UNINTENDED CONSEQUENCES
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Purpose: To report a case of choroidal neovascularization (CNV) following hormonal supplementation during a fertility treatment.

Methods: A comprehensive ophthalmic examination was performed including best corrected visual acuity (BCVA), color fundus examination, fluorescein angiography and optical coherence tomography (OCT). Also blood test, chest x-ray and tuberculin test were practiced.

Results: A 35-year-old woman referred loss of vision in one eye after 4 cycles of ovarian stimulation for intrauterine insemination with no success of pregnancy. After complete eye and systemic examinations idiopathic CNV was diagnosed. She was treated with 3 ranibizumab injections with a significant functional and anatomical improvement.

Discussion: Hormonal therapy for ovarian stimulation during a fertility treatment is a common procedure that could be associated with the development of CNV in healthy young women. Further studies should be performed to investigate this possible association.

SPECTRUM OF NON-PARANEOPLASTIC AUTOIMMUNE RETINOPATHY AMONG ASIAN PATIENTS WITH RETINAL DISEASES
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Introduction: Non-paraneoplastic autoimmune retinopathy (npAIR) encompasses rare immunologic process where circulating serum antiretinal-autoantibodies (ARA) in absence of tumor result in progressive retinal degeneration. npAIR represents a diagnostic challenge with dearth of data in Asian cohort. Thus, we aim to describe demographics of npAIR in an Asian population with retinal diseases.

Methods: Retrospective case review of patients diagnosed with npAIR from 2008 – 2013 was conducted. All patients underwent complete ophthalmic examination and serum ARA was confirmed by western blot.

Results: We found serum ARA positive in 47 patients, with an average age of 49 years. 25 patients (53.2%) were males with mean presenting VA of 6/24. Retinitis pigmentosa (RP) was found in 76.6% patients (n = 36). Remaining patients had Biette’s dystrophy, X-linked retinoschisis, myopic degeneration, diabetic retinopathy, choroiditis, vasculitis and vitreomacular. Common symptoms were rapid deterioration of near vision and photopsias. Half of patients (n = 24, 51%) had vitreous cells, while cystoid macular edema was seen in 10% (n = 5). Majority of patients (n = 35, 74.4%) had antibodies positive against multiple proteins, 46- kDa (enolase) being the commonest. 35 patients (74.4%) underwent immunosuppressive therapy for 3 months, (53%) had oral immunosuppressants while 10% had orbital floor steroids) among which improvement was noted in 71.4% (n = 25), with mean post-treatment VA of 6/15.

Conclusions: In our npAIR study, we found RP was the commonest retinal disease with improvement noted in 71% of patients with treatment. Our study shows that npAIR is treatable and its early detection can reverse visual loss in those affected by this autoimmune condition.

ADVANCED IMAGING OF WHITE SPOT SYNDROMES
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Background and aim: The white spots syndromes remain diseases of unknown etiology and fascinating clinical findings and courses.

Methods: We performed advanced imaging including FA, ICG, SD OCT, OCT angiography, and adaptive optics on patients with placoid diseases and MEWDS.

Results: MEWDS is clearly a disease at the level of the photoreceptors. There is excellent but not complete recovery. The placoid diseases show abnormalities of choriocapillaris but also blockage from overlying retinal changes.

Conclusions: We find that MEWDS is a disease of the photoreceptors where-as important choriocapillaris changes are seen with placoid diseases.

MYSTERIES OF DOME-SHAPED MACULA
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Dome-shaped macula (DSM) is an inward protrusion of the macula as visualized by optical coherence tomography (OCT). Imamura, Spaide and coworkers reported that a DSM was associated with, and caused by, a local thickening of the subfoveal sclera. The mechanism leading to the relative thickening of the subfoveal sclera remained elusive.

By using swept-source OCT, we report 2 new findings associated with DSM; macular Bruch’s membrane defects (MBMD) and peri-dome intrachoroidal cavitation (peri-dome ICC).

1) MBMD and DSM: Out of 1983 highly myopic eyes (1057 patients), 166 eyes (8.4%) showed a DSM and 534 eyes showed a MBMD. In multivariate binary regression analysis, higher prevalence of DSM was associated with a higher prevalence of a MBMD after adjusting for longer axial length. In association with a DSM, three MBMD types were differentiated: MBMDs in patchy chorioretinal atrophy, MBMDs in choroidial neovascularization-related macular atrophy, and MBMDs as temporally extending large parapapillary gamma zone.

2) Peri-dome ICC and DSM: Peri-dome ICC was observed in 53 of the 91 eyes (58%) with DSM. In the areas of the ICCs, the sclera appeared to be displaced posteriorly. In 2 eyes, Bruch’s membrane (BM) appeared to be pushed inwardly by the protruding sclera which could have resulted in the formation of the ICCs surrounding the dome. Defects in BM were detected beneath the areas of the ICCs in 38% of the eyes. In 3 eyes, cross sections of intrascleral blood vessel were observed near the inner surface of the protruded sclera. In 1 eye in which ICG angiography and OCT were both performed, a branch of a vessel originating from the temporally-dislocated Zinn-Haller arterial ring was observed to course parallel to the scleral protrusion that caused the DSM.

