1006 - A569
Interactive Visualization of the Retina in a 3-D Virtual Reality Environment
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Purpose: We describe the development and application of a novel method to visualize the retina within a 3-D, stereoscopic, immersive, virtual reality environment (CAVE). This allows users to collaboratively view, manipulate, interact with (by intuitively changing head/body position and viewing angles), and analyze volumetric and slice based high-resolution OCT in 3-D space, appreciating retinal morphology with full depth perception (Figure).

Methods: We developed a method to interpret raw data from SD-OCT for visualization within the CAVE. Retinal images of AMD, CSR, RD, and VMT were rendered. Using a custom extension to Avizo software, raw data from SD-OCT, including B-scans, IR images, RPE, ILM and NFL surfaces, were read into scalar fields. These were analyzed and visualized with volumetric tools including registration, filtering and segmentation, geometric and volumetric quantification and skeletonization.

Results: High-resolution, 3-D renderings of SD-OCT images of AMD, CSR, RD, and VMT were successfully reconstructed in the CAVE. This allowed 3-D viewing of the retina with the ability to isolate and subtract specific vitreoretinal interfaces and retinal/choroidal structures. This, coupled with the ability to immerseingly interact with the images (Figure), provided a novel modality to view and understand retinal pathology.

Conclusions: This 3-D virtual reality viewing system offers a powerful, intuitive, and interactive perspective for visualizing posterior segment anatomy and pathology in an extraordinary new way. Customization will permit isolation of structures (e.g. choroidal/retinal vasculature) that can enhance understanding of disease pathophysiology.

CR: G.D. Aker, None; J.S. Myung, None; L. Gracia, None; V. Borcherding, None; J.R. Banfelder, None; D.J. D’Amico, None; S. Kiss, None. Support: None

1008 - A571
The Change of Macular Thickness and Retinal Layer Profiles in Spectral Domain Optical Coherence Tomography According to Axial Length in Korea
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Purpose: To evaluate the change of macular thickness and retinal layer profiles in spectral domain optical coherence tomography (SD-OCT) according to axial length in Korea.

Methods: This study was conducted in accordance with the Declaration of Helsinki recommendations. Informed consent was obtained from all participants. Randomly selected 60 eyes of 60 young, healthy individuals underwent auto-refraction (NRK-recommendations. Informed consent was obtained from all participants. Randomly Methods: This study was conducted in accordance with the Declaration of Helsinki recommendations. Informed consent was obtained from all participants. Randomly selected 60 eyes of 60 young, healthy individuals underwent auto-refraction (NRK-recommendations. Informed consent was obtained from all participants. Randomly.

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Conclusions: This 3-D virtual reality viewing system offers a powerful, intuitive, and interactive perspective for visualizing posterior segment anatomy and pathology in an extraordinary new way. Customization will permit isolation of structures (e.g. choroidal/retinal vasculature) that can enhance understanding of disease pathophysiology.

CR: G.D. Aker, None; J.S. Myung, None; L. Gracia, None; V. Borcherding, None; J.R. Banfelder, None; D.J. D’Amico, None; S. Kiss, None. Support: None

1009 - A572
Ethnic Differences in the Relationship of Axial Length With Macular and Retinal Nerve Fiber Layer Parameters

Purpose: To explore the effect of axial length (AL) on retinal nerve fiber layer (RNFL) and macular measurements in different ethnic groups.

Methods: As part of the Sydney Childhood Eye Study, 2267 year 7 students were examined in 2004 - 2005. AL measurement (IOLMaster and StratusOCT scans of the macula and RNFL were acquired. The RNFL was scanned as a circle of 3.4mm diameter centered on the optic disc and divided into quadrants for analysis. The macula was divided into three concentric zones with outer radii of 0.5mm (central macula), 1.5mm (inner macula) and 3.0mm (outer macula). Pearson correlation coefficients (r) between AL and retinal parameters were calculated. The Bonferroni correction was applied to adjust for multiple comparisons.

Results: For the whole sample average, inferior, nasal and superior RNFL were negatively correlated with AL (r = -0.16, -0.22, -0.17, -0.08 respectively; P<0.001), while the temporal RNFL was positively correlated with AL (r = 0.12, P<0.001). Average inner macula, average outer macula and macular volume were also negatively correlated with AL (r = -0.14, -0.25, -0.22 respectively; P<0.001). Although these patterns were also reflected in the Caucasian and East Asian subgroups, East Asian children displayed stronger correlations for average RNFL, inferior RNFL, nasal RNFL, temporal RNFL, average outer macula and macular volume (r = -0.25, -0.36, -0.31, 0.28, 0.35 and -0.31 respectively; P<0.001) compared with Caucasian children (r = -0.14, -0.20, -0.12, 0.08, -0.17 and -0.13 respectively; P>0.05). In Caucasian children, both fovea minimum thickness and central macular thickness were positively correlated with AL (r = 0.11 and 0.13, respectively, P<0.001).

Conclusions: The strength of AL correlations with retinal parameters varied according to ethnicity; with Asian children displaying the strongest correlations. Ethnicity may be a consideration when interpreting OCT scans on individuals with atypical AL.

