to DMEK donor tissue

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Purpose
The purpose of this study was to evaluate the corneal endothelial cell toxicity of the trypan blue dye used in Descemet membrane endothelial keratoplasty(DMEK) donor corneal tissue to enhance visibility before transplant.
Methods
Human cadaver eyes with healthy endothelial cells that were unsuitable for transplantation were obtained. The mean endothelial cell density was 2679±232.76(2273-2994)cells/mm2 and the mean age was 61±13.37(35-73)years. The tissue samples were divided into 3 subgroups based on the application time of trypan blue dye(control, 4,and 6 minutes). Trypan blue dye 0.06%(Vision Blue®) was applied to the endothelium for 30seconds(Control). Descemet membrane was then stripped from the posterior stroma so a sheet of DM with the endothelial monolayer(DMEK donor tissue) was obtained. From the endothelial side, a trephination was made with a 8.25mm corneal trephine. Each sample tissue was stained with 0.06%trypan blue for a duration of 4, 6 minutes. Live/Dead assays using calcein AM and ethidium homodimer was performed to assess endothelial cell viability of DMEK donor tissue using fluorescent microscope.
Results
Endothelial cell damage was expressed as the percent of dead cells/ (live + dead cells). The mean values(cell death rate) were 52.95±10.54 %(control); 61.23±12.96 %(4min.); 81.85±15.17 %(6min.)
Conclusions
Endothelial cell toxicity of staining of DMEK donor tissue with trypan blue(0.06%) up to 4 minutes was similar to that of the control group. However, the endothelial cell death rate was relatively higher in the group for 6 minutes staining than in the group for 4miniutes staining or control. As the staining time of trypan blue increased, the endothelial cell death rate tended to increase(Jonckheere-terpstratest,p<0.05).

• S011

Use of sodium hyaluronate in combination with a blood derivative in the re-epithelialization of rabbit corneas

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Purpose
To analyze if using a bioadhesive (sodium hyaluronate or HaNa) in combination with a blood derivative (s-PRGF) improves the healing rate and quality of corneal epithelial ulcers.
Methods
Rabbit corneas removed 7 and 30 days after an in vivo re-epithelialization assay were include in paraffin and processed for haematoxylin–eosin staining or cryopreserved for immunofluorescent staining. In vitro proliferation and wound healing experiments were performed using the human corneal epithelial HCE cell line and rabbit primary corneal epithelial cultures. We studied the following treatments: 1) 90% s-PRGF 2) 0.22% NaHa 3) s-PRGF + NaHa 4) PBS as control treatment for the in vivo assay. All components in treatments 1, 2 and 3 were half the concentration for the in vitro assays, being 1% BSA the control treatment (4). To manufacture s-PRGF whole blood was collected by venipuncture from healthy volunteers or New Zealand rabbits, respectively.
Results
Healing rate was higher in cultures and in eyes under s-PRGF treatment than in those treated with HaNa or the combination of both. H-E sections at 30 days showed more cells in the anterior stroma in eyes under HaNa treatments. In agreement with it, Ki67 staining as well as in vitro proliferation assays demonstrated that HaNa stimulated cell proliferation. All treatments produced stratified and mature epithelia (CK3 positiveness) with barrier function (ZO-1 staining) and activation of limbal stem cells (CK15 staining), although the HaNa treated epithelia were the less organized. Moreover, eyes treated with only s-PRGF showed the best integrin β4 staining.
Conclusions
HaNa bioadhesive promotes epithelial and stromal cell proliferation, but does not improve the corneal healing capacity of s-PRGF. s-PRGF shows a better healing quality in terms of epithelial-stromal adhesion.

• S012

Evaluation of visual quality parameters after Descemet membrane endotelial keratoplasty (DMEK)

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Purpose
Objectives: To evaluate progressive changes in visual quality parameters in patients who underwent DMEK for Fuchs endotelial dystrophy (FED), and to compare the visual quality results with healthy controls without corneal pathology.
Methods
Methods: Fourteen eyes with FED who underwent DMEK were evaluated for corneal topographic changes using Pentacam (OCULUS, Iberia SL), preoperatively, at 1 month and at 6 months after surgery. Mean keratometry (Km), corneal density (1-2 mm, central and total), high order aberrations (HOA), low order aberrations (LOA) and total aberrations (total RMS) were analyzed in the anterior and posterior cornea. Fourteen healthy subjects were evaluated using the same protocol and compared with the patient's final evaluation data.
Results
Results: Significant improvement was observed in patients at 1 month after surgery in the posterior Km (p=0.005), central posterior density (p=0.034), 1-2 mm posterior density (p=0.006) and central anterior density (p=0.045), and anterior LOA (p=0.026) and total aberrations (p=0.020). After 6 months all densities (anterior and posterior) had improved compared to preoperative results (p<0.05) as well as all posterior aberrations (total, HOA and LOA, p<0.05). Posterior and anterior Km values and corneal densities did not show significant differences compared to healthy subjects (p>0.05). Corneal aberrations (anterior and posterior)remained significantly higher in DMEK subjects (p>0.05)
Conclusions
Conclusions: DMEK surgery improves corneal visual quality parameters in FED patients after the first month postoperatively. Corneal density and mean keratometry values are not different from healthy corneas at 6 months after DMEK. However, despite corneal aberrations decrease after surgery they remain higher than those values found in healthy corneas.

• S013

Interference of TRPA1 function affects background activity of corneal cold thermoreceptors in ageing mice

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Purpose
TRPA1 and TRPM8 channels provide cold sensitivity to cold thermoreceptor neurons, being activated by high- and low-intensity cooling stimuli respectively. Corneal cold sensory nerve terminals (CSNTs) encode both corneal surface temperature reductions and tear osmolarity increases associated with tear evaporation, acting as `dryness detectors´. TRPM8-dependent activity of CSNTs contribute to basal tearing and is disturbed with ageing, while the role of TRPA1-dependent activity is still unknown. In the present work, electrical activity of CSNTs from TRPA1-KO mice was studied to define the contribution of TRPA1 channels to cold thermoreceptor sensory input to CNS.
Methods
Nerve terminal impulse (NTI) activity of CSNTs was recorded in vitro with a glass micropipette applied to the corneal surface of eyes from C57BL/6J (WT) and TRPA1-KO mice (18-22 months old) continuously superfused with physiological saline solution at 34ºC. Background activity at basal temperature (34ºC) and the impulse response to cooling ramps (from 34 to 15ºC) and to TRP channel agonists (menthol, AITC, capsaicin; added to the perfusion solution) were analyzed. Tearing rate was measured with phenol red threads.
Results
Background NTI activity of CSNTs at 34ºC was slightly reduced in old TRPA1-KO mice compared with aged-matched WT (4.5±2.2 imp/s, n=10, vs 7.7±1.2 imp/s, n=11, p=0.22, t-test), due to a reduced proportion of high background-low threshold cold CSNTs. No significant differences were found in response to cooling ramps nor in tearing rate between WT and TRPA1-KO mice.
Conclusions
Knocking TRPA1 alters background activity of CSNTs but not their response to temperature decreases, suggesting that TRPA1-dependent input to CNS is no essential for regulation of basal tearing.
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• S014

Femtolaser-assisted vs manual anterior lamellar keratoplasty in patients with keratoconus

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Purpose
To evaluate anatomic and functional results of ALK using different technics for end-stage keratoconus.
Methods
Anterior lamellar keratoplasty was performed in 21 eyes with progressive keratoconus of IV stage of disease according to the Amsler classification. In 1st group (12 cases) keratoplasty was performed using a femtosecond laser LDV8. Removed corneal disc diameter - 7.5-8.0 mm, thickness - 250-300 mc. In 2nd group (9 cases) manual dissection of anterior stroma was performed. Partial trepanation without penetration of anterior chamber (diameter 7.5-8.0 mm) was done at depth 250 mc using Barron trephine. Corneal graft was fixated by 10/0 sutures. The follow-up was 6 months.
Results
Significant improvements of UCVA and CVA was up to 0.2 and 0.5, respectively, in 1st group. In 2nd group UCVA and CVA improved up to 0.08 and 0.3 in early postop period. Mean corneal astigmatism was 4.6±1.2 D in 1st group and 7.7±2.4 D in 2nd, respectively. In 1 case after manual technic (2nd group) hazing and graft rejection was observed in 2 months after surgery.
Conclusions
The use of femtosecond technologies in anterior lamellar keratoplasty increases the efficiency of the operation due to the greater predictability and accuracy of the procedure and the optimal donor-recipient juxtaposition. This leads to better visual and refractive outcomes by reduction of corneal astigmatism due to good wound apposition, biomechanical stable incision.

• S015

Progressive changes in visual function after Descemet membrane endotelial keratoplasty

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Purpose
Objectives: To evaluate progressive changes in visual function parameters in patients with Fuchs endotelial dystrophy (FED) who underwent Descemet membrane endotelial keratoplasty (DMEK) and to compare visual results after DMEK with visual function parameters in healthy subjects without corneal pathology.
Methods
Methods: Fourteen patients (14 eyes) with FED who underwent DMEK surgery were included in the study. All subjects underwent best corrected visual acuity (BCVA) evaluation using the ETDRS optotype in photopic and scotopic conditions, and contrast sensitivity (CS) assessment using the CSV 1000 and the Pelli Robson tests in different lighting conditions, preoperatively, at 1 and 6 months after surgery. Fourteen eyes of 14 healthy controls were evaluated using the same protocol and compared with the patients' final postsurgery data.
Results
Results: A significant improvement in all visual function parameters was observed in patients 1 month ($p<0.05$) and 6 months ($p<0.05$) after DMEK, compared with preoperative levels. Healthy controls had significantly higher BCVA in photopic and scotopic conditions ($p=0.02$, $p=0.044$, respectively), better CS in spatial frequencies of 6 cpd ($p<0.001$); 12 cpd ($p=0.006$) and 18 cpd ($p=0.006$) measured with the CSV 1000 test, and CS as measured with the Pelli Robson test ($p=0.002$). No significant differences were observed between patients and healthy controls in the spatial frequency of 3 cpd (photopic, $p=0.704$; mesopic, $p=0.596$; mesopic with glare, $p=0.989$).
Conclusions
Conclusions: DMEK improves visual function parameters in patients with FED in the first month after surgery. Patients who underwent DMEK present similar CS to healthy subjects in lower frequencies. However, BCVA and CS in medium and high frequencies remain significantly lower than those values found in healthy corneas.

• S016

Ocular cicatricial pemphigoid secondary to intravitreal implant of ranibizumab: a case report

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Purpose
Mucous membrane pemphigoid is a systemic disorder that primarily affects mucous membranes. When localized to conjunctiva, it is know as ocular cicatricial pemphigoid (OCP), a potentially blinding desease resulting in progressive conjunctival fibrosis and ocular surface failure.Women are affected more than men by a ratio of 8:1. Age on onset is usually age 60 to 80 and rarely younger than 30. We describe the case of a patient with OCP secondary to intravitreal implant of ranibizumab.
Methods
We describe the case of a patient with OCP secondary to intravitreal implant of ranibizumab.
Results
A 85 years old woman with bilateral macular degeneration, treated with intravitreal implants of ranibizumab in the right eye, began with a non specific queratoconjunctivitis in the right eye after the second administration of intravitreal ranibizumab. In numerous ophthalmology follow- up appointments the patient presented red right eye and increased amount of tears. Six months later, after another intravitreal implant of ranibizumab, the patient presented a subepithelial fibrosis, as fine gray-white striae in the inferior fornix. The patient was treated with topic corticosteroid, cyclosporin 0,2%, autologous serum eye 20% with a significant improvement. A systemic treatment with 15 mg methotrexate once a week and the suspension of intravitreal implants of ranibizumab was necessary to control the progression of the OCP.
Conclusions
In some patients, systemic drugs (practolol, D penicilamine…), have triggered the onset of OCP. The term pseudopemphigoid or drug-induced pemphigoid may be used to describe these cases. There are not cases of POC secondary to ranibizumab described on the literature.

• S017

Assessment of endothelial quality of pre-stripped DMEK grafts prepared using the Muraine technique

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Purpose
To determine feasibility of shipping of the DMEK grafts that are pre-stripped in eye bank using the Muraine technique.
Methods
Ten pairs of human corneas were stored in organ culture (OC) for 24±3 days. The mean age of donors was 72±20 years old. For each pair, one cornea was randomized for DMEK preparation using the Muraine technique (Muraine Moria trephine followed by manual dissection on the inverted cornea), the other served as control without dissection. The DMEK grafts of 8 mm in diameter were left attached to the center of the cornea, immersed in the OC medium (without dextran) and shipped to a distant center at room temperature. After 48 hours, the viable endothelial cell density (vECD) was measured with the help of viable cell staining using Calcein-AM and Hoechst 33342 on entire surface of endothelium. Immunostaining on flat mounted endothelium was used to assess the endothelial pump function (Na+/K+ ATPase, COXIV), the apical (ZO-1) and basolateral (CD166, N-CAM) structures of CECs, the roughness of the cleavage between Descemet membrane (DM) and stroma (Collagen I) and the thickness of DMEK grafts.
Results
Before stripping, ECD (classical measurement using a transmitted light microscope) were 2430±175 and 2433±119 cells/mm2 (P=0.9647) in control and DMEK group. After stripping and shipping away, vECD were 2130± 350 and 2190±190 cells/mm2 (P=0.6355). Comparing to controls, no alteration in endothelial pump function, or in characteristic subcellular structures of CECs was noted in DMEK grafts. The thickness of DMEK grafts was 15±2 µm with a smooth cleavage plan.
Conclusions
The technique of Muraine is a good technique for the preparation of DMEK; DMEK grafts attached to the center of the cornea are suitable for long distance shipping.