These results showed that a presence of a DSM was significantly associated with the presence of MBMDs. The morphology of the DSM in association with MBMDs may be associated with a focal relaxation of the posterior sclera, no longer pushed outward by an expanding BM but allowed to partially bulge inward. Defects of BM may also result in a formation of peri-dome ICCs and a posterior displacement of the sclera around the fovea without a displacement of the sclera beneath the fovea may occur. In addition, the relatively inflexibility of the intrascleral vessels within the sclera in the macular area may cause less expansion of macular sclera. These observations occurring around the fovea may be associated with a formation of DSM.
ROLE OF CIRCULATING VASCULAR PROGENITOR CELLS IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION (AMD)  
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Fibrosis is a major contributor to loss of visual acuity in neovascular age-related macular degeneration (nAMD). The comparison of Age-related Macular Degeneration Treatment Trials trial found that fibrotic scars developed in 24.7% of eyes followed in a two-year period while being treated for nAMD. The process leading to this fibrosis has not been fully elucidated. Animal studies of choroidal neovascular (CNV) lesions have shown that cells originating from bone marrow are capable of forming varying cell types in the lesions. This raises the possibility of a similar cell population in human neovascular (nvAMD) subjects. Blood draws were obtained from subjects with active nvAMD while patients were receiving standard care anti-VEGF injections. Peripheral blood mononuclear cells (PBMCs) were isolated and CD34-positive cells purified using magnetic bead sorting (Miltenyi-Biotec). The isolated cells were expanded in StemSpan SFEM media (StemCell Technologies) to increase cell numbers. After expansion, the cells were split and plated in either endothelial or pericyte media (Promo-cell). Phenotype analysis was performed via immunofluorescence and qPCR. Cultures derived in endothelial media showed the typical cobblestone morphology of endothelial cells, and were positive for the endothelial marker vWF. By contrast, cells derived in pericyte media were positive for pericyte marker NG2. Importantly, these pericyte-like cells expressed COL1A1, a vital component of fibrotic scars. This indicates that a single circulating cell population in human nvAMD subjects could contribute to both CNV lesions and fibrotic scars.

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FLUORESCEIN ANGIOGRAPHY BASED TREATMENT IN CHILDREN WITH EARLY COATS DISEASE  
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Background: Coats disease is a rare idiopathic disease which results in vision loss from exudation from abnormal telangiectatic vessels in the retinal periphery. Untreated the disease may progress to total retinal detachment and neovascular glaucoma. Traditionally treatment of early disease has been with laser or cryotherapy to the abnormal telangiectatic vessels but the development of wide field angiography has allowed the full extent of retinal vascular abnormalities to be identified and has led to different approach to treatment.  
Aim: The aim of the study was to review the results of treatment based on intraoperative wide field fluorescein angiography.  
Methods: Retrospective review of children with early Coats disease who underwent intra-operative fluorescein angiography followed by laser or cryotherapy. 25 children with Stage 2 Coats disease managed by a single ophthalmologist (ATM) over a 5-year period were identified and the case notes and retinal imaging were reviewed. Analysis was confined to 20 priests who had at least 3 months follow up.  
Results: Of the 20 children with Coats disease 6 had stage 2a disease and 14 stage 2b. In all cases the fluorescein angiogram (FA) showed more extensive vascular abnormalities than seen clinically and on colour fundus photography. Treatment with laser or cryotherapy was performed immediately after FA. 18 eyes had treatment with laser alone and 2 eyes had additional cryotherapy. 15 eyes need one treatment to stabilise disease and 5 eyes needed two sessions. None of the patients demonstrated progression to a more severe stage. Twelve eyes had a final VA of 0.4 logMAR or better, 6 patients had VA between 0.4 and 1.0 logMAR, and 2 had VA worse than 1.0 logMAR.

Conclusions: The treatment of retinal vascular abnormalities identified by wide-angle intra-operative FA in children with early Coats’ disease is associated with a good anatomic and visual outcome.

CUTICULAR DRUSENS: CLINICAL PHENOTYPES AND NATURAL HISTORY DEFINED USING MULTIMODAL IMAGING  
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Purpose: To define the range and lifecycles of cuticular drusen phenotypes using multimodal imaging. To re-evaluate the histologic characteristics of cuticular drusen.  
Design: Retrospective observational cohort study and experimental laboratory study.  
Participants: Two hundred forty eyes of 120 clinic patients with cuticular drusen and 4 human donor eyes with cuticular drusen (n = 2), soft drusen (n = 1) and hard drusen (n = 1).  
Methods: We performed a retrospective review of clinical and multimodal imaging data of patients with cuticular drusen. Multimodal imaging comprised color photography, fluorescein angiography, indocyanine green angiography, near-infrared reflectance, fundus autofluorescence, high-resolution optical coherence tomography and ultra-widefield imaging. Human donor eyes underwent processing for high-resolution light- and electron-microscopy.  
Main outcome measures: Appearance of cuticular drusen in multimodal imaging and the topography of cuticular drusen distribution. Age-dependent variations in cuticular drusen phenotypes including the occurrence of retinal pigment epithelium (RPE) abnormalities, choroidal neovascularization (NV), acquired vitelliform lesions (AVLs) and geographic atrophy (GA). Ultrastructural and staining characteristics of drusen subtypes.  
Results: Mean age of patients at first visit was 57.9 ± 13.4 years. Drusen and RPE changes were seen in the peripheral retina, anterior to the vortex veins, in 21.8% of eyes. Of eyes with more than 5 years of follow up, cuticular drusen disappeared from view in 58.3% of eyes, drusen coalescence was seen in 70.8% of eyes and new RPE pigmentary changes developed in 56.2% of eyes. RPE abnormalities, AVLs, NV and GA occurred at a frequency of 47.5%, 24.2%, 12.5% and 25%, respectively, and were significantly more common in subjects older than 60 years of age (all P<0.015). Occurrence of GA and NV were important determinants of final visual acuity in eyes with cuticular drusen (both P<0.015). Small cuticular drusen typically demonstrated a homogenous ultrastructural appearance similar to hard drusen, while fragmentation of the central and basal contents was frequently seen in larger cuticular drusen.  
Conclusions: While the ultrastructural characteristics of cuticular drusen appear more similar to hard drusen, their lifecycle and macular complications are more comparable to soft drusen. Cuticular drusen are frequently discovered in patients who are younger than typical age-related macular degeneration and may confer a unique risk for the development of severe vision loss.
PREDICTIVE BIOMARKERS OF TREATMENT OUTCOMES BY MULTIMODAL RETINAL IMAGING IN PATIENTS AFFECTED BY CENTRAL SEROUS CHORIORETINOPATHY