CR: Y.M. Yang, None; C. Samarakoonwansa, None; A. Pai, None; G. Burlutsky, None; P. Mitchell, None. Support: None
1010 - A573
Relationship Between Outer Retinal Thickness Substructures and Visual Acuity in Eyes With Dry Age Related Macular Degeneration (AMD)
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Purpose: Retinal thickness on optical coherence tomography (OCT) has shown variable correlation with visual acuity in patients with retinal disease. The speed and sensitivity of spectral domain OCT has provided increased consistency in the identification of fine outer retinal substructures (ORs) among their quantifications. The aim of this study was to explore the correlation between outer retinal substructures and visual acuity in eyes with dry AMD.
Methods: One hundred eyes of 101 consecutive patients with dry AMD and no other retinal diseases who underwent spectral domain (SD) OCT (Topcon 3D-OCT) were included in this study. Raw OCT data was analyzed using OCTORT software, which permits graders to manually draw boundaries. The internal limiting membrane, inner outer nuclear layer (ONL), outer plexiform layer (OPL), photoreceptor inner and outer segments (IS and OS) junction, outer photoreceptor border, inner and outer retinal pigment epithelium (RPE) borders, and Bruch’s membrane were drawn on all required B-scans, where visible, by certified Doheny Image Reading Center graders. Areas, thicknesses and volumes of RPE, IS, OS, ONL, and the total retina were calculated for foveal central subfield, which were correlated with the logMAR best corrected visual acuity.

Results: Thickness, volume and area measurements of the various quantified layers, as well as the correlation coefficient and P-value with visual acuity are shown in Table. Area, thickness and volumes of the total retina, ONL, IS and OS all showed statistically significant associations (P<0.05) with logMAR best corrected visual acuity.

Conclusions: The integrity of outer retinal substructures in the foveal central subfield does appear to correlate with visual acuity in these patients. The correlation, however, is only moderate and does not fully explain the variability in acuity in these patients. CR: R.K. Pappuru; None; Y. Ouyang; None; H.D. Hemmati; None; P.A. Keane; None; S.R. Sadda; None.

1011 - A574
Segmental Macular Retinal Layer Measurements With HR-OCT in Healthy Subjects of Different Refractive Status
B. Kiss1, H. Resch2, C.H. Resch3, B. Brela1, R. Schubert1, C. Vass4. 1Ophthalmology, Medical University of Vienna, Vienna, Austria; 2UMIT, Hall, Austria.
Purpose: Fast scanning high resolution optical coherence tomography (HR-OCT) enables quantitative analysis of histological retinal layers. Aims of the study was to measure overall macular thickness of retinal ganglion cell plus inner plexiform layers (RGPL) and mean maximum thickness after segmental analysis measured by HR-OCT in healthy subjects in order to assess characteristics to their refractive status. Results: In 62 healthy subjects (refractive between -5.5 sph and +6.0 sph) using ultrafast scanning of a 20x20 field at a resolution of 512x128x1024 voxels. The scans were analysed using a software algorithm for automated segmentation and quantification in retinal layers. The macular area scans were dissected into one central area and 4 concentric rings with an incremental radius of 500µm and further subdivided into 16 sectors each. For each of the 16 axis orientations in respect to the fovea the concentric ring segment with the maximum thickness has been determined and these segments have been averaged to the mean maximum thickness of the retinal layers. This was performed separately for the retinal nerve fiber layer (RNFL), the RGPL and the total retinal thickness (RT).

Conclusions: Differences in mean 8deg RT, RGPL between the refractive groups could not be confirmed when comparing the mean maximum thicknesses of the retinal layers around the fovea. These findings may be explained by a refraction dependent magnification of the macular OCT scans. The effective scan areas of hyperopes were smaller compared to myopes thus fractions of thicker RGPL take up a larger proportion of the image. Our findings indicate that maximum RGPL within the image alone might be a representative parameter for patients with different refractive errors in glaucoma diagnosis.
CR: B. Kiss; None; H. Resch; None; C.H. Resch; None; B. Brela; None; R. Schubert; None; C. Vass; None.
Support: None

1012 - A575
Segmental Macular Retinal Layer Measurements With HR-OCT in Healthy Subjects of Different Refractive Status
B. Kiss1, H. Resch2, C.H. Resch3, B. Brela1, R. Schubert1, C. Vass4. 1Ophthalmology, Medical University of Vienna, Vienna, Austria; 2UMIT, Hall, Austria.
Purpose: Fast scanning high resolution optical coherence tomography (HR-OCT) enables quantitative analysis of histological retinal layers. Aims of the study was to measure overall macular thickness of retinal ganglion cell plus inner plexiform layers (RGPL) and mean maximum thickness after segmental analysis measured by HR-OCT in healthy subjects in order to assess characteristics to their refractive status. Results: In 62 healthy subjects (refractive between -5.5 sph and +6.0 sph) using ultrafast scanning of a 20x20 field at a resolution of 512x128x1024 voxels. The scans were analysed using a software algorithm for automated segmentation and quantification in retinal layers. The macular area scans were dissected into one central area and 4 concentric rings with an incremental radius of 500µm and further subdivided into 16 sectors each. For each of the 16 axis orientations in respect to the fovea the concentric ring segment with the maximum thickness has been determined and these segments have been averaged to the mean maximum thickness of the retinal layers. This was performed separately for the retinal nerve fiber layer (RNFL), the RGPL and the total retinal thickness (RT).

Conclusions: Differences in mean 8deg RT, RGPL between the refractive groups could not be confirmed when comparing the mean maximum thicknesses of the retinal layers around the fovea. These findings may be explained by a refraction dependent magnification of the macular OCT scans. The effective scan areas of hyperopes were smaller compared to myopes thus fractions of thicker RGPL take up a larger proportion of the image. Our findings indicate that maximum RGPL within the image alone might be a representative parameter for patients with different refractive errors in glaucoma diagnosis.
CR: B. Kiss; None; H. Resch; None; C.H. Resch; None; B. Brela; None; R. Schubert; None; C. Vass; None.
Support: None
104 - A57
Choroidal Morphology in Central Serous Chorioretinopathy

**Purpose:** To study morphological change of choroid that related to fluid leakage through the retinal pigment epithelium (RPE) in central serous chorioretinopathy (CSC).