• S018

Discomfort self-perception in contact lens wearers

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Purpose
Chronic use of contact lenses (CLs) disturb ocular surface, leading to loss of corneal epithelium integrity and ocular discomfort. In many patients, there is no correlation between the severity of ocular surface disturbances and the perceived discomfort. In the present work, we analyzed the correlation between discomfort self-perception and ocular surface disease index in contact lens wearers.
Methods
Forty contact lens wearers of both sexes, 18-25 years old participated voluntarily in the study. An ad-hoc questionnaire (Likert scale survey type) was used to score the frequency and intensity of ocular surface discomfort and dryness sensation. Ocular Surface Disease Index (OSDI) adapted for Spanish speakers was also administered. An equivalent group of age and sex-matched volunteers with similar refractive errors that never wore CLs served as control.
Results
Significant differences were found between CL and eyeglasses wearers in medium-high intensity discomfort sensations (72.5% vs 32.5%, CL vs spectacle wearers, p=0.003), eye dryness sensation (87.5% vs 57.5%, p= 0.001), presence discomfort sensation during the day (92.5% vs 77.5%, p=0.011) and frequency of watering eye sensation (90% vs 27.5%, p=0.001). There were no significant differences in the frequency of headache nor in the need to use artificial tears. Surprisingly, no differences were found in OSDI questionnaire between CL and eyeglasses wearers.
Conclusions
Contact lens wearers most frequently perceive eye surface alterations than eyeglass wearers, although there are no significant differences in OSDI questionnaire.
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• S019

Bioactive sphingolipid mediators promote corneal epithelial homeostasis and wound healing

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Purpose
To investigate sphingolipid expression profile in alkali-burned cornea and subsequently evaluate effects of the selected species on corneal epithelial wound healing.
Methods
All experiments were performed using porcine cornea organ culture or porcine corneal epithelial cells (PCEC). For sphingolipid profiling samples were spiked with internal standards, extracted by Bligh&Dyer method and analyzed using liquid chromatography-mass spectrometry. PCEC viability/proliferation and migration were assessed using MTT and Boyden chamber assays, respectively. Epithelial wound healing in cornea organ culture was followed by fluorescein staining. Molecular mechanisms underlying the action of selected sphingolipids were studied using iTRAQ-based quantitative proteomics.
Results
Sphingolipid profiling of alkali-burned corneas revealed early decrease in sphingosine 1-phosphate and lysosphingomyelin with concomitant increase of ceramide 1-phosphate. We tested 7 lipids from aforesaid subclasses for their ability to affect proliferation/viability and migration of PCEC. 2 lipids: A, B improved viability/proliferation of alkali-injured PCEC, induced PCEC chemotaxis as well as promoted re-epithelialization after alkali burn in cornea organ culture. Another lipid: C potently improved viability/proliferation of healthy PCEC in a wide range of concentrations. In response to A/B/C treatments PCEC displayed differential expression of 114/375/47 proteins, majority with binding and catalytic activity functions. Proteins ↑ upon A/B were involved mainly in proliferation, adhesion and glycolysis, while upon C - in maintenance of corneal epithelial homeostasis.
Conclusions
We identified 2 sphingolipids that facilitate cornea re-epithelialization by promoting proliferation and migration of corneal epithelial cells and another that promotes healthy corneal epithelial cell phenotype.

• S020

Corneal haze in juvenile and adult keratoconus patients after corneal cross-linking

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Purpose
Densitometry software for the Oculus Pentacam was used to investigate the treatment outcomes of corneal cross linking (CXL) in adult and juvenile keratoconus patients.
Methods
A retrospective comparative study was carried out at Manchester Royal Eye Hospital. Corneal densitometry measurements collected before and after CXL treatment for 32 eyes from KC patients, aged between 13 and 39, were divided to 2 groups 13-18 years(juvenile group) and 19-39 years (adult group) was compared to pre and post treatment at 3, 6 and 12 months for each group and between both groups.
Results
Analysis of densitometry measurements found higher corneal densitometry after CXL which peaks at 3 months post treatment in both groups. There was significant diversity in corneal densitometry measurements at stromal zone 0-2 and 2-6 mm for all layer except the posterior layer for each group P<0.05). Significant differences were found between both groups at six months in the central (p=0.006), posterior (P=0.004) and full depth (P=0.02) layers for zone 0-2 mm.The same layers differed significantly in the 2-6 mm zone in all layers (p=0.01). One year post treatment significant differences were shown in corneal densitometry level between both groups in the 0-2 mm zone of the central layer (p=0.007), posterior layer (p=0.01) and full depth (p=0.03).The central layer in zone 2-6 mm was significantly different between both groups (p=0.04).
Conclusions
Haze levels post CXL differing in severity in different corneal zones and between both groups.The 0-2 mm and 2-6 mm zones were found to be the most affected area post treatment.Haze reached its maximum level at three months post treatment then appears to differ significantly in improvement level between adult and juvenile group, with the later never returning to pre-treatment clarity in the most anteriorly central zone in juvenile group

• S021

The use of corneal scrubbing associated with matrix therapy in the treatment of chronic ulcers

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Purpose
to treat refractory chronic ulcers with corneal scrubbing and matrix therapy; In dermatology practice, the same method is used in severe burns, the cutaneous scrubbing removes necrotic tissues and helps healthy tissues to progress faster
Methods
Retrospective study on chronic corneal ulcers evolving for several week refractory to conventional treatments; All the corneal ulcers were scrubbed with cotton buds, most of them received matrix therapy at the dose regimen of a drop every other day until corneal healing and preservative free lubricants 3 times a day, for the painful cases, we performed bandage contact lenses, and the remaining patients received the bandage contact lenses without matrix therapy ; ocular examination was performed at D0, D3, D7, D15 and D30, with slit lamp examination, fluorescein coloration and measurement of the size of the ulcers,
Results
18 patients were included and divided on 3 groups Group 1: corneal scrubbing, matrix therapy, lubricant and contact lenses Group 2: corneal scrubbing, matrix therapy, lubricant without contact lenses Group 3: corneal scrubbing; lubricant and contact lenses All the ulcers healed at D30, in the group1 and 2, corneal healing was faster between 7 and 10 days. No complications were reported despite the occurrence of one case of descemetocele at D3, with a good outcome at D15
Conclusions
Corneal scrubbing may accelerate corneal healing and therefore allows matrix therapy to be more efficient.

• S022

Refractive Lenticule Transplantation (RLT) for correction of iatrogenic hyperopia and high astigmatism after LASIK

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Purpose
To describe a novel technique for intrastromal transplantation of stromal lenticules with specific refractive power for correction of post-LASIK induced hyperopia and astigmatism.
Methods
A 28-year-old patient was referred for consultation after complicated LASIK for moderate myopia and astigmatism. The refractive error of the right eye was severely overcorrected due to a data entry error. Post-LASIK refraction showed high astigmatism (OD:+6.50/-9.00/84°) and CDVA of 20/32. The corneal thickness was 282µm. Due to contact lens intolerance, poor visual acuity and severe anisometropia a Refractive Lenticule Transplantation was performed. A toric and myopic lenticule, obtained from a donor using the ReLEx° FLEx technique, was implanted under the flap, in order to reduce the refractive error and restore the corneal volume.
Results
Six weeks after surgery the donor lenticule was spread smoothly in the interface with a minor temporal decentration in relation to the pupil centre. The refraction showed a reduction of astigmatism as expected, but a stronger myopisation compared to preoperative calculations (OD:-6.50/-4.0/70°). At three months, the CDVA returned to preoperative value of 20/32. One year postoperatively corneal tomography showed no signs of ectasia and biomicroscopy showed no signs of rejection. After an additional implantation toric myopic ICL the patient regained an UDVA of 20/40 and a full stereopsis.
Conclusions
The Refractive Lenticule Transplantation technique offers a solution for rare cases of post-LASIK hyperopia and astigmatism while restoring the volume of very thin corneas. Moreover, it is a reversible procedure with low probability of rejection.

• S023

The efficacy of heating devices to warm the lids

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Purpose
To investigate commercially available warming devices for their ability to effectively warm the lids by looking at heat distribution along the lid using thermography.
Methods
Devices that warm the eyelids are a standard treatment for MGD and blepharitis patients. Four commercial devices were tested: Medibeads a microwave activated eye mask, hot flannel, Eyebag instant disposable air activated heating pads, and a faical sauna. Fifteen normal healthy subjects were recruited and acclimated for 15 minutes in a controlled environment chamber at 25°C and 65% RH. Each device was used for 10 minutes over four separate sessions. Lid surface temperature was observed for 3 minutes before and then after treatment using a FLIR ThermaCAM P620.
Results
The mean lid temperature before applying devices was (35.77 ± 0.55 °C). Immediately after treatment, there was a significant increase in lid temperature ($p<0.05$) for all the devices. The Medibeads (38.54 ± 0.53 °C) was significant warmer than the Eyebags (37.96 ± 0.46 °C) ($p<0.03$) and facial sauna (37.62 ± 0.60°C) ($p=0.008$). The hot flannel (38.57 ± 0.79 °C) was significantly warmer than the facial sauna ($p=0.007$).
The facial sauna and the hot flannel leave the skin wet. The wetness may cause evaporative cooling and thereby reduce the beneficial warming effect. The wet devices showed a larger spread. Furthermore, the temperature 1 min after sauna treatment had returned to the pre-treatment value ($p= 0.23$).
The dry devices showed less spread and a longer lasting effect. In addition, the temperature after Medibeads treatment was warmer than after the Eyebags ($p=0.01$).
Conclusions
The dry warming devices were shown to be more consistent. The Medibeads showed the most effective heating. This suggests that the Medibeads offer the most consistent warming for the treatment of MGD and blepharitis patients.

• S024

Corneal melting and perforation under topical moxifloxacin and tobramycin: case report

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Purpose
To describe a case of corneal melting with perforation after treating a corneal abscess with topical moxifloxacin + tobramycin for 2 weeks.
Methods
Retrospective case report.
Results
A 56 year old patient presented 5 weeks after a retinal surgery with a central corneal abscess. Topical tobramycin 0.3% + moxifloxacin 0.5% 1/h + desomedine 1% 8/d was initiated and tapered 3 days later to 1/h, 5/d and 5/d respectively. Four days later a large erosion (3.5x3.5 mm) appeared while the abscess had disappeared. Topical tobramycin 5/d and moxifloxacin 3/d were continued for 1 more week when the patient presented to our clinic with a large corneal melting (3x2 mm) in a clear cornea that perforated centrally (1x1 mm) the next day with Descemet folds, fibrin, anterior cells ++, and, dilated iris vessels and posterior synechiae. Both blood tests and medical history were otherwise unremarkable. Moxifloxacin and tobramycin were discontinued and replaced by preservative free ofloxacin 0.3%1/h tapered quickly, tropicamide 3/d, oral valaciclovir (3g/day), oral levofloxacin 500 mg/d and therapeutic lens. All cultures for bacteria, virus, amoeba or fungi as well as PCR for HsV1, HsV2 and VZV from corneal smear remained negative. Systemic treatment was consequently stopped, cornea healed quickly and therapeutic lens could be removed after a 3 days. No recurrence has been observed for the next 2 months.
Conclusions
This case suggests that topical moxifloxacin (combined with tobramycin) may inhibit the healing of corneal ulcers and induce a corneal melting leading to perforation.

• S025
Mushroom keratoplasty

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Purpose
To report the visual out comes and graft survival rate of mushroom keratoplasty using femto second laser for the treatment of full thickness cornea opacities and healthy endothelium
Methods
retrospective chart view of 23 eyes(low risk of immunologic reactions n=12; high risk n=11)
undergone femtosecond assisted mushroom keratoplasty .
The mushroom shaped graft consisted of a large top hat (9mm diameter+250 microns in thickness) and small stalk (6-6.5 mm) .
the wavelight FS200 laser parameters used on this platform for the donor and recipient corneas are described.
Outcome measures were BCVA best corrected visual acuity refraction , corneal topography,endothelial cell density , graft rejection and graft failure at 1,3,6 and 12.
Results
Average follow up was 9 months(range 6_15) months . All grafts were clear at the last follow up visit.
Excluding eyes with pre existing ocular co_morbidities
the percentage of patients achieving BCVA of 20/40 or better at 1,3,6 and 12 months was 66,7%,90.50%,95,2% and 100% ,respectively .
at last follow up the refractive cylinder was 6 diopters (D) or less in all eyes, averaging 3.7 D.
two eyes (8,7%) had rejection that were easily reversed with topical steroids
Conclusions
femtosecond _assisted mushroom keratoplasty (FAMK) shows faster visual recovery ,better visual acuity and limited postoperative astigmatism with no increase risk of rejection .

• S026
Confocal characterization of recurrent corneal erosion syndrome suspects

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Purpose
To characterize and differentiate recurrent corneal erosion syndrome (RCES) suspects according to cytological findings using in vivo corneal confocal microscopy (IVCM).
Methods
We performed IVCM (Rostock Cornea Module, Heidelberg Engineering Retina Tomograph III) in 58 patients recommended to outpatients clinic with symptoms of recurrent corneal allodynia. First, patients underwent slit-lamp examination with anterior segment photographs. The IVCM was performed with an examination frame of 400x400 µm. Screening, full-thickness corneal scans were performed to evaluate general condition of corneal architectonic. Focal scans aimed to analyze localized changes within corneal epithelium in all corneal quadrants.
Results
From among of 58 analyzed cases, 18 (31%) presented dot-map-fingerprint confocal changes involving epithelial basal membrane. Eight of patients (14%) presented cystic degeneration of epithelial cells, 26 patients were diagnosed with epitheliopathy of inflammatory origin – 13 patients (22%) with Thygesson keratitis and 13 patients (22%) presented features typical for post-adenoviral keratitis. Three patients (5%) suffered from allodynia related to epithelial instability after corneal refractive procedures. There were also 3 (5%) casual cases of allodynia – 1 patient with epithelial squamous cell metaplasia, 1 patient with corneal changes associated with pemphigus vulgaris and 1 patient with post-traumatic neuroma of corneal superficial nerve plexus. The initial clinical diagnosis of RCES was confirmed with IVCM in 34 patients (59%), other 25 patients suffered from recurrent corneal allodynia due to other than RCES causes, mostly inflammatory.
Conclusions
IVCM of corneal epithelium allows differentiating patients with RCES from other causes of recurrent corneal allodynia, which can determine therapeutic decisions.

• S027
Mean shape of the human sclera

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Purpose
To assess the mean shape of the human sclera
Methods
Three-dimensional (3D) maps from the left eye of 27 subjects (26 ± 6 y.o.) were acquired using a corneo-scleral topographer (Eye Surface Profiler). Subjects were asked to open their eyes wide to ensure 360 degrees scleral coverage. For each 3D map, the sclera (maximum diameter 16 mm) and cornea were automatically separated at the level of the limbus, assuming a mean limbal diameter of 12 mm based on recent work. The remaining 3D scleral ring was further fit to a quadratic function, chosen arbitrarily to account for the bulk of surface data. The elevation difference between the original and fit data was calculated. For statistical analysis, sclera was separated in four disjoint quadrants, superior [60,120]°, inferior [240,300]°, nasal [150,210]° and temporal [330,30]°.
Results
Along the horizontal meridian, the temporal aspect of the sclera showed less elevation (mean ± SD: - 240 ± 90 µm) than the nasal aspect (- 60 ± 20 µm), being statistically significant different (paired t-test, p<<0.001). Along the vertical meridian, the inferior aspect of the sclera (- 60 ± 110 µm) showed to be less elevated than the superior aspect (50 ± 100 µm), being statistically significant different (paired t-test, p=0.002).
Conclusions
The sclera is circularly asymmetric. The nasal sclera is higher/flatter, and the temporal sclera is lower/steeper. The insertion of the eye muscles on the eyeball could justify these differences. Scleral shape affects all contact lens designs that interact with the corneo-scleral junction and beyond. Thus, these findings have an important potential impact on contact lens fit.