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Purpose: To identify predictive biomarkers of treatment outcomes by multimodal retinal imaging in patients affected by central serous chorioretinopathy (CSC).

Methods: In this interventional non-randomized clinical study, 27 treatment-naive CSC patients were prospectively enrolled and treated with oral epilerenone for 1 to 3 months. Primary outcomes included presence of pathological findings on indocyaine green angiography (ICGA) and optical coherence tomography-angiography (OCT-A) at baseline associated with different response to the treatment.

Results: A total of 29 eyes of 27 patients (2 females, 25 males) met the inclusion criteria and were included in the study (mean age was 45 ± 7 years). Mean CSC duration at baseline was 13.5 ± 4.4 weeks. After a mean of 10.5 weeks of treatment, mean central macular thickness significantly reduced (p<0.001), and mean best-corrected visual acuity improved (p=0.001). Seventeen eyes (61%) demonstrated total reabsorption of subretinal fluid on structural OCT, 5 eyes (18%) presented a partial response to epilerenone therapy and 6 eyes (21%) showed no response. The complete response to the treatment was associated with absence of CNV at OCT-A and the presence of hotspot at ICGA (p<0.001 and p = 0.002, respectively). None of 8 eyes with CNV in OCT-A imaging had a complete response to epilerenone and none of 3 eyes without hotspot at ICGA showed a complete response to the treatment.

Conclusions: Multimodal retinal imaging allowed us to propose predictive biomarkers (i.e. absence of CNV on OCT-A and presence hotspot on ICGA) for treatment outcomes.

FULLY AUTOMATED IDENTIFICATION OF LESION ACTIVITY IN NEOVASCULAR AMD

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Introduction: The objective of the study was to evaluate the accuracy of the Notal OCT Analyzer (NOA) versus retina specialists (RS) in the automatic detection of fluid on optical coherence tomography (OCT). The diagnosis was a prospective study of the performance of the NOA, which is compared to three retina specialists. The data source was OCT volume scans acquired in a retina clinic. A random selection of anonymization OCT scans (Zeiss Cirrus, Carl Zeiss Meditec, Dublin CA) of 165 AMD patients attending a single tertiary referral center (Belfast HSC, UK).

Methods: OCT scans of AMD patients were exported. Each scan set was analyzed by the NOA, and by three independent RS for the presence of intra-retinal or sub-retinal fluid. NOA also ranked cross-sections of scans for likelihood of CNV activity allowing a second grading session by the three RS.

Results: A total of 29 eyes of 27 patients (2 females, 25 males) met the inclusion criteria and were included in the study (mean age was 45 ± 7 years). Mean CSC duration at baseline was 13.5 ± 4.4 weeks. After a mean of 10.5 weeks of treatment, mean central macular thickness significantly reduced (p<0.001), and mean best-corrected visual acuity improved (p=0.001). Seventeen eyes (61%) demonstrated total reabsorption of subretinal fluid on structural OCT, 5 eyes (18%) presented a partial response to epilerenone therapy and 6 eyes (21%) showed no response. The complete response to the treatment was associated with absence of CNV at OCT-A and the presence of hotspot at ICGA (p<0.001 and p = 0.002, respectively). None of 8 eyes with CNV in OCT-A imaging had a complete response to epilerenone and none of 3 eyes without hotspot at ICGA showed a complete response to the treatment.

Conclusions: Multimodal retinal imaging allowed us to propose predictive biomarkers (i.e. absence of CNV on OCT-A and presence hotspot on ICGA) for treatment outcomes.

Disclosures: Anat Loewenstein is a consultant to Notal Vision, Usha Chakravarthy reports attendance at advisory boards and consultancy fees from Notal Vision. Dafna Goldenberg and Graham Young have no financial interest to declare in relation to the content of this article. Moshe Havilio, Omer Rafaeli and Gidi Benyamini are employees of Notal Vision.

HYPER SPECTRAL AND QUANTITATIVE AUTOFLUORESCENCE (AF): WHAT’S NEW?