**Methods:** Fifty-six eyes 55 patients with CSC were examined with Spectralis OCT (Heidelberg, Germany) by using enhanced depth imaging (EDI) that facilitate to investigate choroidal structure. The EDI-OCT images of the area around fluorescein leakage points were compared with the angiographic findings after magaining (dx) and adjusting the levels of histograms of an EDI-OCT image by using imaging computer software. Routine ophthalmological examination including visual acuity, fluorescein and indocyanine green angiography (IA) was performed for all patients.

**Results:** EDI-OCT delineated a section image of a lobules of choriocapillaris as the layer of high signal intensity beneath the RPE. Choriocapillaris was connected to large choroidal vessels by pre- or post capillary vessels about 20 microns in diameter. Small choroidal vessels about 50-100 microns in diameter aligned with periodicity beneath the layer of choriocapillaris. The high signal intensity layer of choriocapillaris was narrowing (23 eyes, 41%) or interrupted (33 eyes, 59%) around leakage points. 'Narrowing and 'interrupted' were defined as the lesion over 200 microns in length. In this area, small choroidal vessels shifted anterior. These findings corresponded hyperfluorescent spots on IA appeared around the leakage point surrounded by extensive diffuse hyperfluorescence in 54 (96%) eyes.

**Conclusions:** Narrowing or interruption of the choriocapillaris and anterior shift of small choroidal vessels imply collapse or closure of the choriocapillaris around the leakage points because these findings appeared in the area showing hyperfluorescence in IA. The circulatory disturbance of choriocapillaris may cause hyperpermeability in the surrounding area as a result of turbulence of blood flow, which was shown in IA. Failure of choriocapillaris inducing capillary occlusion is potentially the primary lesion of CSC.

CR: T. Sekirya, None; Y. Sugano, None; A. Ojima, None; K. Saito, None; I. Maruko, None; T. Iida, None.

Support: None

105 - A58
Imaging of Choroidal Neovus With Spectral Domain Optical Coherence Tomography

**Purpose:** To describe the spectral domain optical coherence tomography (OCT) findings of choroidal neovus.

**Methods:** 26 patients with choroidal neovus were evaluated by OCT. The mean patient age was 55 years, 14 males and 12 females. Diagnostic imaging was performed with a Spectralis HRA-OCT (Heidelberg Engineering, Heidelberg, Germany).

**Results:** The choroidal neovus was a mean of 4.3 mm in basal dimensions and 1.5 mm in thickness and was located a mean of 2.7 mm from the optic disk and 2.5 mm from the foveola. Related retinal findings by ophthalmoscopic evaluation and at the site of the nevus by OCT included overlying retina edema, subretinal fluid, retinal thinning, drusen, and retinal pigment epithelium (RPE) detachment. Spectral OCT findings of the choroidal neovus included increased thickness of the RPE/choriocapillaris layer (63%) and optical qualities within the anterior portion of the nevus of hyporeflectivity (60%), isoreflectivity (30%), and hyperreflectivity (8%). When comparing OCT with clinical examination, OCT was more sensitive in the detection of related retinal edema, subretinal fluid, retinal thinning, photoreceptor attenuation, and RPE detachment.

**Conclusions:** Spectral domain OCT is a useful diagnostic modality for imaging the retina overlying a choroidal neovus and also it is able to identify the presence of small serous detachments. Numerous overlying changes such as subretinal fluid, retinal edema, retinal thinning, and photoreceptor attenuation are visible by OCT before they become clinically visible.

CR: E. Perrotta, None; U. De Marco, None; S. Salvatore, None; C. Di Crescenzo, None; E.M. Vingolo, None.

Support: None
1018 - A581

**In-vivo Visualization and Quantification of Retinal Pigmented Epithelium (RPE) and Photoreceptor Degeneration in a Rat Retina Model With Ultrahigh Resolution Optical Coherence Tomography**


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**Purpose:** To visualize in 3D and quantify in-vivo outer retinal abnormalities in the rat retina induced by a retinal toxin (NaIO3), by use of a high speed, ultrahigh resolution optical coherence tomography (UHROC) system and novel image processing algorithms.

**Methods:** A high speed, UHROC system, operating in the 1 µm wavelength range was developed for non-invasive retinal imaging. The system provides 3 µm axial and 5 µm lateral resolution in the rat retina and 42 000 A-scans/sec image acquisition rate.

**Results:** 2D and 3D OCT images of healthy rodent retinas showed clear visualization of all retinal layers, RPE, and choroidal vasculature. UHROC tomograms acquired 3 and 7 days post-NaIO3 injection showed progressive loss of the RPE layer, morphological changes in the inner- and outer segments of the photoreceptor layer appearing as clusters of highly reflective spots of ~10 µm - 30 µm in diameter and alternating with areas of abnormally low signal in the RPE, complete loss of the ELM as well as changes in the shape and thickness of the outer nuclear layer. Histological analysis confirms the loss of RPE and fading of the outer retina, loss of photoreceptor outer/inner segments, along with in some areas, complete loss of the outer retina such that the inner retina is in direct contact with Bruch's membrane.

**Conclusions:** We have developed a state-of-the-art, UHROC system for imaging the retina and new image processing algorithms for automatic segmentation and thickness measurement of retinal layers. When applied to a retinal toxicity model in the rat eye, the system allows for in-vivo observation and precise quantification of morphological changes that correlate well with histology.