• S028
The impact of daily disposable soft contact lens wear on tear film surface quality over a three month period

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Purpose
To study the changes in Tear Film Surface Quality (TFSQ) on a Silicon Hydrogel (SiHy) and a Hydrogel (Hy) daily contact lens (CL), during a follow-up period of three months.
Methods
Forty-six subjects aged 25.5 ± 4.3 (mean ± standard deviation) years with a refractive error limited to ±4.50 spherical and ±0.75 cylindrical dioptres were recruited. Based on a pre-clinical analysis which took into account visual acuity (VA), comfort, and fitting, 31 subjects were fitted with SiHy and 13 with Hy lenses. TFSQ was studied based on measurements of the first and the mean non-invasive keratography tear break up time (F/M–NIKBUT). All measurements were acquired at baseline, post four hours (4h) and three months (3m) of CL lens wear. Ocular Surface Disease Index (OSDI) questionnaire was also completed.
Results
The results of the OSDI questionnaire showed an average improvement of 3.09 and 4.16 units for 3m visit for SiHy and Hy lens, respectively. Nevertheless, this improvement was not statistically significant (p=0.144 and p=0.215). For F–NIKBUT, there was no significant difference between 4h and 3m measurements (p=0.490 and p=0.588 for SiHy and Hy lens, respectively). For M-NIKBUT, there was no significant difference for SiHy and Hy groups between baseline and 4h (p=0.052 and p=0.110, respectively). However, there was a significant difference between baseline and 3m for SiHy group (p=0.009) but not for the Hy group (p=0.376). Lastly, no significant differences were observed between 4h and 3m M-NIKBUT measurements for both lenses (p=0.746 and p=0.273 for SiHy and Hy lens, respectively).
Conclusions
The results indicate that estimates of 4h of lens wear NIKBUT can be used to predict those at a 3m visit. Also, Hy lens appeared to have less impact on TFSQ than the SiHy lens.

• S029

Exploratory ocular surface distribution studies of Azithromycin formulations based on semifluorinated alkanes

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Purpose

Purpose: Azithromycin is an antimicrobial agent with broad spectrum activity and anti-inflammatory properties. The aim of this study was to investigate the ocular distribution of azithromycin after a single topical instillation of a new semifluorinated alkane (SFA) based formulation in rabbits.

Methods

Methods: Rabbits were treated with either a single administration of 1.5% or 3% SFA-azithromycin suspensions. Due to the low surface and interface tension of the SFA, and its excellent spreading properties, droplet size is smaller compared to other ophthalmic formulations which lead to a low instillation volume of ~11 µL. Tears (T), aqueous humor (AH), cornea (C), bulbar conjunctiva (BCJ), and eyelids (EL) from individual eyes were collected up to 144 h post dosing and drug concentrations were measured using a validated LC-MS/MS method.

Results

Results: Following a single topical instillation of SFA-azithromycin in rabbit eyes, both formulations were macroscopically well tolerated. The highest exposure was found in the general order of EL > T > C > BCJ > AH. The obtained values were compared with data from a similar experiment of a marketed 1.5% azithromycin formulation in medium-chain triglycerides1, with a single instillation of 25 µL. The comparison showed that azithromycin exposure after administration of 1.5% SFA-azithromycin formulation was similar to the marketed formulation despite the lower absolute dose.

1: Amar et al, Current Eye Research, 33: 149-158, 2008

Conclusions

Conclusion: The preservative-free, multi-dose SFA-azithromycin formulation was well tolerated. Both concentrations resulted in adequate and long-lasting azithromycin levels in T and EL, C and BCJ. Based on these results this azithromycin formulation may lead to a new therapeutic well-tolerated option in treating ocular surface bacterial infections.

Conflict of interest

Any post or position you hold or held paid or unpaid?:
K. Fischer, R. Grillenberger, S. Krösser are paid by Novaliq GmbH.

• S031

Association of incidental epithelialization of corneal endothelium with endothelial barrier impairment

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Purpose

To identify patients with incidental epithelialization of corneal endothelium (IECE) detected in in vivo confocal microscopy (IVCM) and analyze its association with corneal decompensation.

Methods

We performed a retrospective analysis of IVCM (Rostock Cornea Module, HRT III) scans of 327 patients treated in outpatients clinic for various corneal diseases. After identification of cases with IECE, visual acuity (VA), central corneal thickness (CCT) data, endothelial cell density, as well as slit-lamp photographs were collected. CCT measurements were obtained using Pentacam (Oculus).

Results

From among of 327 IVCM examinations, IECE was visible in 8 patients associated with Posterior Polymorphous Corneal Dystrophy (PPCD) in 3 out of 6 patients with an IVCM diagnosis of PPCD; Fuch's Endothelial Dystrophy (FED) in 3 out of 12 FED patients with available IVCM scans. One patient was diagnosed with unilateral IECE after the incident of facial UV-light burn (tanning salon) with the unilateral mild burn of the ocular surface. One patient presented unilateral IECE in superior half of the cornea due to epithelial ingrowth after cataract surgery. PPCD patients with presence of IECE developed corneal edema and greater endothelial cell loss, in contrast to age-matching PPCD patients without IECE. Patients with FCD or cornea guttata developed corneal decompensation and visual impairment at the earlier age (before 50 y.o.) than FCD patients without IECE. Advanced IECE observed in the patient with ingrowth syndrome, as well as epithelial metaplasia after UV-light burn resulted in severe visual impairment.

Conclusions

Diagnosis of corneal diseases should be supplemented by IVCM examination. IECE observed in IVCM could be considered as a prognosis factor of visual impairment in corneal endothelial diseases, however it requires more research.

• S030

Softacort®, preservative-free Hydrocortisone 0.335% drops: A new anti-inflammatory drop with minimal effects on intraocular pressure

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Purpose

The aim of this study was to compare the changes in intraocular pressure (IOP) after instillation of a new preservative-free hydrocortisone 0.335%(Softacort®), prednisolone 1% (Inflanefrane® Forte), lotepredno l etabonate 0.5% (Lotemax®) and rimexolone 1% (Vexol®) in comparison with dexamethasone 0.1% (Maxidex®) in a rat model of glucocorticoid-induced ocular hypertension

Methods

Sixty albino female rats were divided into 5 treatment groups and drops administered twice daily from Day 1 to Day 36. Clinical examination, body weight, and IOP measurements were assessed once weekly during 5 weeks.

Results

Animals treated with Softacort®, Lotemax® or Vexol® had a similar body weight gain. Inflanefran® Forte-treated animals showed a lower body weight gain. Maxidex®-treated animals gained weight up to 7 days but there after lost weight as expected. Animals treated with Softacort®, Lotemax®, Inflanefran® Forte or Vexol® had a similar IOP profile with a slow increase in the mean IOP up until Day 15, and then stabilization at +2 mmHg above baseline throughout the remainder of the study Maxidex®-treated animals showed, as expected, an increase of the mean IOP until Day 36 reaching +4.4mmHg and progressively increasing.

Conclusions

This study shows significant differences in the IOP rise and therefore greater safety of this new preservative-free hydrocortisone and other soft corticoids when compared to Maxidex. Twice daily instillation of Softacort® induced a slight IOP elevation which stabilized after 2-weeks whilst dexamethasone treatment led to a significant continuing IOP increase and drastically reduced body weight gain. Thus, Softacort®, a preservative free hydrocortisone 0.335%, shows a good balance between efficacy and minimal side effects and has just obtained the Marketing Authorization in Europe.

Conflict of interest

Any consultancy arrangements or agreements?:
Consultancy fees from Thea
Any Lecture fee paid or payable to you or your department?:
Speakers fees from Thea

• S032

Femtosecond assisted intracorneal segments implantation for mild to moderate keratoconus: long term Results

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Purpose

To describe the 2 year results of femtosecond assisted intracorneal segments implantation for the treatment of mild to moderate keratoconus with the use of a femtosecond laser.

Methods

Prospective case series including 4 eyes of 4 consecutive patients with keratoconus. Patients where implanted with KC Solutions intrastromal segments (IS). Patients' assessment included visual acuity measurement, manifest refraction, clinical examination and corneal topography and tomography. IS implantation was scheduled in patients with unsatisfying corrected visual acuity (CDVA) and contact lens intolerance. Planning of the operation was done based on the topography and refraction based on nomogram provided by the IS manufacturer. IS were implanted in intracorneal pocket created with the FS200 femtosecond laser. Comparisons were made between pre- to postoperative values with the Wilcoxon signed-rank test.

Results

Preoperative average steep keratometry was 48.45D (range 45.6 to 51.6), whereas at 2 years postoperatively it was 46.73 (44.8 to 48.7), ($p<0.05$). Preoperatively corneal astigmatism on average was 4.95D (2 to 9.1) and refractive astigmatism was 3.94D (2 to 9), whereas postoperatively average corneal and refractive astigmatism was 2.75 (1.2 to 6) and 1.87 (range 0,5 to 5) ($p<0.05$ in both comparisons). CDVA improved in all cases by 1 to 2 lines of Snellen visual acuity. Average spherical equivalent refraction was -3.22 (-1.87 to -4.5) preoperatively, and postoperatively it was reduced to -1,81 (-0.50 to -3,5) ($p<0.05$). No statistically significant differences were found between the last and 6th month follow up results.

Conclusions

According to our pilot long term study, Implantation of KC Solutions intrastromal segments with the aid of a femtosecond laser improved all patients' topographic and refractive astigmatism, visual acuity and refraction.

• S033

Complete corneal ring (MyoRing) implantation combined with corneal collagen crosslinking in keratoconus treatment

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Purpose
To evaluate functional results of complete corneal ring (MyoRing) implantation with corneal collagen crosslinking (CXL) for progressive keratoconus
Methods
MyoRing implantation with corneal CXL was performed in 39 eyes with progressive keratoconus of the II-III disease degree according to the Amsler classification. Implantation of a MyoRing in the corneal pocket was performed using a PocketMaker microkeratome and corneal intrastromal implantation system. Saturation of the cornea was performed with a solution of 0.1% riboflavin injected into the corneal pocket through the incision tunnel within 10-15 minutes. Standard surface UV irradiation (370 nm, 3 mW/cm2) was carried out for 30 minutes. The follow-up was 36 months.
Results
Significant improvements in uncorrected distance visual acuity and corrected distance visual acuity were observed. Keratometry was reduced for 9.43 D, the spherical equivalent decreased from from 9.43 D to 6.25 D. The cylinder decreased to 3.31. Corneal thickness decreased from baseline (from 426.93±46.58 µm to 401.24 ± 39.12 µm) 36 months postoperatively, which corresponds with pachymetry reduction after conventional CXL. Dynamic observation after 36 months showed stabilization of clinical and functional results.
Conclusions
Combination of CXL and MyoRing implantation was effective for keratoconus treatment. Complete corneal ring implantation combined with corneal collagen crosslinking allows not only correct the keratoconus followed ametropia but also slow down the progression of the disease.

• S034

Corneal clarity measurements in patients with myopia undergoing laser assisted in situ keratomileusis and laser assisted sub-epithelial keratectomy

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Purpose
To compare the preoperative and postoperative corneal densitometry of patients undergoing Laser Assisted in Situ Keratomileusis (LASIK) and Laser Assisted Sub-epithelial Keratectomy (LASAK) and to determine how result differed between the 2 types of surgery.
Methods
A retrospective and comparative study was performed at Manchester Royal Eye Hospital,UK. Preoperative and postoperative corneal densitometry data were collected from the Oculus Pentacam. The data were taken at 3 corneal depths (anterior,centre and posterior) and at 3 corneal annulus ring diameter (0-2 mm, 2-6 mm and 6-10 mm). Postoperative data were collected at the time 6 weeks, 3 and 6 months post treatment. Quality of vision pre and post-surgery was determined by BCVA.
Results
Data of 60 eyes from 16 LASIK and 14 LASEK patients were collected with a mean age of 37.06±10.0 and 37.7±6.6 respectively. There was statistically significant increase of corneal densitometry in all concentric zones in all corneal layers after 6 weeks in the LASIK treatment group ($p<0.05$). There was a statistically significant increase in densitometry after LASEK but only in the central and posterior layers at all concentric zones ($p<0.05$). Pre and Postoperative BCVA did not significantly differ after LASIK but found statistically difference at 6 weeks and 3 months in post LASEK ($p<0.05$).BCVA post treatment was significantly different between groups at 6 weeks ($p<0.0001$) and 3 months ($p=0.001$).
Conclusions
Corneal wound healing plays an important role in determining corneal transparency and may be responsible for an increase in corneal haze following refractive surgery.This response differs based on the type of procedure used shown by the increased haze in the anterior layer of the LASIK group which corresponds to the region where the flap was cut which will lead to increased would healing and inflammation.

• S035

Recombinant human heat shock protein 27 can inhibit ultraviolet B-induced differentiation in pterygial-derived fibroblast

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Purpose
To investigate the effect of recombinant human heat shock protein 27 (rhHSP27) on the differentiation of human pterygial-derived fibroblast.
Methods
Human conjunctival and pterygial fibroblasts were isolated and cultured from specimens of normal conjunctiva and pterygium head, which were donated during pterygium excision. Cultured conjunctival and pterygial fibroblasts were exposed to 20 mJ/cm2 of ultraviolet-B (UVB) irradiation with and without 4 ug/mL rhHSP27 pre-treatment. Western blot analyses of α-smooth muscle actin (α-SMA), a marker for myofibroblast, were performed in each group and quantified using Image Gauge 4.0 software. The ratios of α-SMA / GAPDH and phosphorylated HSP27 / GAPDH were compared.
Results
The α-SMA level in Pterygial fibroblasts showed 2.85 ± 0.11 fold greater than that of normal conjunctival fibroblasts ($P<0.001$). The level of α-SMA was increased by 1.92 ± 0.02 times ($P<0.001$), when normal conjunctival fibroblasts were exposed to UVB irradiation without rhHSP27 pre-treatment. However, when normal conjunctival fibroblasts were exposed to UVB irradiation with rhHSP27 pre-treatment, the fibroblasts demonstrated 0.82 ± 0.04 fold smaller α-SMA level than control did ($P=0.04$).
Conclusions
The rhHSP27 revealed inhibitory effects on the UVB irradiation-induced differentiation from normal conjunctival fibroblasts to pterygial myofibroblast. The rhHSP27 can be a preventive treatment against pterygium growth.

• S036

Corneal clarity after Descemet membrane endothelial keratoplasty versus Descemet stripping endothelial keratoplasty: Two-year outcomes

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Purpose
To compare the course of Scheimpflug corneal densitometry (CD) after Descemet membrane endothelial keratoplasty (DMEK) versus Descemet stripping automated endothelial keratoplasty (DSAEK) versus age-matched controls.
Methods
From two consecutive series of 130 DMEK and 49 DSAEK cases, 54 DMEK and 25 DSAEK cases without prior corneal surgery, complicated intraoperative or postoperative course or vision-limiting ocular comorbidities were included in this study. Pseudophakic eyes of age-matched subjects were recruited as controls (n=20). Scheimpflug CD of the optically relevant zones (0-2mm and 2-6mm), best-corrected visual acuity (BCVA) endothelial cell density (ECD) and central corneal thickness (CCT) were evaluated preoperatively and at 3, 6, 12 and 24 months postoperatively.
Results
CD was significantly lower after DMEK at 3 and 6 months compared to DSAEK ($P\leq0.012$). The two groups reached similar levels of CD at 12 and 24 months after surgery ($P\geq0.056$). Compared to healthy pseudophakic controls, central CD at 24 months after DMEK did not differ significantly ($P=0.152$). Postoperative BCVA was significantly higher after DMEK for every examination time point compared to DSAEK ($P<0.001$). ECD was similar in both groups ($P\geq0.081$).
Conclusions
The first 6 postoperative months CD was lower and BCVA higher after DMEK compared to DSAEK. Notably, although CD reached similar levels in the midterm after both DMEK and DSAEK, BCVA remained significantly better after DMEK. Two-year CD after DMEK was similar to CD of healthy pseudophakic eyes indicating an excellent restoration of corneal clarity in the midterm.