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The standard clinical AF image is produced by the fluorescence of retinal pigment epithelium (RPE) lipofuscin (LF) when excited by blue light. It is an excellent reporter of the health of the RPE and an important marker in retinal degenerative disease, especially Age-related Macular Degeneration (AMD). The technical advances of hyperspectral (ex vivo) and quantitative (in vivo) AF imaging now provide further information on the molecular sources of this image and their tissue levels in health and disease. qAF imaging of normal and AMD subjects demonstrates that LF levels in early AMD appear to be decreasing, rather than increasing. This in turn suggests that early AMD is not driven by LF accumulation or LF toxicity. We will present such results by our group in pseudophakic patients with clear posterior capsules, further confirming the results of Gilem et al (JAMA-O; 2016) in phakic subjects. Hyperspectral AF imaging (ex vivo) records AF emissions at 10 nm intervals, 420-720 nm. We have demonstrated that there are three main AF spectral signatures of human RPE, S1, S2, and S3, and a drusen hyperspectral signature SDR in AMD. The RPE spectra for AMD and normal are strongly to moderately correlated, whereas the drusen spectra are all tightly correlated (mean CCs 0.99) The non-LF spectrum SDR is also sensitive and specific for drusen/ sub-RPE deposits (peak ~510 nm, 436 nm excitation). The important clinical AF image may now be quantified by qAF, with significant implications for AMD pathogenesis, and the spectral signatures of its complex molecular sources identified by hyperspectral AF for understanding RPE function in health and disease. While AMD and normal tissue differ somewhat in their main RPE spectra, the drusen signature SDR, present in all AMD tissues with drusen, is the most specific spectral change in AMD. The biochemical role of this fluorophore may be important in AMD pathophysiology.

IMPROVING THE AGE-RELATED MACULAR DEGENERATION CONSTRUCT: A NEW CLASSIFICATION SYSTEM

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Previous models of disease in age-related macular degeneration (AMD) were incomplete in that they did not encompass subretinal drusenoid deposits (pseudodrusen), subtypes of neovascularization, and polypoidal choroidal vasculopathy. In addition, Type 3 neovascularization starts in the retina and may not necessarily involve the choroid. As such the term choroidal neovascularization is not appropriate for these eyes. The new aspects in the AMD construct are to include specific lipoprotein extracellular accumulations, namely drusen and subretinal drusenoid deposits, as early AMD. The deposition of specific types of deposit seems to be highly correlated with choroidal thickness and topographical location in the macula. Late AMD includes macular neovascularization or atrophy. The particular type of extracellular deposit is predictive of the future course of the patient. For example, eyes with subretinal drusenoid deposits have a propensity to develop outer retinal atrophy, complete outer retinal and retinal pigment epithelial atrophy, or Type 3 neovascularization as specific forms of late AMD. Given Type 3 neovascularization may never involve the choroid, the term macular neovascularization is suggested for the entire spectrum of neovascular disease in AMD. In contrast to older classification systems, the proposed system encompasses the relevant presentations of disease and more precisely predicts the future course of the patient. In doing so the concept was developed that there may be genetic risk alleles, which are not necessarily the same alleles that influence disease expression.
SWIFT SOURCE OCT ANGIOGRAPHIC PREVALENCE, INCIDENCE, AND NATURAL HISTORY OF SUBCLINICAL NEOVASCULARIZATION IN AGE-RELATED MACULAR DEGENERATION

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Purpose: Swift-source optical coherence tomography angiography (SS-OCTA) was used to determine the prevalence, incidence, and natural history of subclinical macular neovascularization (MNV) in eyes with non-exudative age-related macular degeneration (AMD).

Methods: In this prospective, observational, consecutive case series, patients were enrolled with non-exudative AMD in one eye and exudative AMD in their fellow eye. All patients were imaged using both the 3 mm × 3 mm and 6 mm × 6 mm SS-OCTA field-of-views (FOVs) (PLEX Elite 9000, Carl Zeiss Meditec). The en face slab used to detect the MNV extended from the outer retina to the choriocapillaris (ORCC slab), and projection artifacts were removed using a proprietary algorithm. Outcomes included the prevalence and incidence of subclinical MNV and time to anti-VEGF therapy using Kaplan-Meier cumulative estimates of treatment at one year.

Results: SS-OCTA imaging was performed on 160 patients (110 eyes with iAMD and 50 eyes with GA) from August 2014 through March 2017. SS-OCTA identified subclinical MNV at the time of first imaging in 23 of 160 eyes for a prevalence of 14.4%. Of 134 eyes with follow-up visits, the annual incidence for developing subclinical MNV was 5.4% and a total of 13 eyes developing exudation. Of these 13 eyes, 10 eyes were found to have pre-existing subclinical MNV. By 12 months, the Kaplan-Meier cumulative incidence of exudation for all 134 eyes was 6.8%. For eyes with subclinical MNV at the time of first SS-OCTA imaging, the incidence was 21.1%, and for eyes without subclinical MNV, the incidence was 3.6%. There was no difference in the cumulative incidence of exudation from pre-existing MNV in eyes with iAMD or GA (p = 0.847, log-rank test). After the detection of subclinical MNV at the time of first imaging, the incidence was 21.1%, and for eyes without subclinical MNV, the incidence was 3.6%. There was no difference in the cumulative incidence of exudation from pre-existing MNV in eyes with iAMD or GA (p = 0.847, log-rank test).

Conclusions: By 12 months, the risk of exudation was 15.2 times greater for eyes with documented subclinical CNV compared with eyes without detectable MNV. For eyes with subclinical MNV, recommendations include more frequent follow-up and home monitoring. Intravitreal therapy for subclinical CNV is not recommended until prospective studies are performed.