**Support:** The Natural Sciences and Engineering Research Council of Canada (NSERC), the Collaborative Research Centre (CRC) and Peter & Louise Walter Retinal Regeneration Laboratory, St. Michael's Hospital.

1019 - A582

**Ultrahigh Speed Spectral / Fourier Domain OCT Imaging of the Rodent Retina**


*Department of Electrical Engineering and Computer Science and Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, MA; Advanced Imaging Group, Thorlabs, Inc., Newton, NJ; New England Eye Center and Tufts Medical Center, Tufts University, Boston, MA.*

**Purpose:** Non-invasive imaging technologies for measuring rat and mouse retinal structure and physiology at the micron level could be useful tools for ocular biomedical research. Spectral / Fourier domain OCT imaging is a promising technique for rat and mouse retinal imaging. Ultrahigh speed spectral / Fourier domain OCT enables novel protocols which can be used for measuring rodent retinal structure and retinal blood flow in vivo.

**Methods:** An ultrahigh speed spectral / Fourier domain OCT prototype instrument has been developed for small animal imaging using high-speed CMOS imaging technology. This technology achieves imaging speeds over 100 000 axial scans per second with axial image resolutions of ~3 µm. A microsphere delivery system was developed for focusing and scanning the OCT beam in the animal eye. Three dimensional OCT 3D-3D OCT data sets of the rodent retinas were acquired. Projection OCT fundus images were created from axial summation of 3D OCT data. Doppler OCT analysis of blood flow in the rodent retina was performed.

**Results:** Ultrahigh speed imaging enables high pixel density 3D OCT data with minimal eye motion artifacts. Residual motion artifacts can be reduced or eliminated using more advanced image processing methods. At such high speeds, the OCT fundus images offer more precise registration of individual OCT images to retinal fundus features. Projection OCT fundus images of normal rodent retina show anatomic features such as the nerve fiber layer, retinal capillary network, and choroidal vasculature. Doppler OCT provides measurements of blood flow in retinal blood vessels.

**Conclusions:** Ultrahigh speed imaging of the rodent retina was demonstrated at speeds over 100 000 axial scans per second using spectral / Fourier domain OCT. Optimal OCT image sets obtained at high speeds show reduced motion artifacts. Projection OCT fundus imaging enables visualization of fine retinal features. Doppler OCT provides non-invasive measurements of retinal blood flow in vivo and may benefit studies of diseases such as glaucoma and diabetic retinopathy. Therefore, ultrahigh speed spectral / Fourier domain OCT is a promising tool for monitoring disease progression in rat and mouse models to characterize ocular disease pathogenesis and response to treatment.

**Support:** J. J. Liu, None; B. Potsaid, Thorlabs, Inc., E.; J. S. Duker, Carl Zeiss Meditec, Inc., F.; J. G. Fujimoto, Optovue Corporation, F.; Carl Zeiss Meditec, Inc., F.

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1021 - A584

**Biometric Measurements Inside the Model Eye Using a Two Wavelengths Spectral Domain Interferometer**

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**Purpose:** Biometric measurements inside the eye using spectral domain interferometry are limited by the measuring depth (in the order of 6-8 mm) basically due to the spectral resolution. Therefore the measurement has to be divided in several fragments. To minimize data acquisition time two spectral domain interferometers with different wavelength ranges are combined for simultaneous biometric measurement in terms of corneal thickness, anterior chamber depth, and axial length. **Methods:** Two spectral domain interferometers were combined to measure the anterior and posterior parts of a model eye simultaneously. For the anterior part a SLD with a wavelength of 954±17 nm (Superlum Ltd.) and for the posterior part a SLD with a wavelength of 812±12 nm (Exalos AG) were used. The applied powers were below the German laser regulations for continuous exposure. The interference signal is detected by a self constructed spectrometer. The spectrometer has a theoretical resolution of 0.03 nm for the anterior part and 0.056 nm for the posterior part. The necessary offset between both optical paths in the combined setup was calibrated with a known reference object. The feasibility is tested by using a self constructed human model eye. The model consists of a contact lens, small lens, and a reflecting surface. The model eye is filled with water.

**Results:** The axial length, the corneal thickness, and the anterior chamber depth of the model eye were simultaneously measured. The measuring time including exposure time, transfer to the computer, and visualization by LabVIEW was approx 20 ms. The maximal detectable depth of the setup was 6.1 mm (anterior part) with a maximal sensitivity of 83 dB and 5.9 mm (posterior part) with 83 dB.

**Conclusion:** The combined setup of the two wavelengths Fourier interferometer allows a biometric measurement within a very short time frame. Therefore potential improvements should have no influence to the result. No additional algorithms are necessary to combine results of multiple single measurements. Beside the fast measurement this setup provides the possibility to adjust the laser power of both sections independently. This may help in the case of dense cataracts.

**Support:** University funding AKF-program 239-0-0

CR: T. Bende, None; S. Birkner, None; J. Einighammer, T. Oltrup, None; B. Jain, None.

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The prevalence of Diabetic Retinopathy (DR) has been growing at a dramatic rate and is the leading cause of new cases of blindness in patients 20-74 years of age in the U.S. The extra cost and inconvenience of seeing an eye specialist causes many patients to be non-compliant with recommended yearly dilated screening exams. The proposed diagnostic camera aims to circumvent these problems by low-cost retinal photographic screening within the primary care physician’s clinic that is easy to use with minimal training.