• S037

Short-term in vivo morphologic changes of amniotic membrane after fibrin glue-assisted pterygium surgery on anterior segment optical coherence tomography: a case series

LIM S

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Purpose

The evaluations of morphologic changes of amniotic membrane (AM), even after successful AM transplantation surgery without complications, may be difficult. Moreover, there was no report regarding morphologic changes after fibrin glueassisted AM transplantation with pterygium excision. Here, we highlight and describe the use of spectral domain optical coherence tomography (OCT) for the evaluation of the morphologic features of amniotic membrane (AM) and of associated in vivo structural changes after fibrin glue-assisted pterygium surgery.

Methods

Retrospective Case Series

Results

All three patients underwent cryo-preserved AM transplantation using the permanent inlay technique (epithelial side up) with fibrin glue. In vivo morphologic changes of AMs were evaluated using a spectral domain OCT equipped with an anterior segment imaging module (RTVue-100, Optovue, Inc., Fremont, CA, USA). Anterior segment OCT examinations demonstrated morphologic changes, that is, re-absorption of fibrin glue or subconjunctival hemorrhage, migration of epithelium, and integration of AM into sclera, of AMs over first postoperative months.

Conclusions

Anterior segment OCT might provide additional structural information, including quantitative and qualitative data, on AMs after pterygium surgery as compared with conventional slit-lamp examination.

• S038

Ultraestructural analysis of human pre-Descemet's tissue

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Purpose

To analyze the elastic component of the posterior corneal stromal using electron transmission microscopy and inmunohistochemical techniques.

Methods

Four pieces of cornea and sclero-corneal angle were included in the study which were obtained from three deceased donors. The mean age was 57,67 years. From each piece a sample of tissue was processed for transmission electron microscopy examination and another sample was paraffin-embedded for their study using optic microscopy. The optical sections were immunostained with anti-fibrillin1 antibody.

Results

The ultrastructural study showed that the posterior corneal stroma was comprised of fibrillary collagen lamellae.The number of lamellae vary from 3 to 10 in a random distribution from the line formed by the last queratocytes to the Descemet´s membrane. Mainly, the lamellae were separated by type IV collagen and elastic tissue. There were no differences between fibrillary collagen lamellas of the stroma anterior and posterior to the last line of queratocytes.In all cases, an electrodense band was observed alongside being closely related to the Descemet's membrane. This band was interrupted with gaps between the interruptions that vary in size and shape, like stitching. This band was continued towards the trabecular meshwork, where this material was located principally inside the trabecular sheets. This material appeared to be elastic tissue, this was confirmed by inmunostaining with anti- Fibrillin 1 antibody.

Conclusions

Posterior stroma does not constitute a special layer of the cornea. However, a band of elastic tissue is observed close to the Descemet membrane that is continued into the trabecular meshwork. This elastic band could contribute notably to corneal biomechanical properties.

• S039

Early signs of microglial activation in mice retinas contralateral to experimental glaucoma: quantitative analysis of cells number, processes retraction and reorientation

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Purpose
To quantify retinal microglia signs of activation after 24 h of unilateral laser-induced ocular hypertension (OHT) in OHT-eyes and their contralateral eyes.
Methods
Albino Swiss mice were divided into two groups, naïve (n=6) and lasered (n=6). Retinal whole-mounts were immunolabeled with anti Iba-1 to quantify the: i) number of microglial cells in the photoreceptor layer (PRL), outer plexiform layer (OPL) and inner plexiform layer (IPL); ii) the area of the retina occupied by Iba-1+ in the nerve fiber layer-ganglion cells layer (NFL-GCL) and; iii) the arbor area of microglial cells in the OPL and IPL. iv) the number of microglial vertical processes connecting the OPL and PRL.
Results
In OHT eyes and contralateral eyes had no significant differences in cell number with respect to naïve. OHT eyes presented a significant decrease in microglial arbor area in the OPL in comparison with control ($p<0.01$) and in the IPL in comparison with control and contralateral eyes ($p<0.01$ and $p<0.05$ respectively). However the retinal area occupied by Iba-1+ cells in the NFL-GCL was significantly increased: i) in both contralateral and OHT eyes with respect to control ($p<0.01$ in both instances); and ii) in OHT eyes with respect to contralateral eyes ($p<0.05$). In contralateral untreated eyes, the number of microglial vertical processes connecting the OPL and PRL were significantly increased in comparison with control and OHT eyes ($p<0.01$ and $p<0.05$ respectively).
Conclusions
At 24h, laser-induced OHT produces a reactive non-proliferative microgliotic response both in OHT eyes and in contralateral untreated eyes. Whether this response favors neuroprotection or neurodegeneration needs to be clarify.

• S040

Comparative study of retinal nerve fiber layer and ganglion cell complex thickness between Korean patients with unilateral exfoliation syndrome and normal control

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Purpose
To compare retinal nerve fiber layer (RNFL) thickness and ganglion cell complex (GCC) thickness by using spectral domain optical coherence tomography (OCT) in unilateral exfoliation syndrome (XFS) and age matched control.
Methods
This prospective case control study include total of 54 eyes of 27 unilateral XFS patients and 27 age matched control subjects. The retinal nerve fiber layer and ganglion cell complex measurements were performed using spectral domain OCT (RT-Vue 100, Optovue) after pupillary dilation. Statistical analyses were performed using SPSS for Windows software version 18.0. Independent t test and chi-square tests were used to compare baseline characteristics of unilateral XFS and Control.
Results
Mean age of XFS was 73.3 years and Age-matched control was 74.3 years. Both group demonstrated male preponderance; however, there was no statistical difference. Average circumpapilary RNFL and inferior RNFL were significantly thinner in XFS than healthy age matched control. Moreover, average GCC and inferior GCC were thinner in XFS than control.
Conclusions
Patients with XFS without visual field defect showed thinner RNFL thickness and GCC thickness. This findings implicit XFS itself might be an risk factor for development of glaucomatous optic disk and retinal nerve fiber layer damage.

• S041

Efficacy and safety of the pars plana clip in the Ahmed valve device in patients with refractory glaucoma.

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Purpose
To evaluate the efficacy and safety of the pars plana clip (PPC) in the Ahmed valve tube PC7 inserted via the pars plana in patients with secondary refractory glaucoma.
Methods
Prospective and interventional case series that included 8 patients with secondary refractory glaucoma. The pars plana vitrectomy and the implant of the modified tube were performed during the same surgery. Control of intraocular pressure (IOP) and the development of intra- and postoperative complications were evaluated during the follow-up.
Results
Follow-up time was twelve months in all the patients. Control of IOP was achieved in 85% of patients, and 75% needed no antiglaucoma treatment. The complications that occurred were transient hypotony in two cases, choroidal detachment in two cases, and one case of intraocular hemorrhage and one case of hyphema. No case of tube extrusion was observed.
Conclusions
Our clinical experince suggests that implantation of the Ahmed tube modified with the PPC via the pars plana is safe and effective in patients with secondary refractory glaucomas.

• S042

Three year results of iStent + Phacoemulsification cataract surgery for glaucoma

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Purpose
To evaluate long-term safety and efficacy of iStent trabecular micro-bypass stent implantation + cataract surgery (phaco) in glaucoma: A retrospective, interventional, open label study.
Methods
Cases of glaucoma who had phacoemulsification surgery planned, were included. Preoperative and postoperative evaluations included intra-ocular pressure (IOP), topical ocular hypotensive agent use, best corrected visual acuity, perioperative complications and adverse events.
Results
A single trabecular micro-bypass iStent was implanted at the time of phacoemulsification cataract surgery. A temporal incision approach was used in all cases. The results from 35 eyes in 25 patients were analysed for 3 years postoperatively. 49% (n=17) were male. Mean age was 80 ± 7 (SD). 3 eyes had angle closure with previous peripheral iridotomies.
Mean preoperative IOP was 18.5 ± 3.2 mmHg; this was significantly reduced at 12 months ($p=0.008$), 24 months ($p=<0.001$) and 36 months ($p=<0.001$). Mean IOP was 15.9 ± 4.5, 15.0 ± 4.5 and 15.6 ± 3.6 respectively. The mean number of preoperative IOP lowering agents was 2.3 ± 1.0 and 2.5 ± 1.0 at 36 months. This was not significantly reduced at any follow up time period. Secondary interventions were required in three eyes. Cyclodiode laser was required in 2 patients. ALT was carried out in 2 eyes. There were no significant intraoperative complications and no post-operative hypotony. At 36 months, visual acuity was ≥6/12 in 29 eyes (83%).
Conclusions
Trabecular micro-bypass stent implantation during cataract surgery is safe and effective for patients with glaucoma. We measured a sustained reduction in IOP over 36 months in the real world clinic setting.

• S043

Supracilliary Micro-Stent (CyPass®) is associated with lack of disease progression and minimum usage of IOP lowering medications in patients with POAG 2-Years Post-Implantation

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Purpose
Glaucoma is a progressive disease marked by deterioration in the visual field, optic nerve cupping and nerve fiber layer thinning. Glaucoma treatment is aimed at slowing disease progression through control of intraocular pressure (IOP). Minimally invasive glaucoma surgery (MIGS) has become available as a treatment modality offering effective IOP lowering without the high rate of complications associated with traditional glaucoma surgery or the reliance on strict patient adherence required for pharmacological intervention.
Methods
One such MIGS device, a supracilliary micro-stent (MS), implanted during cataract surgery, has recently completed a large 2-year trial in the US (COMPASS trial) - 505 patients were randomized to MS (n=374) or cataract surgery control (n=131).
Results
MS showed sustained 24-month efficacy > than phacoemulsification alone. Importantly, visual fields (VF) did not progress with MS treatment over control (baseline and 2-year mean deviation [MD] -3.4, -3.2 MS; -3.7, -3.2 control) while the percent of patients requiring IOP lowering medications was 15.2% for CyPass group versus 40.9% for control. The percentage of patients with VF progression (≥2.5 dB MD decrease) was 6.7% for MS and 9.9% for control. There was a three-fold lower incidence of disc hemorrhage for MS vs. control (0.5% vs.1.6%), fewer IOP spikes (≥10 mmHg) over the 30-day post-op period (6.4% vs. 20.6%), and fewer subsequent glaucoma surgeries (0.6% vs.3.8%).
Conclusions
While these are post-hoc descriptive observations, the data suggest that the benefits of reliable, effective, sustained IOP-lowering through the use of a supracilliary micro-stent implant may include limiting disease progression in patients with mild-to moderate primary open-angle glaucoma. Additional studies aimed at monitoring progression in patients with the micro-stent are warranted.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Medical Affairs Lead Surgical Glaucoma EMEA at Alcon

• S044

Follow-up of non-complicated filtering surgeries under ambulatory care with no control at Day 1

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Purpose
In most cases, filtering glaucoma surgery is performed as an outpatient procedure and recommendations suggest performing follow-up at least at Day 1, Day 8, Day 15 and Day 30. As many of our patients have difficulties to come to follow-up and because of the economical cost of medical transportations we decided to evaluate the results of a group of patients without clinical control at Day 1.
Methods
Retrospective monocentric study in the department of ophthalmology. All patients (naïve of surgical treatment for glaucoma) underwent of surgery of a primary open-angle glaucoma in an ambulatory care unit between May 2014 and July 2016. A nurse made a phone call to the patients at Day 1. Clinical controls were due at Day 5 and Day 21. In case of problems detected during the phone call, patients were examined earlier.
Results
One hundred and forty-four eyes (126 patients) were consecutively included in our study. The mean preoperative IOP was 20,4+/-6,4mmHg. After the phone call, only five patients were examined before the first planned control at Day 5. For 3 of them the examination revealed the presence of a hyphema and their topical treatment was changed. The others two patients had no medical modifications. At Day 5, the mean IOP was 10,6 +/- 5,9 mmHg. Thirty-two eyes (22,2%) needed a change in their treatment at Day 5. The mean IOP at Day 21 was 12,9 +/- 4,6 mmHg. Our success rate (IOP<21mmHg with no topical) at day 21 was 95,6%.
Conclusions
We replaced the Day 1 control with a phone call. We didn't notice a substantial rate of complications. The criteria of success of a filtering glaucoma surgery vary according to the different articles in the literature. Our success rate seems to be similar to those we find in the literature and may suggest that the control at Day 1 is not necessary if the surgery is not complicated.

• S045

IOP-lowering efficacy of prostaglandin analogues adjunctive to a Supercilliary Micro-Stent (CyPass®)

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Purpose
Minimally invasive glaucoma surgery (MIGS) procedures are proving to be a safe, efficacious alternative to medical management of glaucoma. Most frequently employed concomitantly with cataract surgery, they add little if any additional risk while, in many instances, decreasing or even eliminating the need for ocular hypotensive medication. The optimum target intraocular pressure (IOP) varies from patient to patient and is dependent on multiple factors including degree of glaucomatous damage, rate of progression, age and race, central corneal thickness. The purpose of this work is to investigate IOP lowering effect of PGAs added to MS in patients with mild to moderate POAG.
Methods
In a recent large randomized controlled trial (the COMPASS Trial; n=505, 374 micro-stent, 131 control), the supracilliary micro-stent (MS) used in conjunction with phacoemulsification demonstrated superior IOP lowering effectiveness at 24 months compared to phacoemulsification alone (CON) and allowed 85% of patients to remain off of all ocular hypotensives. Despite this success, 8 (2%) patients in the MS group and 15 (11%) in the CON group required a prostaglandin (PGA) in addition to the MS to reach their IOP target. Mean pre-PGA IOP for MS and CON groups were 24.4 and 18.7 mmHg.
Results
Addition of the PGA resulted in mean percentage IOP reductions of 23% and 18.5% for the MS and CON groups respectively. Measurement of IOP post-PGA was at 24 months post-surgical visit so that the duration of treatment with the PGA was variable but was initiated over 3 months earlier, on average, in the CON group than in the MS group.
Conclusions
Addition of a PGA in MS patients provided IOP reductions at least as good and numerically better than for CON patients, albeit somewhat less than IOP reductions observed (~ 30%) for PGA monotherapy when used in the overall OAG population.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
Medical Affairs Lead Surgical Glaucoma at Alcon

• S046

Ultrasound ciliary plasty to treat glaucoma: efficacy and safety results on 152 patients