CORRELATING ISCHEMIA ON ULTRA-WIDE FIELD FLUORESCEIN ANGIOGRAPHY WITH OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN DIABETIC RETINOPATHY

Baumal CR, Alibhai Y, Arya M, Rebhun CB, Moreira-Neto C, Ivana N, Despotovic IN, Witkin AJ, Duker JS, Waheed NK, for areas of capillary non perfusion (mm²) using the built-in software, and an ischemic index was calculated (area of non-perfusion as a fraction of the total area of visible retina). Vessel density of the superficial and deep capillary plexus separately were generated for 3 × 3 mm and 6 × 6 mm OCTA scans using the built-in ReVue software. Spearman’s rho was used to assess the relationship between FA obtained ischemic index and OCTA obtained vessel density.

Results: Twelve eyes from 8 diabetic patients were included in the final analysis. The mean area of capillary non perfusion was 172.6 mm² (range 26.7 to 662.7 mm²), while the mean total visible retinal area was 593.5 mm². The UWF-FA calculated ischemic index did not correlate well with automated vessel density values for the superficial (R = -0.434, p = 0.159) and deep (R = -0.608, p<0.05) plexus on the 3 × 3 mm OCTA scan. However, there was a strong correlation observed between the UWF-FA calculated ischemic index and vessel density values for the superficial (R = -0.874, p<0.01) and deep (R = -0.881, p<0.01) plexus on the 6 × 6 mm OCTA scan.

Conclusions: Automated 6 × 6 mm vessel density analysis using OCT Angiography appears to predict peripheral capillary non perfusion in patients with diabetic retinopathy. Our results suggest that OCTA may have a role in screening for peripheral retinal ischemia, and may identify eyes at higher risk for developing proliferative diabetic retinopathy.

CORRELATION BETWEEN FOVEAL AVASCULAR ZONE (FAZ) AREA BY OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY (OCTA) AND PERIPHERAL RETINAL ISCHEMIC INDEX IN PATIENTS AFFECTED BY DIABETIC RETINOPATHY AND ITS CORRELATION WITH A PERIPHERAL RETINAL ISCHEMIC INDEX WAS PROSPECTIVELY INVESTIGATED

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Purpose: To investigate the foveal avascular zone (FAZ) area by optical coherence tomography angiography (OCT-A) in patients affected by diabetic retinopathy and its correlation with a peripheral retinal ischemic index.

Design: Prospective observational study.

Subjects, participants, and/or controls: Consecutive patients with treatment naïve diabetic retinopathy were prospectively recruited between October 2015 and January 2017.

Methods: All patients underwent a comprehensive ocular examination including optical coherence tomography (OCT), OCT-A, ultra-widefield (UWF) color fundus photography and UWF fluorescein angiography.

Main Outcome Measures: Variables analyzed included best-corrected visual acuity (BCVA) expressed in logarithm of the minimal angle of resolution (logMAR), diabetic retinopathy grading, FAZ area in full-thickness (internal limiting membrane to Bruch’s membrane) and from the OCT-A angiogram, superficial capillary plexus, deep capillary plexus, ischemic index and central macular thickness (CMT) were analyzed.

Results: Twenty-two eyes of 22 patients (21 males, mean age 54.9 ± 15.8 years) were included. Mean FAZ areas at full thickness, superficial and deep plexuses were 0.331 ± 0.137 mm², 0.340 ± 0.140 mm² and 1.028 ± 0.447 mm², respectively. Mean ischemic index was 13.6% (range 0%-50.2%). A significant correlation was found between the ischemic index and FAZ area at both full thickness (r = 0.60, p = 0.0035) and superficial (r = 0.68, p = 0.0005) layers. Disease severity correlated to ischemic index (r = 0.49, p = 0.0204), and FAZ area at full-thickness (r = 0.53, p = 0.0108) (Fig 4B) and superficial (r = 0.47, p = 0.0292) plexuses. No significant correlation between ischemic index and FAZ at deep plexus was appreciated. BCVA correlated only with CMT (r = 0.66, p = 0.0008).

Conclusions: The association between peripheral and macular perfusion found in this study supports the hypothesis that both conditions share a common pathogenic mechanism that leads to capillary non-perfusion.

FLUCINOLONE ACETONIDE INTRAVITREAL IMPLANT FOR DIABETIC MACULAR EDEMA IN HIGHLY TREATED EYES: VISUAL OUTCOMES, COMPLICATIONS AND NEED FOR RESCUE THERAPY

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Background and aim: To assess 0.19 mg flucinolone acetone (FA) intravitreal implant in a cohort of treatment experienced eyes with diabetic macular edema (DME).
**Methods:** Patients treated with FA intravitreal implant for DME were studied. Inclusion criteria were eyes receiving a single FA implant for the treatment of DME with a history of prior treatment for DME.

**Results:** Twenty eyes were identified. Four were male and 11 were female. Nineteen eyes were pseudophakic and 1 eye was phakic. Steroid challenge (SC) was performed with DX (n = 19 eyes) and IVTA (n = 1 eye). Average IOP was 17.9 mmHg at baseline and 15.8 mmHg at 1 year F/U (p = 0.03). Average CTR was 382.4 μm at baseline and 284.3 μm at 1 year F/U (p = 0.02). Average logMAR VA was 0.538 (Snellen 20/69) at baseline and 0.480 (Snellen 20/60) at 1 year F/U (p = 0.22). Ocular hypertension (OHT) from steroid response following FA implant occurred at a mean of 143 days. Five eyes (25%) received rescue intravitreal injections after FA. Eight eyes (40%) were treated with OHT medications at baseline and 11 eyes (55%) were on OHT medications at 1-year F/U. A single eye required selective laser trabeculoplasty (SLT). Eleven of 14 (79%) eyes that had a negative steroid challenge (SC), did not receive rescue intravitreal injections after FA. Eight eyes (40%) were treated following FA implant occurred at a mean of 143 days. Five eyes (25%) were treated.