Conclusions: The fundus camera design consists of a novel optical attachment integrated with a Canon consumer digital camera (Canon G11). Illumination of the retina is achieved through the use of LEDs and Xenon flash via fiber optic cable coupling along with a combination of beam-splitters and additional optics to produce standard ring illumination at the retinal surface. A front-mountital holographic lens directs light from the eye and transmits the fundus image to the camera, providing a standard 60 degree field of view. Images are then captured and stored on the camera’s SD memory card. Results: By taking advantage of recent improvements in the consumer digital camera industry, such as image stabilization and LiveView, the proposed device succeeded in being compact while maintaining the user friendliness of a common point-and-shoot digital camera. The device is low cost (£8000 in parts), is able to be used by untrained medical personnel, is hand-held with no external power supply, and is capable of taking superior quality images of the fundus (Fig. 1).

Conclusions: The current prototype fundus camera produces images of sufficient quality for screening purposes. When coupled with an automated off-site image review service for the primary care provider, we believe this device can have a substantial impact on providing appropriate eye care for diabetics within the US. It may also find use for low cost fundus photography in developing nations.

Figure 1: (A) Typical fundus image from current camera prototype (B) Prototype camera image of a fundus image with an internal filter that is an overtone of Canon G11 camera with novel lens attachment and fiber optic coupled flash.
1026 - AS99
Measurement Maps of Dynamic ICG for Neovascular Conditions
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Purpose: Work was carried out to develop and test software algorithms that derive quantitative measures from dynamic indocyanine green (d-ICG) movie sequences and produce image maps of these measures. The main application is in the assessment of response to therapies for neovascular conditions, such as laser photocoagulation of feeder vessels to neovascular lesions and anti-VEGF injection therapy.

Methods: Six movie pairs were processed, that were obtained from Heidelberg Retinal Angiograph (HRA) and Spectralis models of scanning laser ophthalmoscopes. Each pair contained a baseline and follow-up movie, taken before and after treatment, respectively. Some of the movie pairs were of feeder-vessel laser photocoagulation therapy and some were of anti-VEGF treatment. The cases were categorized as responders and nonresponders, by standard clinical methods, where the term responder means that the neovascular lesion responded positively to the treatment and nonresponder means that the neovascular lesion progressed to a worse condition after treatment. Quantitative measures were produced for each pixel in the image that reflected the time-delay for dye filling, the overall fluorescences magnitude that is affected by blood volume and flow associated with the pixel, dispersion of the temporal fill pattern that reflects diffusion of the dye, and, (4), pulsation magnitude that is affected by cardiac activity.

Results: The resulting images were examined for information that may serve as adjunct information to assist the physician in evaluating the response to therapy or in identifying pathological anatomy such as the feeder vessel, drain vessel and capillary network of the lesion in planning and deciding treatment options.

Conclusions: The measures that showed the most promise for augmented clinical information to the physician were the time-delay (1) and magnitude (2) image maps. The time-delay is an aid to identifying the feeder, drain and capillary network because the earliest fill occurs in the feeder, while the middle and late fills occur in the capillary network and drain, respectively. The magnitude showed decreasing activity in the feeder and drain, and sometimes in the capillary network with responders.


1028 - AS91
Non-Invasive Measurement of the Absolute Hemoglobin Value in the Retinal Arteries of Anemic and Healthy Subjects Using a New Approach
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Purpose: To test a new non-invasive tool to measure absolute hemoglobin concentration in retinal arteries.

Methods: 50 healthy volunteers as well as 40 anemic, otherwise healthy pregnant patients from the Triemli Hospital, Zurich, were included. Hemoglobin concentration was quantified by a blood draw of a cubital vein using Advia®2120 hematology system. A non-myrdiatic digital Fundus Camera (Noked AFC-230) pictures of the central fundus were taken from each study patient. Segments of retinal arteries were selected by the investigator. The intensity of the green channel - according to the absorption maximum of hemoglobin - of the camera chip was determined with the aid of the law of Lambert Beer. Absolute hemoglobin concentration was calculated in relation to the vessel volume.

Results: 83 females and 7 males were included. Mean age was 32 (range 18-63). Hemoglobin levels from the cubital veins ranged from 8.1-11.9 g/dL (mean 10.0), hemoglobin levels below 11.4 g/dL calculated from the non-invasive technique corresponded to the venous value with $r = 0.99$.

Conclusions: This new technique is suitable for monitoring hemoglobin concentrations in a non-invasive way and allows us for measuring hemoglobin on the site of the retinal pathology and therefore may give us further information about hemodynamic alterations in retinal diseases and may provide a new possibility in finding therapy options.

Support: None

1027 - A590
Oxygen Saturation Analysis With the Pulsation of Choroid Observed by a Dynamic Two-Spectral-Band Fundus Camera
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Purpose: We have been working on the functional imaging of the retina using a two-spectral-band fundus camera (730-780 nm, 820-880 nm). When we analyzed the spatio-temporal independent components (IC), we noticed the IC having choroidal spatial pattern in the image and fluctuation caused by the pulse in the time course. We investigated if this IC may be used for estimating oxygen saturation in the choroid.

Methods: Two eyes of two cats were studied under general anesthesia. The total time of the experiment was six minutes. For the first cat, we provided artificial ventilation with 50% oxygen for 30 seconds at the beginning of the experiment, then no ventilation for three minutes, and again provided the artificial ventilation for 2 minutes 30 seconds. For the second cat the durations of three ventilation conditions were 30 seconds, 1 minute 20 seconds, and 4 minutes 10 seconds. We obtained images from a cat retina using the fundus camera during the experiment. We repeated one-second imaging every 2.5 seconds for 150 times. The one-second imaging consisted of 40 images for each spectral band. We analyzed the 40 images using an independent component analysis (ICA). We manually chose a time-invariant pattern IC (TIC) and a choroidal spatio-temporal pattern IC (CIC) from the ICs obtained by the ICA. Because the spatial pattern in the CIC was normalized in power spectrum, we could calculate the power ratio in the pulse portion of the choroidal pattern by comparing the power spectrum of the time course at pulse frequency in the CIC to the average value of the time course in the TIC. Finally, we calculated a ratio of those in the two spectral bands and investigated if the values could be used for possible oxygen saturation measurement.