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Purpose
To evaluate the efficacy and safety of the Ultrasound Ciliary Plasty (UCP) procedure using Focused ultrasound with second generation probe on a consecutive series of 152 glaucoma patients.
Methods
Prospective clinical series of 169 eyes of 152 patients with primary and secondary open angle or angle closure glaucoma treated between April 2015 and September 2016 in 2 University Hospitals. Procedures were conducted with second generation therapy probe comprising 6 piezoelectric transducers, with 8 seconds exposure time per transducer (standard protocol). Complete ophthalmic examinations were performed before the procedure, and at 1 day, 1 week, 1, 3, 6 and 12 months after. Primary outcome was IOP reduction compared to baseline. Secondary outcomes were success rate (defined as IOP reduction from baseline ≥ 20% and IOP > 5mmHg without adding medication compared to baseline), vision-threatening complications, hypotensive medication use, complications, and re-interventions.
Results
No major intra- or post-operative complications occurred. Ocular exam did not reveal lesions of ocular structures other than ciliary body and no or few signs of anterior chamber inflammation. Semi-mydriasis was observed on fifteen eyes, reduced or resolved in a few weeks/months. Intraocular pressure was significantly reduced from a mean preoperative value of 27.1 ± 9.3 mmHg (3.1 hypotensive medications) to a mean value of 19.1 ± 7.6 mmHg (3.2 hypotensive medications) at last follow-up, corresponding of a mean IOP reduction of 27%. Nineteen patients were re-treated using focused ultrasound, 7 patients were considered as failure and treated by filtering surgery, and 8 patients with Diode laser cyclo-destructive procedure.
Conclusions
Ultrasound Ciliary Plasty using High Intensity Focused Ultrasound is an effective method to reduce intraocular pressure in patients with glaucoma.
Conflict of interest
Any consultancy arrangements or agreements?:
Consultant of EyeTechCare

• S047

Computational fluid dynamics simulations of aqueous flow through the CyPass® Micro-Stent

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Purpose
In normotensive eyes, aqueous humor is eliminated through Schlemm's canal and through the iris root in approximately equal fractions. But in glaucomatous eyes, the hydraulic resistance of the trabecular meshwork restricts outflow through the canal and causes the IOP to rise. The CyPass® supraciliary micro-stent is a device implanted by minimally invasive glaucoma surgery (MIGS) which is designed to reduce IOP by allowing an alternative pathway for aqueous humor outflow. The device, a fenestrated polyimide tube, is inserted between the sclera and the ciliary muscle creating an adjacent fluid space which communicates directly with the suprachoroidal outflow pathway.
Methods
To better understand and illustrate the mechanism of action for this device, computational fluid dynamics simulations of aqueous flow were conducted in human eye models with and without implanted devices. The configuration of the device and fluid space in the eye was obtained from a separate mechanical simulation of device implantation using an explicit solver. Hydraulic resistances of the vitreous and sclera were obtained from the literature.
Results
The resistances of the trabecular meshwork and ciliary muscle were adjusted to produce an IOP of 24.4 mmHg (the mean untreated IOP in the COMPASS trial) and a suprachoroidal elimination fraction of 80%. With the device implanted the hydraulic resistance of the fluid in the space adjacent to the device was reduced ~4 orders of magnitude to achieve the post-surgical IOP of 16.8 mmHg observed in the COMPASS study. It was found that the device reduces IOP by decreasing the overall resistance of the eye to hydraulic flow by more than 30%.
Conclusions
The model confirms that substantial IOP lowering is achievable through aqueous egress via a supracilliary stent even when there is substantial trabecular resistance.
Conflict of interest
Any post or position you hold or held paid or unpaid?:
All authors are Alcon employees thats own Cypass properties

• S049

Clinical manifestations of reverse pupillary block after scleral-fixated intraocular lens implantation: Pre- and post-laser peripheral iridotomy

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Purpose
To present the clinical features and intraocular pressure (IOP) changes of patients with reverse pupillary block (RPB) after scleral fixated intraocular lens (IOL) implantation treated with laser peripheral iridotomy (LPI).
Methods
A chart review of patients presenting with elevated IOP and RPB after sclera fixated IOL implantation was carried out. LPI was performed in 5 eyes of total 6 eyes included in the study. Ultrasound biomicroscopy (UBM) and Goldmann applanation tonometry (GAT) was also performed before and after laser treatment.
Results
Five men who underwent LPI at a mean of 38.2 months (range 9 to 75 months) after scleral-fixated PC IOL implantation were included. Two patients had history of retinal detachment, one subject had a history of trauma, and one patient was previously diagnosed with open angle glaucoma. Angle recession was not observed in all cases. The mean axial length was 24.24±1.14 mm (range 22.86 to 25.44). Scleral fixated IOL implantation with pars plana vitrectomy was performed in all cases. All eyes showed extremely deep anterior chamber with pigment (trace to 1+), a concave iris configuration and angle pigmentation before LPI. On UBM, all eyes showed RPB. After LPI, RPB was resolved on slit lamp examination and UBM in all cases. IOP decreased within normal range (from 29.00±12.37 to 13.40±2.88 mmHg, p=0.043) temporarily, but IOP elevated again (to 30.20±15.39mmHg, p=0.068) few weeks after LPI and all patients needed IOP lowering medications.
Conclusions
LPI is effective for relieving the RPB. But, in some patients, IOP was still elevated and IOP lowering eye drops were needed persistently. Even though RPB is reloved, regular check up of IOP after LPI is recommended. Also it is necessary to consider the possibility of previously decreased TM function.

• S048

Trabeculectomy: evaluation of the area exposed to mitomycin C

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Purpose
Mitomycin C (MMC) is used to increase the durability of filtering procedures in glaucoma. However, the ideal time and area of exposure, as well as the associated side effects remain to be fully understood. This study aims to analyse the association of the MMC-exposed area in trabeculectomy with safety and efficacy outcomes.
Methods
Prospective, interventional pilot study of 25 eyes of 25 open-angle glaucoma patients enrolled for a primary trabeculectomy with MMC 0.4mg/ml. The antimetabolite solution was visually highlighted by mixing it with a vital dye (trypan blue 0.1%). The area of MMC application was evaluated using a software analysis program (ImageJ). The primary outcome was the association of surgical intraocular pressure (IOP) lowering efficiency with the area of MMC application. Absolute success was defined as 30% IOP reduction and less than 18 mmHg, with no further medication. Relative success was similarly defined but IOP-lowering medication was used.
Results
The mean MMC-exposed area was 122.6 ± 40.0 mm^2 (median 116mm^2). The mean time of follow-up was 7.2 ± 4.8 months. Mean IOP reduction after trabeculectomy was 12.5 ± 8.0 mmHg with absolute and relative success rates of 60% and 76%, respectively. Overall, no relationship between the MMC-exposed area and parameters of efficacy nor safety were observed (p=0.40). Interestingly, all patients with a MMC exposure area >150mm^2 had a 100% absolute success rate. All failed trabeculectomies (6 eyes, 24% of the total) had a MMC-exposed area <150mm^2. Lastly, only (but one) patients with MMC-exposed area <150mm^2 needed more than on laser suture lysis.
Conclusions
Our study gives an approximate absolute value of the MMC-exposed area during trabeculectomy and suggests it may be related to the hypotensive efficacy, with exposed MMC areas >150 mm^2 being associated with better IOP-lowering outcomes.

• S050

Positional and shape changes of lamina cribrosa after trabeculectomy in pseudoexfoliative and primary open angle glaucoma

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Purpose
To evaluate positional and shape changes of anterior lamina cribrosa (LC) after trabeculectomy and compare them between eyes with pseudoexfoliative (PEXG) and primary open angle glaucoma (POAG).
Methods
The prospective study included 99 eyes (78 PEXG and 21 POAG) planned for trabeculectomy. The morphological parameters of LC and intraocular pressure (IOP) were measured pre- and postoperatively (1 week and 1, 3, 6 and 9 months after the surgery). LC was imaged using enhanced depth imaging spectral domain optical coherence tomography. The mean and sectoral LC depth (LCD), global shape index (GSI), curvedness and curvatures in main meridians were calculated using Morphology 1.0 software. LC parameters were compared across the follow-up visits and in-between PEXG and POAG groups.
Results
The mean IOP reduced in PEXG and POAG eyes after the trabeculectomy at all follow-up visits ($p<0.001$). There was a decrease in mean and sectoral LCD ($p<0.001$), curvedness ($p<0.001$), nasal-temporal (N-T) and superior-inferior (S-I) curvatures ($p<0.001$, p=0.045, respectively) during whole postoperative period. LC GSI did not change significantly postoperatively and stayed in-between a trough and rut shape (p=0.065). There were no differences in the changes of LC morphology between PEXG and POAG eyes (p>0.05); however a tendency of greater reduction in LCD and curvature was observed. The decrease in LCD, N-T and S-I curvatures correlated positively with IOP reduction($\rho=0.326$, $\rho=0.3$, $\rho=0.261$, $p<0.01$ after 1 week, respectively).
Conclusions
Trabeculectomy induced a long term mean and sectoral anterior displacement as well as flattening of LC. However, the overall shape of LC was not affected postoperatively. Despite a potential elastinopathy of pseudoexfoliative syndrome PEXG and POAG eyes did not show differences in positional and shape behaviour of LC after the surgery.

• S051

Interest of analysis of circumpapillary retinal nerve fibers layer thickness at different measurement diameters

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Purpose
The analysis of the circumpapillary retinal nerve fiber layer (RNFL) is a major data in structural analysis in glaucoma. Since OCT development, analysis is on a circle of 3.4mm diameter. This study evaluates the diagnostic capability of an RNFL analysis with different diameter measurements.
Methods
60 glaucomatous and 58 control patients had a complete ophthalmological exam to exclude patients with papillary morphological abnormalities (coloboma, dysversion ...). Others had an OCT Spectralis (Heidelberg Engineering, Germany) of RNFL on 4 circles of different diameters: 3.4, 3.5, 4.1 and 4.7mm. Only one eye per patient was randomly included. The diagnostic capability of each of these circles was analyzed for global mean thickness and for each sector (temporal, temporal-superior, nasal-superior, nasal, nasal-inferior and temporal-inferior) by calculating areas under ROC curve (AUROC).
Results
Patients were comparable for clinical characteristics. In glaucomatous patient group, 58.9% of the patients were early glaucoma (MD> -6dB) and 21.4% of the patients were severe (MD <-12dB). For conventional RNFL measurement (3.4 mm), the temporal-inferior sector had the highest diagnostic capability with an AUROC of 0.916. For the 3.5mm measurement, the global mean thickness of the RNFL had the highest diagnostic capability (AUROC = 0.909). For the 4.1mm measurement, the global mean thickness of the RNFL had the highest diagnostic capability (AUROC = 0.915). For the 4.7mm measurement, the average thickness of the temporal-inferior sector had the highest diagnostic capability (AUROC = 0.909). There was no statistically significant difference between these 4 AUROC.
Conclusions
Regardless of the diameter of RNFL analysis, the diagnostic capability remains very good with no significant difference in patients with normal papillary morphology.

• S052

Screening for glaucoma progression by using non-parametric tests

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Purpose
Automated perimetry still represents the gold standard in long term glaucoma monitoring.Early detection of progression tendency in glaucoma patients is crucial. Purpose of this study was to assess an alternative fast and convenient method compared to GPA (Humphrey Perimeter, Carl Zeiss®) for detecting glaucoma progression shortly after diagnosis-24 months.
Methods
We studied in a longitudinal manner 41 eyes from 41 patients with early open angle glaucoma forms, followed in the first 24 months after diagnosis. Glaucoma was defined according to EGS criteria and a minimum of 5 valid visual fields were required form each patient. All specific glaucoma clinical data were recorded and progression was verified by two distinctive methods: Glaucoma Progression Analysis (GPA) software from Hymphrey Visual Field Analyzer and a non parametric analysis (NPA) according to Wesselink protocol.
Results
In GPA analysis, a positive „event" (progression) was detected in 11/41 eyes, 26.82%. NPA confirmed progression in all GPA cases, but additionally detected 8 moreprogression cases (46.34% eyes). The concordance between tests was good (k=0.596, p=0.000), with positive correlation (Mc Nemar test r=0.652, p=0.008). In the first 2 years after diagnosis, GPA sensitivity was 26.82% and a specificity of 73.33%, whereas NPA sensitivity was 46.34% and comparable specificity 72.41% to GPA. Likelihood ratio for progression (LR) in GPA was 1.00 vs 1.51 for NPA analysis.
Conclusions
NPA tends to overestimate progressor number in a cohort, but its purpose is to allert and orient the clinician on the progression profile of the followed patients. In the first years, the GPA analysis can be highly inaccurate, therefore combining two methods with similar specificity might aid this purpose and ease the glaucoma care management.

• S053

Prospective comparison of global visual field indices and cluster progression in glaucoma and their relationship to structural changes

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Purpose
Glaucoma diagnosis and follow up of progression is often based on structural and functional assessments. This study aimed to assess clustered progression in comparison to global indices and structural measures from HRT and OCT.
Methods
16 eyes of OHT and glaucoma patients with a minimum of 5 visual fields (HFA II i 24-2) over a year were assessed prospectively. MD and VFI rates of progression were used for trend analysis. Linear regression of clusters defined by the Glaucoma Hemifield Test (GHT) was performed based on the mean threshold in each cluster. Rim Area (HRT 3) and mean parapapillary RNFL(SD-OCT) analysis were assessed and correlated with functional clustered measures. Rates of progression were flagged as statistically significant if the gradients over time were negative with p<0.05.
Results
Cluster analysis showed significant progression: 11 of 16 eyes in at least 1 cluster (68.75%) with an average rate of progression of -2.18 ± 2.2 dB/year. RNFL thinning was found in 12 of 16 eyes with an average rate of progression of 2.58 ± 1.43µm/year. 7 out 16 eyes were progressing at HRT RA (43.75%) while 5 of 16 and 6 of 16 were progressing at VF VFI (31.25%) and VF MD (37.5%) respectively. The agreement between GHT Cluster and VF VFI and VF MD was 0.34 and 0.2, respectively. The best agreement was found between GHT Cluster and OCT RNFL (k= 0.61).
Conclusions
Visual field clusters well detected spatial locations of sensitivity loss showing greater sensitivity than global indices (MD; VFI) and better concordance with structural changes .This suggests GHT clusters to be a sensitive method for the early identification of glaucomatous visual field loss.

• S054

Reproducibility of angle metrics in children using hand-held spectral domain optical coherence tomography: intra-observer and inter-observer variability

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Purpose
To evaluate intraobserver and interobserver agreements of anterior chamber angle measurements in children using hand-held spectral domain optical coherence tomography (HH-SDOCT).
Methods
HH-SDOCT (Leica Microsystems Ltd) was used to scan the anterior chamber of 30 normal children (mean age = 5.12 ± 3.5 years, range: 2 days to 12 years). Two independent observers analysed the same B-scan showing both clear nasal and temporal angles using ImageJ. They identified iridocorneal angle landmarks: scleral spur (SS), Schwalbe`s line (SL) and angle recess (AR) and used them to calculate parameters such as trabecular meshwork length (TML), SS angle opening distance (SSAOD), SL angle opening distance (SLAOD), SL angle (SLA), SS limbal distance (SSLD), SL limbal distance (SLLD), trabecular iris surface area (TISA500), nasal to temporal SS distance (SS-SSD) and pupil diameter (PD). The reproducibility of measurements were assessed using interclass correlation coefficients (ICC) and Bland-Altman plots.
Results
Repeated measurements of anterior chamber were calculated in 141 images. Both intra-observer and inter-observer agreements of most measurements ranged from fair to excellent (0.66 to 0.97). Intra-observer and inter-observer ICC for SSAOD, SLAOD, SLA, SSLD, SLLD, TISA500, SS-SSD and PD were 0.74, 0.78, 0.81, 0.72, 0.80, 0.76, 0.96, 0.96 and 0.83, 0.85, 0.77, 0.91, 0.89, 0.83, 0.84, 0.97, respectively. TML reproducibility was poor, ICC were 0.42 and 0.33, respectively. Bland Altman plots showed no significant difference between repeated measurements (P value were >0.05) for parameters with ICC reproducibility ≥ 0.7.
Conclusions
Reproducible quantitative measurements in children using HH-SDOCT was possible with ICC of up to 0.97. Anterior segment OCT could be a potential method in understanding the normal and abnormal ocular development of children.