**Conclusions:** Exposure to FA resulted in a statistically significant improvement in CRT in highly treatment-experienced eyes with DME. Steroid-induced OHT can occur despite negative steroid challenge and can present later than seen with other steroid agents.

**BESTROPHTHIN ONE GENE BUT MANY PHENOTYPES**

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**Purpose:** To describe four patients with peripapillary plaques and visual field defects.

**Methods:** All patients presented between 2009 and 2011 and underwent an ocular examination, imaging and systemic investigations. Clinical features and treatment responses were the outcome measures.

**Results:** Three women and one man aged 37 to 55 years were included. All had new scotomas and three had photopsias or other visual phenomena. None had anterior chamber inflammation, vitritis or retinitis. Fluorescein angiography did not reveal damage to the inner arterial wall, but showed a surrounding band of hypofluorescence. Telangiectatic changes in the capillaries immediately outside this band were present, along with focal staining of an adjacent venule. Fellow eye involvement had occurred in three in the previous one to seven years and was asymptomatic at presentation in the fourth. Investigations for infectious, inflammatory and embolic disease were negative. Neuroimaging and fluorescein angiography did not suggest Susac’s syndrome. Recurrent field defects in two patients prompted systemic corticosteroids. All noted improved field defects, and the plaques disappeared or faded over a few months.

**Conclusions:** Four patients with symptomatic retinal peripapillary plaques, distinct from Susac’s syndrome and other inflammatory and infectious disorders, are described. Although this condition appears self-limited, two responded to systemic corticosteroids. This condition appears to be new and not previously described.

**BESTROPHTH IN ONE GENE BUT MANY PHENOTYPES**

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**Purpose:** To describe four patients with peripapillary plaques and visual field defects.

**Methods:** All patients presented between 2009 and 2011 and underwent an ocular examination, imaging and systemic investigations. Clinical features and treatment responses were the outcome measures.

**Results:** Three women and one man aged 37 to 55 years were included. All had new scotomas and three had photopsias or other visual phenomena. None had anterior chamber inflammation, vitritis or retinitis. Fluorescein angiography did not reveal damage to the inner arterial wall, but showed a surrounding band of hypofluorescence. Telangiectatic changes in the capillaries immediately outside this band were present, along with focal staining of an adjacent venule. Fellow eye involvement had occurred in three in the previous one to seven years and was asymptomatic at presentation in the fourth. Investigations for infectious, inflammatory and embolic disease were negative. Neuroimaging and fluorescein angiography did not suggest Susac’s syndrome. Recurrent field defects in two patients prompted systemic corticosteroids. All noted improved field defects, and the plaques disappeared or faded over a few months.

**Conclusions:** Four patients with symptomatic retinal peripapillary plaques, distinct from Susac’s syndrome and other inflammatory and infectious disorders, are described. Although this condition appears self-limited, two responded to systemic corticosteroids. This condition appears to be new and not previously described.

**ULTRA WIDE-FIELD OCT FOR PATHOLOGIC MYOPIA**

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A posterior staphyloma is a hallmark of pathologic myopia, and has been defined by Spaide as an outpouching of the ocular wall with a curvature radius being smaller than the curvature radius of surrounding ocular wall. Although typical for pathologic myopia, posterior staphyloma can also occur in non-highly myopic eyes. A new prototype of a wide-field swept-source OCT system uses not only one but multiple scan lines and generates scan maps allowing the three-dimensional reconstruction of posterior staphylomas in a region of interest of 16 mm × 14 mm and a depth of 5 mm. Applying wide-field OCT (WF-OCT), we conducted this study to visualize posterior staphylomas in highly myopic eyes in their full three-dimensional extent, to compare the detectability of staphylomas by WF-OCT and by 3D-MRI, and to describe OCT-based characteristics of staphylomas found particularly at the edge of a staphyloma.

The results showed that all staphylomas detected on the 3D-MRI images, except for two very large staphylomas, were visualized on the WF-OCT images.
Morphological hallmarks of the staphylomas were smoothly configured staphyloma border with a gradual thinning of the choroid and an inward protrusion of the sclera at the staphyloma edge. A spatial relationship between the staphylomatous areas and the macula and optic nerve head was observed by WF-OCT.

In conclusion, WF-OCT can provide tomographic images of posterior staphylomas in a resolution and size unachievable so far, and may replace 3D-MRI in assessing posterior staphylomas. Future studies using WF-OCT may explore the detailed morphologic characteristics of posterior staphylomas and give clues to the etiology of staphylomas.

**OCT-A CHANGES IN CNV IN EXUDATIVE AMD DURING ANTI-VEGF-THERAPY**

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**Introduction:** OCT-Angiography (OCT-A) is a new diagnostic tool to differentiate the vascular structures in exudative AMD. In order to transfer these new findings into clinical and therapeutic praxis, two major challenges have to be approached. The first is the definition of OCT-A characteristics of different CNV phenotypes (type 1 and type 2 CNV) and the second is the description of changes in the vascular network during and after anti-VEGF-treatment.

**Methods:** OCT-A images (Optovue, Zeiss-Angioplex and Zeiss-SS; CC-segmentation below the RPE was used as “characteristic” CNV slab) of 25 patients with new, treatment naive type 1 and type 2 CNV were obtained together with BCVA, SD-OCT, FAF and FA. Also after initial 3 Anti-VEF-Treatments as well as every 4 weeks thereafter these examinations were repeated. CNV were qualitatively (minor or good demarcation) and quantitatively (internal and external flow-parameter) classified and compared with FA as well as observed during treatment.