Results: It was easy to select a TIC and a CIC from each one-second duration. The ratios of pulsation portion in the two spectral bands were 0.604 and 0.657 for two cats under the regular 50% oxygen condition. After the three-minute non-oxygen condition in the first cat, the ratio was 0.825 for one cat. In the other cat with one-minute-20-second non-oxygen condition, the ratio did not vary and stayed around 0.65. Theory of the pulse oximetry predicted that the ratio is the larger when the oxygen saturation is less, so the tendency of the first cat results was consistent with the theoretical prediction.

Conclusions: The results suggested possibility of choroidal oximetry using pulsation observed by a multi-spectral-band fundus camera.

Support: None
**1032 - A599**

**Noninvasive Estimation of Oxygen Saturation Using the Scanning Laser Ophthalmoscope**


**Purpose:** Practical implementation of retinal oximetry must lead to early detection of retinal diseases. As the retina consumes a large amount of oxygen similarly to the cerebrum, insufficient oxygen induces retinal necrosis and the cytokines generated from hypoxic tissues make fragile neovessels, which may cause retinal detachment, blood vessel destruction, or glaucoma. Therefore, we developed the spectroscopic scanning laser ophthalmoscope (Spectroscopic SLO) to measure the oxygen saturation non-invasively. The spectroscopic-SLO can be used without the mydriatic and the injection of contrast dye, which is suitable for screening tests.

**Methods:** We added a spectroscopic feature to a SLO produced by Nidek Co., Ltd. (Gamagori, Japan). The spectroscopic filter, a white-light illumination, a highly sensitive detector were installed in it to get spectroscopic images. The wavelengths between 450 nm to 700 nm can be selected to measure the Q-band of hemoglobin. The five spectrum images detected by the spectroscopic-SLO were translated to the oxygen saturation using the partial least square analysis. We employ the pre-dispersed illumination method for preventing too much exposure on retina. In our system, the exposure power was between 10-30 pW for getting the retinal spectral images.

**Results:** We applied this system to clinical research under approved method by the Institutional Review Board (IRB). The one result for a healthy volunteer is shown below. Brightness of the picture shows the oxygen saturation on the retina. Arteries can readily distinguishable from veins for a healthy retina. We show some cases focusing on diabetic retinopathy.

**Support:** None.

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**1033 - A596**

**Simultaneous Probing of the Structure and Function of the Rat Retina in vivo With a Combined UHROCT and ERG System**

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**Purpose:** The main objective of this study was to establish a correlation between the retinal structure and function in a rat retina model by use of a combined high speed, ultrafast high resolution optical coherence tomography (UHROCT) and full filed electroneurogrammetry (ERG) system.

**Methods:** We developed a prototype, combined UHROCT + ERG (full field) system for simultaneous probing of the retinal structure and function in rodent retinas. The UHROCT system operates in the 1060nm wavelength region, outside the spectral range of the ERG visual stimulus, and provides 3um axial and ~5um lateral resolution in the rat retina at the imaging rate of 46 fps. The UHROCT was combined with a commercial full field ERG system (Dignosys LLC) for simultaneous acquisition of the OCT images and the ERG traces. UHROCT + ERG data was acquired from healthy and damaged (drug induced toxicity) rat retinas of female Long Evans rats using visual stimuli of various duration, luminance, frequency and spectral characteristics.

**Results:** UHROCT tomograms acquired from healthy rat eyes showed clear visualization of all intra-retinal layers, the choroid and the sclera were associated with normal ERG traces. In the retinas of drug treated animals, dose-, time- and drug type- dependent morphological changes were observed, including thinning of the neural layers, disruption of the ILM and ELM, development of highly reflective and highly transmissive spots in the photoreceptor and RPE layers and overall change of the optical properties (image contrast) in some of the retinal layers. ERG traces acquired simultaneously with the optical images showed reduced magnitude of the a and b-waves and in some cases, complete loss of the ERG signal. Depending on the type of drug and the dose used, the loss of the ERG trace was temporary or permanent. The observed structural changes coincided with the elimination of the a-wave and downstream loss of function in the ERG traces.

**Conclusions:** Our preliminary results suggest a direct link between the changes in retinal morphology and functional response to visual stimuli as measured with ERG in damaged retinas. The combined UHROCT + ERG system could provide ophthalmologists with the means to achieve a deeper understanding of the origins and progression of neurodegenerative retinal diseases.

**Support:** The Natural Sciences and Engineering Research Council of Canada (NSERC), the Ontario Research and Development Fund (ORDFC), and the Peter & Louise Walter Retinal Research fund.

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**1030 - A593**

**Noninvasive Estimation of Oxygen Saturation Using the Scanning Laser Ophthalmoscope**


**Purpose:** The metabolic function of the retinal tissue is likely altered due to disease, therefore measurements of retinal tissue oxygen tension and consumption may be beneficial in assessment of retinal health. The purpose of this study is to report measurements of outer retina oxygen tension (PO2) and oxygen consumption (Q) by a phosphorescence imaging technique in rats under hypoxia and normoxia.