• S055

UBM evaluation of mechanisms that drive intraocular pressure (IOP) decrease after ultrasound ciliary plasty (UCP) with high intensity focused ultrasound (HIFU), towards a new explanation of the role of uveoscleral pathway outflow

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Purpose
Ultrasound ciliary plasty technique is a new therapeutic approach in refractory glaucoma under maximal hypotensive medication, with coagulation of ciliary body. Our UBM evaluation found an atrophy of the ciliary body (ACB) as well as an widening of the uveo-scleral pathway (UP). We evaluated the correlation between UBM observations and IOP decrease.
Methods
We conducted a prospective, observational, monocentric study, with 24 eyes from 19 patients, recruited between July 2015 and October 2016, undergoing systematic pre-operative and postoperative visits at D7, M1, M3 with IOP measurement and UBM in 8 axes (the 6 ultrasound-treated zones and 2 non-treated zones).The evaluation of the UBM pictures was conducted by 2 experienced surgeons, analyzing the existence or absence of a de novo UP as well as the ACB.
Results
ACB was found to be significant in UBM pictures and predominant in the therapeutic success group (60% of the axes analyzed for at least one of the reviewers for patients with IOP decrease maintained at M3 follow-up versus 46% of axis in case of failure (p=0.17). An opening of the UP was observed in the UBM pictures, observable in 53% of axes with patients in success group versus 45% of axis in patients whose IOP had failed to decrease. UBM found a gradual narrowing of the possible UP during the follow-up in more than half of the axes analyzed irrespective of the IOP result.
Conclusions
The mechanisms of action responsible for IOP decrease after UCP have not been studied in great enough detail so far. Our study highlights several mechanisms contributing to IOP decrease: on the one hand, the decrease of the aqueous humor production by means of atrophy of the ciliary processes; and on the other, a second - and less expected phenomenon - of an increase in aqueous humour outflow due to a wider uveoscleral pathway, clearly visible in UBM pictures.

• S056

Modifications in corneal biomechanics and intraocular pressure after deep sclerectomy

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Purpose
To compare preoperative and postoperative measurements of corneal biomechanical properties and intraocular pressure (IOP) using Goldmann applanation tonometry (GAT) and the ocular response analyzer (ORA, Reichert Inc, Depew, NY) in eyes undergoing deep sclerectomy with implant (DSCI).
Methods
Ninety eyes of 90 glaucomatous patients undergoing deep sclerectomy with SNOPER® implant and and 30 eyes of 30 normal subjects were included were included. Goldmann applanation IOP, central corneal thickness (CCT), and ORA measurements [corneal compensated IOP (IOPcc), Goldmann-correlated IOP (IOPg), corneal resistance factor (CRF), and corneal hysteresis (CH)] were taken the day before deep sclerectomy with collagen implant and on days 1, 8, and 30 and three months after surgery.
Results
Preoperative CH and CRF values of the glaucomatous patients were statistically significantly lower than the values in normal subjects. Corneal hysteresis values increased significantly on day 1 after DSCI, and then showed a statistically significant decrease up to day 30. GAT IOP and all the other ORA parameters changed significantly on day 1 after DSCI, but there was no time effect variation up to 3 months. Only CH showed variations up to 3 months after surgery.
Conclusions
CH statistically increased between preoperative and postoperative day 1 DSCI. On days 8 and 30, the change in CH values was statistically significant.

• S057

Glaucoma in screening of diabetic retinopathy programme

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Purpose
To assess the proportion of new glaucoma suspects among diabetic patients aged 18 years or older attending photographic screening for diabetic retinopathy arranged by the City of Helsinki.
Methods
Two 60 degree monochromatic digital fundus images, one macula and the other disc centered were taken with Canon DF-60 DSi Digital Fundus Camera using a green filter by trained nurses after instillation of mydriatic drops (tropicamide and if needed, cyclopentolate). All images with abnormalities were analyzed by one ophthalmologist. Patients screened during the year 2012 were included in the analysis. Glaucoma suspicion was based on disc hemorrhage and/or glaucomatous cupping and nerve fiber defects.
Results
Of 6937 patients attending fundus photography for screening of diabetic retinopathy, 24 (0,3%) had glaucoma diagnosed earlier and two were currently under examination for glaucoma suspicion. Altogether 520 patients were referred to further examination (7.5%, 95% confidence interval (CI) 6.9-8.1), and of them the cause for referral was glaucoma suspicion in 50 (9.6, CI 7.3-12.5). Excluding the known glaucoma patients or those currently under examination, the suspicion of new glaucoma, 50 out of 6911, was 0.72% (95% CI 0.55-0.95). Ten patients had disc hemorrhage, one advanced nerve fiber defect and the rest suspiciou disc cupping. The majority, 44 patients with glaucoma suspicion had type 2 diabetes, 5 had type 1 diabetes and one had secondary diabetes.
Conclusions
Diabetes is a risk factor of glaucoma and changes related to it are thus not unusual in diabetic population, especially in elderly patients with type 2 diabets. Glaucoma suspicion constituted ca. 10% of all referrals. Graders of fundus images need to be aware of these changes. Known glaucoma patients in ophthalmologist's follow-up are, however, not expected to attend screening programme

• S058

Analysis of changes in individual retinal layer thickness after cataract surgery using spectral-domain optical coherence tomography

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Purpose
To evaluate whether there were significant changes in macular thickness and each retinal layer thickness after cataract surgery using spectral-domain optical coherence tomography (OCT)
Methods
From February to August 2015, a prospective study of 24 eyes of 14 patients, who underwent cataract surgery was conducted. The thickness of each retinal layer was measured with OCT before and one month after surgery. The changes in OCT signal strength and retinal thickness before and after surgery were compared, and the layers more affected were confirmed. Also, correlation analysis was performed to determine the relationship between changes in signal strength, severity of cataract, and changes in refractive index and retinal thickness.
Results
The mean macular thickness was significantly increased from 263.33 μm to 269.75 μm ($p = 0.019$). When examining the changes in each retinal layer thickness, there was a significant increase in the thickness of the inner plexiform layer ($p = 0.034$), outer nuclear layer ($p = 0.015$) and retinal pigment epithelium (RPE) ($p = 0.012$). The signal strength of OCT was significantly increased from 28.79 dB to 31.67 dB ($p = 0.005$), which was significantly correlated with postoperative macular thickness changes ($p = 0.046$). However, the severity of cataract ($p = 0.219$) or the change of refractive index ($p = 0.098$) was not significantly correlated with macular thickness changes.
Conclusions
After cataract surgery, both improvement of signal strength and structural changes of the retina may increase macular thickness. In particular, the thickness of the inner plexiform layer, outer nuclear layer, and retinal pigment epithelial layer increased. Therefore, the thickness of ganglion cell-inner plexiform layer after cataract surgery may increase, so it should be carefully considered in the assessment of glaucoma progression.

• S059

Application of 3D-ASL technique in observation on cerebral blood flow changes in early and mid-stage primary open angle glaucoma

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Purpose
Based on Three Dimensional Arterial Spin Labeling (3D-ASL) was used to examine the cerebral blood flow CBF changes of cerebrum for patients with early and middle stage primary open-angle glaucoma (POAG) and to explore the characters of CBF changes and Central nervous system injury in early and middle stage POAG in order to providing a new thinking of preventing POAG.
Methods
According to the inclusion and exclusion criteria of POAG, Seventeen POAG patients and seventeen gengder-age-matched healthy control were enrolled in the study. For each participant high-resolution structural brain image was acquired on a 3.0 scanner. CBF images were obtained after being preprocessed by SPM8. REST were used to analyze CBF changes of whole brain and correlation analysis between CBF changes and RNFL and MD.
Results
1) whole brain CBF analysis : compared with control group, CBF is mainly decreased in POAG. The area include : right cerebellum, left superior occipital gyrus, right precentral gyrus, left cerebellum, right superior frontal gyrus, left fusiform gyrus, corpus callosum, left calcarine, the left parahippocampal. Increased CBF area : inferior frontal gyrus, caudate nucleus, orbitofrontal. 2) correlation analysis : RNFL was shown positive correlation with right inferior temporal gyrus, left calcarine, right cerebellum and right occipital gyrus. It has positive correlation between MD and right superior frontal, right calcarine and left middle frontal.
Conclusions
POAG in early and middle stage POAG could cause cerebral blood flow decrease, and these changes were positive correlation to RNFL and MD. Cerebral blood flow may be a potential biomarker for the brain involvement in glaucoma.

• S060

ISNT rule applicability based on optical coherence tomography parameters in a normal Portuguese population

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Purpose
We aim to determine the applicability of the inferior, superior, nasal and temporal neuroretinal rim (NRR) area characteristic configuration (ISNT rule) in adult normal Portuguese population based on spectral-domain optical coherence tomographic (SD-OCT) and assess demographic variations by age, sex, race and relation to optic disc area.
Methods
Prospective study with 188 eyes of 94 patients that underwent SD-OCT with the new glaucoma module premium edition software (v.6.0). Patients with confirmed or suspected glaucoma, visual field defects, other optic disk or retinal abnormalities were excluded. Optic Nerve Head parameters such as Minimum Rim Width (MRW), Bruch's membrane opening (BMO) and thickness of peripapilar nerve fibre layer (RFNL) on four quadrants were analysed.
Results
The mean age group was 55 years, 44% were men, 83% caucasian and 17% melanodermic. Mean spherical equivalent was 0.10 (min -6.5, max +5), and mean best-corrected visual acuity was 20/20 (min 20/40, max 20/16). NRR thickness area (MRW) was 376.0µm±75.9, 345.4µm±81.8, 365.1µm±86.8, 240.5µm±57.4, respectively on inferior, superior, nasal and temporal quadrants and ISNT rule was present in 23%. When excluding nasal quadrant (inferior>superior>temporal (IST) or inferior>superior (IS)) such configuration was present in 71% and 73% of patients, respectively. Mean age and mean optic disk/scleral area was higher in those with ISNT rule present (58.8 vs 53.7 years and 2.08 mm^2±0.4 vs 1.98 mm^2±0.5, respectively) but was not significant (p>0.05) as were not sex and race differences.
Conclusions
ISNT rule in normal population is not confirmed by SD-OCT assessed with ONH parameters and it is only present in 23% of eyes. The authors propose that a "IS/IST rule" seems more representative in a normal population as exclusion of nasal quadrant consideration increases prevalence.

• S061

Macular thickness after intraocular pressure reduction following trabeculectomy

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Purpose
The aim of the study was to assess changes of macular thickness after trabeculectomy and compare them in respect to the usage of preoperative prostaglandins and status of diabetes mellitus.
Methods
The prospective observational study included 93 glaucomatous eyes (90 patients) that underwent trabeculectomy. 81 (87.1%) patients were on prostaglandins treatment preoperatively. 5 (5.38%) patients had type 2 diabetes. The foveal and sectoral macular thicknesses were measured preoperatively, 1 week, 6 months and 12 months after the surgery using spectral domain optical coherence tomography. Retinal thickness was compared across the follow-up visits and in respect to the preoperative use of prostaglandins and diabetes.
Results
There was a reduction in mean ±SD intraocular pressure of 18.5 ±8.6mmHg 1week, 15.4 ±7.9 mmHg 6 months and 14.4 ±8.3 mmHg 12 months after trabeculectomy (p<0.001). 1 week postoperatively retinal thickening was observed in all macular subfields (p<0.001); the central macular thickness increased from 267.23 ±19.20µm at baseline to 271.12 ±19.59µm. 6 months postoperatively macula remained slightly thicker in central, nasal, inner superior and outer temporal sectors (2.10 ±5.97µm, p<0.001 in central subfield). 12 months after trabeculectomy retina showed thinning in the outer nasal and superior subfields (-3.54 ±8.57 µm; -1.94 ±7.02; p<0.01, respectively). There were no differences

in the changes of macular thickness when compared in respect to preoperative prostaglandins (p>0.05). The retinal changes did not differ between diabetic and nondiabetic patients (p>0.05).

Conclusions

Trabeculectomy induced mild macular thickening, more pronounced in the early postoperative period. Neither diabetes nor the use of prostaglandins before surgery had impact on these changes regardless their potency to increase vascular permeability.

• S062

First real-life data of use of the new PF-MD glaucoma device (EasyGrip®): Results of the ISY study from Spain and France.

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Purpose

Preserved eye drops can cause local side effects, some of which appear more rapidly, that can impact the patients' quality of life. The new availability of the first Preservative-Free (PF) Dorzolamide/Timolol (DT) Fixed Combination (FC) in a new MD bottle (EasyGrip®) could improve patient satisfaction, treatment compliance and ultimately treatment efficacy.

Methods

ISY is an international, multicentre, observational and cross-sectional study. It is still ongoing to recruit a total of 1880 glaucoma patients from DK, FI, FR, DE, NO, ES and SE. The patients were treated and stabilised for at least 28 days with the PF-MD DTFC (Duokopt®/Dualkopt® - Laboratoires Théa-France). The questionnaire is divided in two parts to be completed independently by the ophthalmologist and the patient during one routine visit. The primary endpoint is the prevalence of patients satisfied with the new PF-MD bottle. Other parameters: medical history; intraocular pressure (IOP); use of the new PF-MD bottle; ophthalmologist satisfaction; assessment of compliance and persistence; and visual acuity.

Results

The results of the first 268 patients (188 Spain, 80 France) are presented here for the first time. 97.5% of ophthalmologists are satisfied or very satisfied to prescribe the new PF-MD device with DTFC. 79.0% of patients, who were previously using a preserved MD bottle, are satisfied enough to continue with the new PF-MD device. 44.5% of patients declared the new PF-MD bottle better or much better than the previous preserved MD eye drop.

Conclusions

The first results of ISY study confirm the interest of switching from a preserved MD glaucoma treatment to a PF-MD device EasyGrip® whilst keeping the efficacy.