**Results:** Type 1 CNV demonstrated at a minor demarcation, while type 2 CNV showed a good demarcation towards the surrounding CC. During anti-VEF treatment, the size of the flow in the CNV decreased in both CNV types. Quantitatively also predominantly the size but not the flow ratio regressed. On „reactivation“ in SD-OCT especially the capillary part at the border of type 2 CNV demonstrated reestablished flow, resulting in larger flow-size.

**Conclusions:** The analysis of OCT-A 2D-images with CC-segmentation below the RPE permits a differentiation of type 1 and type 2 CNV in exudative AMD. Also therapeutic changes during anti-VEGF therapy can be observed and an additional „activity“ parameter tot he SD-OCT findings is available. Therefore this new method is a very interesting addition to visualize CNV structures before and under treatment. Especially if further methods for the 3-D visualisation of the obtained OCT-A data will be available, the threedimensional structure of the CNV pathology will be observed and differentiated in much more detail and may result in a more individualized therapeutic strategy.

**NEW INSIGHTS INTO MACTE2 BASED ON ADVANCES IN RETINAL IMAGING**

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**Purpose:** To describe new findings made possible by recent advances in retinal imaging and the potential pathophysiologic insights they offer for macular telangiectasia Type 2 (MacTel2).

**Methods:** To review recent studies performed using optical coherence tomography (OCT), OCT angiography, volume rendered angiographic and structural optical coherence tomography, and vector field mapping in MacTel2.

**Results:** In MacTel2 right angle veins appeared in association with vascular proliferation external to the deep vascular plexus. The origin of a right angle vein was surrounded by a stellate arrangement of radiating retinal vessels, apparently caused by contraction of surrounding tissue in the temporal macula. Cavitations were found in the fovea and varied in size and configuration from one examination to the next. Many smaller cavitations, called microcavitations, were seen in the surrounding macula. Vascular invasion occurred into the subretinal space. In eyes with extended follow-up, there was increasing grayish opacification in the temporal macula with straightening and displacement of the macular vessels, even those in the nasal macula. The warp field vectors pointed to the temporal juxtapfoveal macula. There was never any cavitation at the epicenter of the retinal distortion in any patient, although cavitations were found around this area. OCT imaging showed a circumscribed region of hyperreflectivity in the temporal macula. OCT angiography showed a deep angular condensed network of vessels within the hyperreflective region.

**Conclusions:** There are contractile features of the tissue in the temporal macula and the number, size, and temporal variations in the cavitations have not been in not mentioned in previous published descriptions of MacTel2. Tissue contraction with retinal vascular displacement and contortion appear to be integral aspects of disease manifestation in MacTel2. The induced vascular changes may lead to secondary effects that increase morbidity in this disease. Vascular invasion of deeper layers occurs in the temporal macula through the nuclear outer layer.

**TWELVE-MONTH OUTCOMES OF RANIBIZUMAB VS AFLIBERCEPT FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: DATA FROM AN OBSERVATIONAL STUDY**

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**Introduction:** We compared visual acuity (VA) outcomes at 12 months in treatment naïve eyes with neovascular age-related macular degeneration treated with ranibizumab vs aflibercept in routine clinical practice.

**Methods:** Database observational study. Main outcome measures were change in mean VA, number of injections and visits, and proportion of eyes with inactive CNV over 12 months. Eyes that switched or discontinued treatment were included with last observation carried forward.

**Results:** 394 eyes were identified (197 ranibizumab, 197 aflibercept). Baseline parameters were well matched. Mean VA increased in both groups: ranibizumab treated eyes +3.7 [95%CI 1.4-6.1] letters, aflibercept treated eyes +4.26 [95%CI 2.0-6.5] letters. The difference in change in crude VA of 0.6 letters was not statistically significant (p = 0.76), nor was difference in adjusted mean VA (p = 0.26). Among completers, the number of injections (8.1 vs 8.0) and visits (9.6 vs 9.5) did not differ between the two groups. The adjusted proportion of eyes with CNV graded inactive was similar between the two groups (74% ranibizumab vs 77% aflibercept).

**Conclusions:** In this real world observational study, VA outcomes at 12 months did not differ between ranibizumab and aflibercept, nor was there a difference in treatment frequency.

**IMPLEMENTATION OF NATIONAL OBSERVATIONAL STUDIES AND HOW TO INTERPRET THE DATA**

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There are many reasons why collecting Real World Evidence benefits all stakeholders in medical care, not least payers and patients. Implementation of systems to do this regionally is possible but faces some challenges, which we identify here:

1. Identifying a national committee to be custodians of the national data and to direct the registry nationally.
2. Interaction with the local college or society to direct the registry nationally.
3. Privacy issues (particularly in Europe)
4. Single point data entry
5. Motivating training and supporting clinicians to participate
6. Fragmented market of Electronic Medical Record providers
7. Legislation in various host institutions
8. Funding

These issues were encountered and addressed in the first phase of a project in the Netherlands, the NOG has now approved the next phase of the project there. This foundation may assist the development of systems to track and analyse real world outcome data in other countries in Europe.
GENE THERAPY FOR DRY AMD USING A TERMINAL INHIBITOR OF THE COMPLEMENT CASCADE

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Background and aim: Gene therapy, utilizing an adeno-associated virus that produces soluble CD59 (AAVCAGsCD59) as a transgene, has been developed. CD59, also known as protectin, blocks membrane attack complex (MAC) from forming. MAC is implicated in the development of AMD.