**Methods:** Retinal tissue PO2 maps were generated in rats using our optical section spectroscopic laser ophthalmoscope (SLO) system. A narrow vertical laser line at 532 nm was projected on an angle on the retina after intravitreal injection of an oxygen-sensitive molecular probe. Phosphorescence lifetime and PO2 were calculated at each pixel on the depth-resolved retinal tissue image. Three repeated retinal PO2 maps were being acquired for each of 9 and 10 rat eyes under hypoxia (10% O2 breathing) and normoxia (30% O2 breathing), respectively. Retinal PO2 profiles through the retinal depth were derived by plotting PO2 values vertically averaged over 100-micron segments along the image. For each profile, the outer retinal Q was calculated by fitting the curve to a steady-state one-dimensional oxygen diffusion model. Coefficients of variation (COV) for maximum outer retinal PO2 (PmaxO2), minimum outer retinal PO2 (PminO2) and outer retinal Q were calculated. Statistical t-test and ANOVA were performed to compare measurements.

**Results:** The systemic arterial PO2 measurements under hypoxia and normoxia were 44 ± 10 mm Hg (mean ± SD, N = 9) and 106 ± 18 mm Hg (N = 10), respectively and were significantly different (p < 0.001). The COV of repeated measurements of PmaxO2, PminO2 and Q were on average 9%, 11% and 15% under normoxia, respectively, and not significantly different (p > 0.09). P OR maxO2 and POR minO2 measurements were 16 ± 44 ± 10 mm Hg and hypoxia and 59 ± 15 and 39 ± 13 mm Hg under hypoxia and normoxia, respectively. Outer retinal Q measurements were 0.31 ± 0.12 and 0.75 ± 0.28 ml O2/100g/tissue/min under hypoxia and normoxia, respectively (p < 0.001). Q measured under normoxia was linearly correlated with PO2 (r = 0.84, p < 0.0001; N = 19). The COV of PmaxO2, PminO2 and Q measurements along the image were on average 16%, 21%, and 32%, respectively and significantly different (p < 0.001).

**Conclusions:** An imaging method was utilized to measure outer retina oxygen tension and oxygen consumption and report alterations under hypoxia and normoxia in rats. This technique may be of value for quantitative mapping and monitoring of retinal metabolic function over time.

**Support:** None.

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**1031 - A594**

**Measurement of Retinal Tissue Oxygen Consumption in Rats by Phosphorescence Lifetime Imaging**


**Purpose:** The metabolic function of the retinal tissue is likely altered due to disease, therefore measurements of retinal tissue oxygen tension and consumption may be beneficial in assessment of retinal health. The purpose of this study is to report measurements of outer retina oxygen tension (PO2) and oxygen consumption (Q) by a phosphorescence imaging technique in rats under hypoxia and normoxia.

**Methods:** Retinal tissue PO2 maps were generated in rats using our optical section spectroscopic laser ophthalmoscope (SLO) system. A narrow vertical laser line at 532 nm was projected on an angle on the retina after intravitreal injection of an oxygen-sensitive molecular probe. Phosphorescence lifetime and PO2 were calculated at each pixel on the depth-resolved retinal tissue image. Three repeated retinal PO2 maps were being acquired for each of 9 and 10 rat eyes under hypoxia (10% O2 breathing) and normoxia (30% O2 breathing), respectively. Retinal PO2 profiles through the retinal depth were derived by plotting PO2 values vertically averaged over 100-micron segments along the image. For each profile, the outer retinal Q was calculated by fitting the curve to a steady-state one-dimensional oxygen diffusion model. Coefficients of variation (COV) for maximum outer retinal PO2 (PmaxO2), minimum outer retinal PO2 (PminO2) and outer retinal Q were calculated. Statistical t-test and ANOVA were performed to compare measurements.

**Results:** The systemic arterial PO2 measurements under hypoxia and normoxia were 44 ± 10 mm Hg (mean ± SD, N = 9) and 106 ± 18 mm Hg (N = 10), respectively and were significantly different (p < 0.001). The COV of repeated measurements of PmaxO2, PminO2 and Q were on average 9%, 11% and 15% under normoxia, respectively, and not significantly different (p > 0.09). P OR maxO2 and POR minO2 measurements were 16 ± 44 ± 10 mm Hg and hypoxia and 59 ± 15 and 39 ± 13 mm Hg under hypoxia and normoxia, respectively. Outer retinal Q measurements were 0.31 ± 0.12 and 0.75 ± 0.28 ml O2/100g/tissue/min under hypoxia and normoxia, respectively (p < 0.001). Q measured under normoxia was linearly correlated with PO2 (r = 0.84, p < 0.0001; N = 19). The COV of PmaxO2, PminO2 and Q measurements along the image were on average 16%, 21%, and 32%, respectively and significantly different (p < 0.001).

**Conclusions:** An imaging method was utilized to measure outer retina oxygen tension and oxygen consumption and report alterations under hypoxia and normoxia in rats. This technique may be of value for quantitative mapping and monitoring of retinal metabolic function over time.

**Support:** None.

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**CR:** H. Furukawa, None.

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**CR:** H. Furukawa, None.

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1034 - A597
Properties of Flash-Evoked Retinal Activity Revealed by Functional Optical Coherence Tomography (fOCT) in the Macaque Retina

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Purpose: fOCT can detect flash-evoked light scattering changes following neuronal activation in the neural tissues. This is called functional OCT (fOCT) technique. The basic properties of the fOCT signals, however, have not been well investigated. We have measured fOCT signals with both diffuse and focal stimuli from macaque retina to precisely investigate their properties and possible sources.

Methods: We have developed a fOCT system based on spectral domain OCT (SLD, 840 nm; band width 50 nm) through the same optical pathway. Following dark-adaptation, the posterior retina was stimulated by (1) diffuse flashes (duration: 1ms) with different intensities or (2) focal flashes. The evoked signals were calculated by dividing the images obtained by the stimuli by those obtained during the pre-stimulus level by pixel after spatial alignment of the images.