• S064

Wait before extrapolating rather than wait between two eyedrops! ... The 1974 Chrai et al.'s study on the albino rabbit may not apply to humans

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Purpose
The recommendation of having patients waiting 5 minutes between two eyedrops instillation is based on an experimental work conducted by Chrai et al. in 1974 on the albino rabbit. In this work, instillation of pilocarpine eyedrops was followed by instillation of saline eyedrops after 30 seconds and 2 minutes with as few as 4 rabbits and permitted a decreasing of the maximum difference in pupillary diameter respectively by 44% and 17.5%. The present study was undertaken to assess the validity of these findings in humans.
Methods
Twenty-four healthy volunteers were enrolled from March 2016 to April 2017. Eyeballs were photographed in a completely dark room with an infrared camera at baseline, 40 minutes after instillation of 1% pilocarpine and 40 minutes after instillation of 1% pilocarpine eyedrops followed by the instillation of saline eyedrops immediately afterwards or 5 minutes later . Pupil to iris surface ratios were calculated and differences of ratios between baseline and 40 minutes (i.e. myosis gain) were compared with Wilcoxon test.
Results
The mean (SD) myosis gain was 0.176 (0.089) with 1% pilocarpine alone; 0.165 (0.086) with 1% pilocarpine immediately followed by saline eyedrops (p = 0.652) and 0.167 (0.087) with pilocarpine followed 5 minutes later by saline eyedrops (p = 0.731). Only some eye colours significantly influenced the myosis gain in multivariate analysis.
Conclusions
Despite using pupil/iris surface ratios (more sensitive than diameter measurements), and more subjects (24 versus 4) our study fails to confirm the results found by Chrai et al.'s in the albino rabbits. While awaiting for the issue of the time interval between eyedrops in humans to be further investigated, one should be cautious with extrapolation of Chrai et al.'s conclusions in the albino rabbits to humans.

• S065

Prescription pattern of ocular hypotensive drugs in Portugal and its comparison with the European guidelines – PEM Study

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Purpose
There are few studies in Europe addressing the adherence to antiglaucomatous prescription guidelines. This study aims to describe the nationwide yearlong analysis of the prescription patterns of these drugs in Portugal, discussing how guidelines are being applied and identifying opportunities for improvement.
Methods
Cross-sectional study including all patients who were prescribed at least one IOP-lowering medication in Portugal, in 2015. Data was obtained from the common electronic drug prescription system used by all hospitals and clinics in the country. Current National and European Guidelines on Glaucoma Management were used as a reference. Statistical analyses were performed using STATA.
Results
A total of 833 871 prescriptions were provided to 231 634 patients (57% women). Over half of them were under monotherapy, but only 76% complied with first-line treatment choices (prostaglandin analogues or beta blockers). Among patients who were prescribed two IOP-lowering drugs, only two thirds adhered to the treatment strategy of using them as a fixed combination (FC). The guidelines orientation to use FC treatments was more likely to be followed by the ophthalmologist than the patient's General Practitioner. Nationwide, this topical IOP-lowering therapy accounted for a total of 26 million euros (M€) in costs, shared between patients and the national health system. The prescription rate per 100 000 people ranged from 13 180 to 2 257 among the seven Portuguese regions.
Conclusions
Guidelines for glaucoma treatment seem to apply to the majority of Portuguese patients taking IOP-lowering medication. However, a significant number of treated patients are not being prescribed first line IOP-lowering drugs. Non-ophthalmologist may be less aware of the preferred practice patterns in the management of this disease.

• S066

Missed opportunities of optimizing glaucoma medical therapy – A nationwide cross-sectional analysis of glaucoma topical therapy in Portugal (PEM Study)

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Purpose
Approximately 2,2% of the Portuguese population are under intraocular pressure(IOP)-lowering medication. However, an analysis based on the number of drugs may neglect how fixed combinations can minimize the burden of topical therapy and adherence to treatment. We aimed to analyse the prescription pattern of these drugs in Portugal and to identify improvement opportunities on the daily topical antiglaucomatous therapy.
Methods
Cross-sectional nationwide study, resorting to the PEM database from 2015 – which retrieved prescription data from all hospitals and clinics in the country. All data was provided in an encrypted form and anonymously extracted. Statistical analyses were performed for only one-month data (January) to guarantee a cross-sectional view and reduce the likelihood of misinterpreting changes in medication during the year. STATA was used as statistical package.
Results
In January 2015, a total of 53.053 people were prescribed IOP-lowering drugs in Portugal, with only 4,5% of these being preservative-free formulations. The vast majority of the patients instilled up to two drops a day (72%), either using monotherapy (63%) or fixed-combination (9%). Among the remaining 28%, half could have reduced at least two daily drops by using more fixed combinations.
Conclusions
Although most patients were under either monotherapy or one fixed combination, instilling up to 2 drops a day, the use of preservative-free drugs is far from the ideal scenario. Our results also suggested the number of daily drops may be significantly reduced in as many as 14% of the patients, thus potentially reducing ocular surface side effects and improving adherence.

• S067

Enzymatic Activity of CYP1B1 in primary congenital glaucoma goniodysgenesis and its relation with histological alterations

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Purpose
To analyze de CYP1B1 genotype activity, the histological findings and the clinical phenotypes in human primary congenital glaucoma (PCG).
Methods
Transmission electron microscopy was used to study surgical pieces from trabeculectomy from PCG patients (n=5) and normal cadaver donors sclerocorneal rims (n=3). Genomic DNA was extracted from the peripheral leukocytes of the same patients for the CYP1B1 study.
Results
The histological analysis allowed us to classified patient samples into three groups depending on goniodysgenesis findings: A) no visualization of the Schlemm's canal (SC); B) presence of the SC and no visualization of the collector channels (CC); C) presence of the SC and CC. Patients from groups A and B had extensive trabecular endothelial cell necrosis, and abnormal trabecular beam and null enzymatic activity of CYP1B1. Patients from group C in addition to presence of the SC and CC, showed a more developed trabecular meshwork than groups A and B and trabecular endothelial cells alive and with signs of phagocytic. This group showed a 60% of enzymatic activity of CYP1B1. All groups shared an abnormal insertion of the ciliary muscle although in group C the insertion was in a more posterior position.
Conclusions
In the samples analyzed, it seems to have a relationship between enzymatic activity of CYP1B1 and histological changes. The lower the CYP1B1 gene enzymatic activity, the greater the goniodisgenesys and the trabecular endothelial cell death extent. A greater understanding of histological changes associated with the enzymatic activity of CYP1B1 could be useful for clinicians to plan treatment strategy. This data could be useful for clinicians to plan treatment strategy

• S068

Qualitative early signs of microglial activation in mice retinas contralateral to experimental glaucoma

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Purpose

To analyze qualitative retinal microglia signs of activation after 24 h of unilateral laser-induced ocular hypertension (OHT) in OHT-eyes and their contralateral eyes.

Methods

Albino Swiss mice were divided into two groups, naïve (n=6) and lasered (n=9). Retinal whole mounts were immunolabeled with antibodies against Iba- 1 and MHC-II.

Results

Both in OHT eyes and in contralateral eyes Iba-1+ cells: i)had morphological signs of activation, being these more intense in OHT eyes than in the contralateral eyes. Iba-1+cells showed hypertrophy, soma displacement both in their own retinal layer and towards the nearest one and in some instances, reoriented microglial processes from being parallel to being perpendicular to the retinal surface. ii) were dystrophic in some instances in the photoreceptor layer (PRL); iii) in the outer plexiform layer sent processes to the PRL and this was mainly found in contralateral eyes; iv) overall, did not up-regulate the expression of MHCII .

Only in OHT eyes MHCII+ rounded cells were observed in the nerve fiber layer-ganglion cell layer, being more numerous in the peripheral superior zone of the retina and near the optic disc. These cells were surrounded and phagocyted by numerous ameboid Iba-1+ cells. In addition, beneath the retinal areas where this event was occurring, microglial cells of the inner plexiform layer and outer plexiform layer oriented their processes towards those areas and surrounding them.

Conclusions

At 24 h after unilateral OHT, microglial features of activation were observed not only in OHT eyes but, interestingly, also in the contralateral untreated eyes. Whether this activation favors neuroprotection or neurodegeneration needs to be clarify.

• S070

Association of apolipoprotein E with a risk of primary open-angle glaucoma

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Purpose

Glaucoma is classified as a neurodegenerative disorders. It is characterized by loss of retinal ganglion cell (RGC) and changes in the structure of the optic nerve. The exact mechanism of RGC death is multifactorial and unclear. Many reports have focused on the possible role of apolipoprotein E (APOE) in the development risk of glaucoma.

Methods

The study involved 30 patients with primary open-angle glaucoma (POAG) and 30 age-matched healthy subjects. Material for the study was the whole blood and the aqueous humor. The main goal of this study was to assess the expression level of APOE in whole blood and serum of patients with POAG compared with a control subjects without glaucoma. Moreover, we evaluated the expression level of APOE protein in the aqueous humor in POAG patients. The level of mRNA expression was determined by QRT-PCR and the protein level was evaluated by ELISA. The statistical analysis was performed using the non-parametric Mann-Whitney U test.

Results

The results of APOE mRNA expression level in the blood have shown no statistical differences between POAG patients and control subjects ($p>0.05$). However, the analysis of protein level in the serum has showed a higher expression of APOE of POAG patients compared with the control group ($p \leq 0.05$; 5106.07 ng/ml vs 4294.70 ng/ml). Additionally, we have observed a tendency to increase in concentration of APOE in the aqueous humor in POAG patients (262.12 ng/ml) compared with controls (173.83 ng/ml).

Conclusions

Our research suggests that altered level of APOE may be related to the development of primary open angle glaucoma.

• S069

Aqueous inflammatory proteasome in open angle glaucoma in Caucasian patients

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Purpose

Primary open-angle glaucoma is characterized by loss of retinal ganglion cells and their axons, resulting in optic nerve cupping and visual field loss. Until now, no specific cause was attributed to POAG development, but multiple pathogenic theories have been approached, beside IOP elevation and aging.The aim of this study was to assess the inflammatory and immune dysregulation theory in POAG.

Methods

We included in a cross-sectional study 40 eyes, from 40 patients: 16 eyes with POAG and 24 eyes from healthy subjects. Aqueous was collected during conventional cataract surgery. 21 inflammatory markers were quantified and compared between groups using a Luminex® Performance Assay multiplex kit based on flowcytometric methods.

Results

Mean age in POAG group was 75.69+/-5.54 years vs 72.33+/-11.26 years in controls ($p=0.23$). Mean IOP in healthy controls was 14.21+/-2.68 mmHg compared to 18.19+/-4.3 mmHg in glaucoma patients, controlled by 3+/-0.87 topical substances. Mean MD level in POAG group was -13.59+/-9.35 dB, whereas PSD mean level was 4.25+/-4.22dB. Cytokines expression in glaucoma patients compared to healthy controls was found significantly different for CXCL5 ($p=0.008$), CXCL8 ($p=0.048$), IL-1α ($p=0.005$), IL-2 ($p=0.015$) and TNFα ($p=0.041$). Therefore, a prediction statistical model for these cytokines was created. All markers point out a common inflammatory pathway that triggeres TNFα release. A mathematical model proved that CXCL5, CXCL8, IL-1α and IL-2 can accurately predict TNFα level in this study (r square=0.842, $p=0.000$).

Conclusions

Our results show that in POAG patients there is an increased production of inflammatory cytokines in aquoeous humor. Moreover our statistical predictions point out TNFα molecule and its signalling pathways as the determinant pathogenic pathway involved in the inflammatory compound of POAG caucasian patients.

• S071

Glaucoma assessment tools used by clinicians: old or gold?

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Purpose

Glaucoma is the main cause of irreversible blindness worldwide. Early detection and personalized management is the key to prevent or slow disease progression. Our group previously evaluated the quality of within-hospital referral to a glaucoma subspecialty department (GSD), raising awareness to the importance of doing applanation tonometry (AT), gonioscopy and visual fields (VF) before referral. The aim of this work was to perform an audit cycle, one year after the awareness training session in December 2015.

Methods

Retrospective analysis of a random sample of within-hospital referrals to the GSD, in Lisbon Academic Medical Center (January 2016 to May 2017). Electronic records were screened for clinical data, exams, medical and surgical treatments prior to referral. Descriptive statistics were performed with SPSS.

Results

A total of 150 patients (69 males) were included in this analysis, with a mean age of 65 years [range 10-93]. Mean intraocular pressure (IOP) was 19.8 mmHg. Almost 20% of patients were not on any IOP-lowering drugs, while nearly half were under ≥2 classes of treatment. AT and VF were performed respectively in 43% and 59% of the referred patients, both versus 49% in 2015 ($p>0.05$). Gonioscopy was described for 23% of patients, more than the 12% mentioned in 2015 ($p = 0.014$). Optical coherence tomography (OCT) was performed in the large majority, 85%, as in the first analysis. Only 6% of patients had all AT, gonioscopy and VF; and 19% were referred with none of these exams, comparing to the 22% in the original 2015 screening ($p>0.05$).

Conclusions

Overall, training session did not significantly improve the quality of GSD referral, though more physicians reported gonioscopy results. It seems many clinicians still prefer more expensive and sophisticated exams as OCT, often forgetting valuable and simpler tools.

• S072

Calcium signaling in human lens epithelial cells after mechanical stimulation

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Purpose
The purpose of this study is to explore and identify intra- and inter-cellular calcium (Ca2+) signaling in human lens epithelial cells (LECs) upon local mechanical stimulation, to understand better the role of Ca2+ in intercellular communication related to cataract formation, lens regeneration and posterior capsular opacification (PCO).
Methods
The anterior lens capsule (aLC: basement membrane and associated LECs) were obtained from cataract surgery. Primary human LEC cultures were established by placing adherently the intact human aLC onto Petri dishes. LECs were stained with Fura-2 dye, the fluorescence of which was imaged to monitor spatio-temporal changes in cytosolic free Ca2+ concentrations in response to localized, micropipette induced mechanical stimulation.
Results
Analysis of the intra- and inter-cellular Ca2+ signaling from postoperative aLCs and cultures showed that the Ca2+ signal spreads radially and its propagation speed increases with the degree of cataract. While in aLC Ca2+ signals travels between the first few neighbor LECs in the order of seconds, in confluent culture the propagation is slower and it covers smaller distances. LECs from aLC with less developed cataracts exhibit faster and bigger changes in intracellular Ca2+ concentration. Moreover, in aLC and in LEC cultures, the duration of Ca2+ transients prolongs with increasing distance from stimulation site, whereas their amplitude decreases.
Conclusions
The modifications of Ca2+ homeostasis in LECs, which are associated with different degrees of cataract, affect Ca2+ signaling upon the local mechanical stimulation. Impairment of Ca2+ signaling might be the basis of cataract formation. LEC's cultures have less developed Ca2+ signaling capabilities, what might be reflected on lens regeneration and PCO.