Methods: A phase 1, open-label, dose-escalating safety and tolerability 26 week study using a single intravitreal injection of AAVCA GsCD59 in patients with advanced non-exudative (dry) age-related macular degeneration with geographic atrophy was started in March 2017.

Results: AAVCA GsCD59 appears to be safe both in pre-clinical studies and in early phase 1 dose escalation.

Conclusions: Intravitreal injection of AAVCA GsCD59 is being developed for the treatment of geographic atrophy. AAVCA GsCD59 is a novel approach in inhibiting overactivity of the complement system in AMD.

CORRELATION OF LOW LUMINANCE VISION (LLD), LOW LUMINANCE CONTRAST SENSITIVITY (LL-AULCSF), ROD FUNCTION AND DRUSEN VOLUME AS MARKERS OF AGE-RELATED MACULAR (AMD) PROGRESSION

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Decreased low luminance visual acuity and LL-AULCSF as measures of cone dysfunction and reduced scotopic sensitivity (sMPS) as an indicator of rod dysfunction are observed in patients with AMD. Diffuse retina pigment epithelial dysfunction leading to both rod and cone dysfunction has been hypothesized as a major pathologic mechanism in AMD. The goal of the present study was to test this hypothesis by examining the relationships between LLD, LL-AULCSF, sMPS and drusen volumes in patients with AMD.

VA was assessed by standard ETDRS testing at 4 meters while CSF was determined with the Sentio platform (Adaptive Sensory Technology, San Diego, CA), a novel device that applies Bayesian adaptive algorithms to measure the full CSF across a wide range of spatial frequencies. The full CSF was summarized by the area under the Log CSF (AULCSF) from 1.5 to 18 cyc/deg. Low luminance VA and CSF were obtained following placement of a 2 ND filter over the study eye. Low luminance deficits (LLD) for VA and AULCSF were calculated by subtracting low luminance VA and AULCSF from normal luminance VA and AULCSF, respectively. Drusen volume was determined by automated segmentation of the sub-RPE – Bruch’s membrane volume (Spectralis – Heidelberg, Heidelberg, Germany) following by manual corrections (control = 0.1 ± 0.1 (AMD = 0.16 ± 0.06) (3 cm³; mean ± SD). For this portion subjects with early AMD (n = 3), intermediate (n = 14), non-foveal geographic atrophy (GA) (n = 4), and age-matched controls (n = 9) with VA of ≥20/60 were examined. An additional 17 intermediate AMD subjects underwent scotopic microrimetry. Following 30 minutes of dark adaptation, sMPS’s were measured at 56 locations with a spot size 3 within 10° of the fovea, aligned to OCT using a modified fundus microperimeter (MP-1S, Nidek Technologies) and neutral density filters to adjust the dynamic range. Points falling on patches of GA were eliminated. All relationships were evaluated using Kruskal-Wallis test of medians and Pearson’s correlation coefficient (r).

Under normal and low luminance, there were correlations between VA and AULCSF (r = 0.69; r = 0.76). However, low-luminance deficit scores calculated for VA and AULCSF were not correlated (r = -0.02). While there was no statistically significant difference in normal luminance VA between control and AMD (p = 0.68), AULCSF at both normal (p = 0.02) and low luminance (p = 0.005), and VA at low luminance (p = 0.04), showed statistical differences between control and AMD subjects. While there was a statistical difference in drusen volume between control and AMD patients (p = 0.02), in the AMD subjects there was no correlation between drusen volume and VA and AULCSF either under normal or low luminance conditions. In addition there was no correlation between LLD and scotopic sensitivity in the intermediate AMD group (R² = 0.04, p = 0.27).

AULCSF may be a more sensitive indicator of visual function deficits in AMD both under normal and low luminance conditions. However there does not appear to be a correlation between increasing drusen on either CSF or VA under normal or low luminance conditions. In addition there was no correlation between rod and cone functions in intermediate AMD subjects. These results support the hypothesis that cone dysfunction in AMD is distinct from rod photoreceptors abnormalities and drusen accumulation.

COLOR FUNDUS AUTOFLUORESCENCE IMAGES

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Purpose: To evaluate the possibility to visualize different fluorophores of the fundus of the eye with color autofluorescence (AF).

Methods: Color fundus AF images were obtained with a modified EIDON AF scanning ophthalmoscope (CenterVue - Padova, Italy) employing a blue LED as the excitation light (440-475 nm), a high-pass barrier filter (500 nm cutoff) and a color digital sensor (14 MP) with sensitivity extending from 400 nm to 750 nm. Conventional blue AF was obtained by means a Heidelberg Spectralis (Heidelberg Engineering - Heidelberg, Germany) averaging 9 images.

Results: 250 patients with normal fundus and different pathologies such as age-related macular degeneration (early, intermediate and advanced), Stargardt’s diseases, Best disease, Retinitis pigmentosa, adult vitelliform lesions and central serous choroidopathy, were studied.

The images present color content with predominance of orange pixels (lipofuscin, emission peak at approx. 600 nm) and with green regions (non-lipofuscin emission) possibly due to other retinal fluorophores (e.g. A2PE, AGE, FAD) and collagen.

Conclusions: This technique is able to discriminate the different color components of a black and white AF which correspond to different fluorophores. This preliminary data suggests the possibility to use color autofluorescence for a better differential diagnosis.