• S073

Effects of short oxidative stress exposure on lens epithelial cells

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Purpose
To observe the reactions of lens epithelial cells (LECs) to a short exposure of an elevated oxidative stress. To help find future treatments for the prevention of posterior capsule opacification. Using cultured human lens capsules as an experimental model and hydrogen peroxide (H2O2) as the stress inducer.
Methods
Lens capsule-ciliary body complexes were extracted from human donor eyes. Samples were exposed to 30mM H2O2 for 5 min (n=8) or used as untreated controls (n=9). H2O2 was applied after lens extraction through intercapsular irrigation using a silicone irrigation ring. Samples were cultured on average for 30 days, during which dark field and lateral illumination photos were taken every 2 to 3 days. These photos were used to observe and quantify, time until cellular growth and subsequent confluence on the posterior capsule. Three of the controls were not cultured, in order to observe starting conditions.
Results
All control samples showed signs of normal cellular growth on the posterior capsule on average by day 6. LEC proliferation and migration was not observed on H2O2 samples until day 22. Four H2O2 samples showed signs of growth. The overall delay of cell growth compared to control was significant (H2O2 $p<0.001$). Until day 29 none of the exposed samples that had shown growth reached confluence. Half of controls were confluent on day 10, 83% on day 20 and all by day 26. The average cellular migration speed of controls and H2O2 samples were very similar, being 3.2 and 3.0 (mm2/day) respectively.
Conclusions
Exposure of lens epithelial cells to an elevated concentration of H202 for a short period of time does not seem to lead to immediate cell death as expected, but rather arrests the cell cycle. Surprisingly, after cells have recovered from the oxidative stress, they grow at a normal rate.

• S074

Changes in the X-ray diffraction pattern of porcine lens before and after simulated accommodation

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Purpose
Introduction: During the accommodation process, the morphology of the lens changes. The crystallin proteins within the lens fibres are the primary structural unit of organisation at the cellular level, and play a major role in maintaining transparency and refractive power. All the structural information about the lens from X-ray scattering techniques have so far been performed on samples in the relaxed accommodated state. It is thought that largest structural changes occur in the lens nucleus during accommodation.
Aims: To measure any changes in the average distance between the crystallin proteins, and their ordering within the lens fibres before and after stretching using small angel x-ray scattering.
Methods
Fresh porcine lenses were mounted into a commercially available lens stretching device (Bioniko, Florida, USA). Samples were placed in the X-ray beam at the Diamond synchrotron and 2D grid scans performed. Scans were taken in the same lens in both the accommodated and unaccommodated states, before and after a stretching.
Results
All patterns show a reduction in both the X-ray intensity and in the average spacing between the crystallin proteins, in the centre of the lens compared with the periphery. This is consistent with the increase of protein concentration from the lens cortex to the nucleus. No significant changes in the average spacing between the crystallin proteins was observed upon stretching. Substantial changes in both the X-ray intensity, and in the ordering of the proteins were recorded at the peripheral margins of lenses in the stretched state.
Conclusions
The changes in the X-ray intensity, and in the ordering of the crystallin proteins at the peripheral margins of the lens are somewhat in contrast to the notion that the nucleus under goes the largest structural changes.

• S075

Intraocular implant calculation based on the fellow eye measurements

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Purpose
To estimate the postoperative refractive error when the use of the IOL-Master is not possible in Cataract Surgery and the calculation of the Intraocular Lens (IOL) is based on the fellow eye measurements.
Methods
The records of 150 patients who underwent Cataract surgery between September 2015 and September 2016 were reviewed. Performing IOL-Master measurements was not possible and the calculation of the IOL was based on the IOL-Master measurements of the fellow eye.
Results
The refractive error was -0,75 sph with a standard deviation from -1,25 to +0,75.
Conclusions
IOL calculation can be based on the IOL-Master measurements of the fellow eye, when measurements of the eye that is about to be operated cannot be performed.

• S076

Persistent pupillary membrane associated with cataract

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Purpose
Persistent pupillary membranes represent remnants of the tunica vasculosa lentis. In general, it does not affect vision, although cases of deprivation ambliopia have been described. There are few reported cases of associations with other ocular pathologies.
Methods
Interventional case report showing bilateral Persistent Pupillary Membrane associated with cataract.
Results
A 17-year-old male underwent routine ophthalmologic examination. Best corrected visual acuity (BCVA) was 0.2 (+4.25, -4.50ª 90º) in the right (RE) and 1.0 (- 0.50, 0.75 to 40 °) in the left eye (LE). Slit-lamp biomicroscopy examination demonstrated a bilateral persistent pupillary membrane associated to cataract in the RE. Goldmann applanation intraocular pressure (IOP) and fundoscopy were normal. In order to improve visual acuity we performed a membranectomy with cataract extraction. Nevertheless, BCVA following surgery showed no changes.
Conclusions
We describe the association of bilateral persistent pupillary membrane to unilateral cataract, as well as to hyperopia and anisometropic amblyopia. Conservative management should be considered in patients whose visual development has concluded. Surgery entails risks and visual gain may not be significant.

• S077

Visualization of the light field of multifocal intraocular lenses using a dual wavelength approach

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Purpose
To implement a setup which allows simultaneous visualization of the far and near distance light field of multifocal intraocular lenses (MIOL) with two different wavelengths.
Methods
We used two different laser systems (532 nm and 405 nm) in junction with Powell lenses to create vertical laser lines. One laser line was collimated to simulate far distance imaging while the second laser line was diverging simulating near distance imaging at approximately 0.3 m distance. The MIOL was placed in a glass cuvette filled with balanced saline solution which was doped with two different fluorophores. The fluorophores were chosen to have a large Stokes shift and good separation between their excitation and emission bands. Image acquisition was performed with a slit lamp bio microscope and a digital single reflex camera. We investigated three different IOL types: a bifocal MIOL, a trifocal MIOL and an extended depth of focus IOL.
Results
We found that Propidium iodide and Fluorescein were appropriate fluorophores. Propidium iodide was excited at 532 nm and showed a red fluorescence while Fluorescein was excited at 405 nm showing the green fluorescence. Both lasers required a high power of approximately 30 mW in order to create a visible fluorescent reaction in the cuvette. All three MIOL types provided a good separation between far and near distance light. The regions of overlapping light fields were visible as yellow fluorescence.
Conclusions
In contrast to the previously published setups using a single wavelength with collimated excitation light and axially separated far and near distance foci the current setup allows superposition of the far and near distance foci which is more realistic compared to the situation in the eye. The dual wavelength approach enables an easy optical separation of far and near distance light.

• S078

Robotic surgery - a new way to perform cataract surgery

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Purpose
To demonstrate the feasibility of robot-assisted simulated cataract surgery
Methods
We performed cataract surgeries on a Kitaro cataract wet lab training system using simultaneously the DaVinci Xi robotic surgical system and a phacoemulsification system. For each procedure, duration and successful completion of the surgery with or without ocular complications were assessed.
Results
Procedures were successfully performed on 27 lens nuclei. Feasibility of robot-assisted simulated cataract surgery is confirmed. The DaVinci Xi system provided the intraocular dexterity and operative field visualization necessary to perform the main steps of the phacoemulsification procedure: corneal incisions, capsulorhexis, grooving, cracking, quadrant removal and infusion-aspiration of the viscoelastic. The intervention of a second surgeon was required for the intraocular injections of viscoelastic, balanced salt solution and intraocular lenses. Mean operative time was 26 minutes. All lens nuclei were removed. Inadvertent enlargement of the main corneal incision caused by the phaco hand piece was observed in 2 cases.
Conclusions
Experimental robot-assisted cataract surgery is technically feasible using the new DaVinci Xi robotic Surgical System combined with a phacoemulsification machine.

• S079

Usefulness of Ret-Cam imaging in diagnosis, treatment and monitoring of retinoblastoma

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Purpose
To present a group of children with retinoblastoma whose diagnostic, therapeutic and monitoring decisions were made using Ret-Cam
Methods
Children treated in the Department of Ophthalmology and Ophthalmic Oncology for retinoblastoma in the 1900s. Diagnosis was made after ophthalmic examination under general anesthesia with Ret-Cam and ultrasonography. Treatment was performed with VEC chemoreduction, iodine and ruthenium brachytherapy, cryotherapy, and transpupillary thermotherapy.
Results
The results of treatment and control were documented on a Ret-Cam camera. Photographs of intraocular tumors have been made prior to treatment, after chemoreduction, after local treatment and during the follow-up. Tumors regression, vitreous seeds and possible radiation retinopathy were monitored.
Conclusions
Photographic documentation using the Ret-Cam is very useful in treating retinoblastoma. The biggest advantage is the objective possibility to compare and evaluate the results of treatment and control

• S080

Preliminary results: Comprehensive national retinoblastoma cohort in Finland - RB1 mutation spectrum

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Purpose
Retinoblastoma (Rb), a malignancy of developing retina, emerges almost always after biallelic mutation and inactivation of tumor suppressor gene RB1. In heritable Rb, a child carries germline RB1 mutation. Identifying this will help in future risk management and family planning. Recently, we have made an effort to create a comprehensive national register for Rb. DNA sequencing for mutations in RB1 is being offered to every patient not previously tested and the results are included in the register.
Methods
Of the 226 Rb patients registered in the Finnish Retinoblastoma Register until January 2016, 72 have so far underwent germline DNA testing and 40 patients from 32 unrelated families tested positive for mutation. RB1 mutation detection methods varied depending on the time period. Mutations were checked for pathogenicity from the Leiden Open Variation Database (http://rb1-lsdb.d-lohmann.de).
Results
RB1 mutations comprised 90% of heritable (bilateral, familial or both) Rb and 10% were sporadic unilateral tumors (unifocal or too advanced to assess focality). The distribution of mutation types was 46% nonsense, 15% frameshift, 15% splice site, 3% large indel, 8% missense, 13% chromosomal deletions and none promoter. Two novel mutations (c.1A>C and c.2042_2203+?del) were detected. Five mutations (13%) had been reported only once and nine mutations (23%) three times or less.
Conclusions
The frequencies of the type of mutation in the RB1 gene in the preliminary results of our national cohort expectedly follow the mutation spectrum described worldwide.

• S081

High-dose chemotherapy with autologus hematopoeitic stem cell transplantation in relapsing Vitreoretinal Lymphoma, a LOC network study

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Purpose
The management of isolated vitreoretinal lymphoma (VRL) remains controversial due to his rarity. The aim of this study was to evaluate the efficiency and safety of high-dose chemotherapy with autologous hematopoietic stem cell transplantation (HCT-ASCT) as a treatment of recurrent relapsing VRL.
Methods
We retrospectively studied medical records of patients included in the French LOC network database between 2011 and 2016 with isolated vitreoretinal relapse of either primary vitreoretinal lymphoma or oculocerebral lymphoma treated with HCT-ASCT. Hematologic, neurologic and ophtalmologic datas were screened.
Results
32 patients (16 F/16 M), all immunocompetent, were included in the study. Median age at HCT-ASCT was 62 (range 44 years-73 years). Median Karnofsky Performance status before HCT-ASCT was 90. At diagnosis, 17/32 had primary vitreoretinous lymphoma (PVRL), 7/32 Primary Central Nervous Cells Lymphoma (PCNCL), 8/32 PVRL and PCNL. Patients had previously received a median number of 1 line of treatment including high-dose methotrexate before HCT-ASCT. All patients received a thiotepa-based HCT. 81% of the patients experienced a complete response. 2 « toxic deaths » occurred. Mean follow-up was 41,6 months (range: 5-96). 9/32 patients had recurrences. The 5-years OS was 81%. The 5-years OS was respectively 91% in the PRVRL groups, 85% in ocular and cerebral group and 64% in PCNCL group. The 5-years PFS rate was 58%. The 5-years PFS was respectively 66% in the PRVRL groups, 75% in ocular and cerebral group and 43 % in PCNCL group. 4 deaths occurred overall.
Conclusions
Intensive chemotherapy followed by autologous stem cell transplant is an aggressive therapeutic approach but appears to give interesting results especially in young and fit patients with recurrent refractory vitreoretinal lymphoma.

• S082

Case of IgG4-related eye disease requiring differentiation from carotid-cavernous fistula

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Purpose
Purpose: We report our findings in a case of IgG4-related eye disease that was confused with carotid-cavernous fistula (CCF).
Methods
Case report: A 61-year-old man visited to our department for exophthalmos with dilated conjunctival vessels in both eyes. He had hyperthyroidism. At the first visit, his ocular movements were disturbed, and MRI showed funicular-like appearance of the superior ophthalmic veins. However, enlargements of the extraocular muscles were not detected, and thyroid ophthalmopathy was excluded. Cerebral angiography showed no flow from either internal carotid arteries to the cavernous sinus, and CCF was also excluded. Blood tests showed high level of IgG4 (281 mg/dl) and a IgG4-related eye disease was considered. Systemic examinations showed no other lesions. Although histological examinations could not be performed, we treated the patient with 30 mg prednisolone as a possible IgG4-related eye disease. However, the reduced vision and critical fusion frequency did not improve. Then we switched to steroid pulse therapy, and all findings including the MR images were improved. A biopsy could not be performed because of the high risk of bleeding. Thus, malignant lymphoma could not be completely excluded. The patient is being followed continuously to detect any recurrences.
Results
Conclusions
Conclusion: We report our findings in a very rare case of IgG4-related eye disease with funicular-like appearance along the superior ophthalmic veins requiring differentiation from CCF. Ophthalmologists should consider IgG4-related eye diseases in cases with signs and symptoms of CCF and thyroid ophthalmopathy.

• S083

Protein kinase inhibitors for targeting tumor-initiating cells in uveal melanoma

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Purpose

Uveal Melanoma (UM) is the most common intraocular tumor in adults. Surgery and brachytherapies have improved survival rates, but up to 40% of patients develop liver metastases.

Mutations in the Gαq family members GNAQ and GNA11 are present in 80% of UM tumors whereas BRAF mutations are much less common. Consequently, Protein Kinase signaling pathways are dysregulated and specific targets can be identified for precise therapeutic approach. On the other hand, it has been proposed that tumors contain a specialized subset of cells defined as tumor-initiating cells (TICs) that may be responsible for de novo resistance to drugs and metastatic disease. Thus, targeting TICs may be imperative for achieving a cure.

Methods

To this end, we performed an in vitro screening using the Screen-Well® Kinase Inhibitor Library (BML-2832-0100) on TIC-enriched populations of UM cells harboring either GNAQ /GNA11 or BRAF mutations.

Results

These UM-TICs have the capacity to self-renew and generate tumor spheres (melanospheres) in low-adherent culture conditions. Furthermore, they display stem cell-like features such as high expression of CD133, CD44, Nestin or ABCB5 specific markers. The metastatic ability of OMM-2.5-enriched TIC cells is currently explored in vivo after their orthotopic injection into the uvea of HL-SCID mice.

Our results revealed that metastatic and TIC-enriched populations were more resistant to antiproliferative effects of kinase inhibitors. Several kinase inhibitors such as Tyrphostin 51 (EGFRi), DES (PKCi), DRB (CK2i) and ML-9 (MLCKi) differentially affected growth and survival of TIC-enriched population from parental cell line Mel270.

Conclusions

Taken together, we showed that EGFR, MAPK, PKC and PI3K signaling pathways are activated in TICs and their respective inhibitors may represent attractive therapeutic candidates for metastatic UM.

All authors index

All authors of abstracts are listed alphabetically.

One letter and three digit numbers refer to posters.
Four digit numbers refer to oral presentations.
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