Results: With diffuse flash stimulation, increases in the fOCT signals were observed in the outer segment of photoreceptor layer (OS). The magnitude of the fOCT signals increased (> 40 % for the strongest stimulation at fovea) with flash intensities. In the inner segment and outer segment (IS/OS) junction, fOCT signals were also observed, but with opposite polarity to those in the OS. fOCT signals were not observed either in the RPE or choroid. With focal stimulation, increases of OCT signals were observed both in the OS of the stimulated region and in the ganglion cell layer of the non-stimulated region. The polarities of the fOCT signals were not different in stimulated and non-stimulated regions, not like in the case of the intrinsic signal imaging.

Conclusions: The fOCT signals reflect the stimulus-evoked neural activities both in the outer and inner retinas. However, their polarities of the signals are not same as those in the intrinsic signal imaging, indicating that fOCT signals may be generated by the different mechanisms from those of the intrinsic signal imaging.

Support: SENTAI, JST.

1035 - A598
Static and Dynamic Retinal Fixation Stability in Microperimetry

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Purpose: To evaluate retinal fixation stability, obtained by microperimetry, both in static and dynamic patterns, in normal and pathologic eyes.

Methods: One hundred and thirty-one pathologic eyes (58 diabetic retinopathy, 35 age-related macular degeneration (AMD), 37 glaucoma and 21 vitreo-retinal interface disorders) and 152 age-matched normal eyes were included in this study. Retinal fixation characteristic (stability) was studied during a pure fixation task (static fixation: 60 seconds) and during a differential light threshold quantification (dynamic fixation) by MP-1 microperimeter (Nidek, Gamagori, Japan). Fixation stability was quantified with both the automatic clinical score (central 2° and central 4°) and the automatic calculation of the bivariate contour ellipse area results (BCEA).

Results: Using MP-1 automatic clinical score of fixation stability in both static and dynamic condition, pathologic group was statistically different to normal group (p<0.0001). There was not significant difference between static and dynamic retinal fixation in normal group whereas in pathologic group the difference between static and dynamic retinal fixation was statistically significant (p<0.0001). Analyzing BCEA the difference between pathologic and control groups was statistically significant both in static and in dynamic retinal fixation (p<0.001). The difference between static and dynamic fixation is statistically significant both in normal and in pathologic eyes (p<0.0001). Fixation stability is related with both techniques, to the etiology of macular disorders (static, p<0.001; dynamic, p<0.001).

Conclusions: Fixation stability may be characterized, using microperimetry, by static and dynamic patterns. BCEA can be useful for monitoring minimal quantitative changes of the fixation area, related to the standard clinical results. Fixation stability remains the most important clinical parameter of retinal fixation in macular disorders.

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Support: None.

1036 - A599
Regional Age-Related Changes on Macular Function as Measured by Scanning Laser Ophthalmoscopy Microperimetry

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Purpose: To evaluate the relationship between age and regional macular sensitivity values in normal subjects by scanning laser ophthalmoscopy microperimetry (SLO-MP).

Methods: We prospectively enrolled 147 normal subjects (147 eyes), mean age 44.4±14.7 years (range 21-85 years). After a complete ophtalmological examination, all patients underwent microperimetry testing using a SLO-MP device (Spectral OCT/SLO, OPKO-OCTI, Miami, FL). The “Polar3” scan was used and the macular area was divided into 3 concentric circles (inner, middle and outer regions). Test parameters were Goldmann III size stimulus, 200ms stimulus duration, stimulus interval of 1.5 sec and 4-2 threshold strategy. SLO-MP thresholds in each macular region were compared among age groups using analysis of variance (group 1, 21 - 39 yrs; group 2, 40 - 59 yrs; group 3, ≥60 yrs). Testing purposely included points within and just adjacent retina and correlate structure with functional findings.

Results: The SLO-MP thresholds for all macular regions were significantly reduced with increasing age in all macular regions, with a steeper decrease in the outer macular regions. Average age was 25.75 years (SD= 14.02). Average testing time was 10 minutes 47 seconds. The sensitivity both in static and adjacent retina decreased with age. This was more pronounced in areas adjacent to the coloboma in an attempt to delineate thresholds for each of these retinal areas. Patients with forme fruste, small “nervous doubling”, and large colobomas were included in the study.

Conclusions: Fixation stability may be characterized, using microperimetry, by static and dynamic patterns. BCEA can be useful for monitoring minimal quantitative changes of the fixation area, related to the standard clinical results. Fixation stability remains the most important clinical parameter of retinal fixation in macular disorders.

CR: E. Convento, None; S. Vujosevic, None; E. Pilotto, None; G. Bonini, None; I. Fregona, None; A. Ghirlando, None; E. Midena, None.
Support: None.

1037 - A600
Microperimetry Thresholds for Complete and Forme Fruste Chorioretinal Colobomas and Adjacent Retina


Purpose: To measure differential light thresholds in chorioretinal colobomas and adjacent retina and correlate structure with functional findings.

Methods: 13 eyes of 8 patients with chorioretinal coloboma were examined using the MP1 microperimeter (NIDEK, Italy) and a program customized to examine the inferonasal retina involved with the coloboma. Examination settings included an adaptive Goldmann III stimulus and a 4-2 staircase strategy. The stimuli were projected on a white background with background illumination set to 2.72 cd/m2 and a stimulus presentation time of 200 msec. Testing purposely included points within and just adjacent to the coloboma in an attempt to delineate thresholds for each of these retinal areas. Patients with forme fruste, small “nervous doubling”, and large colobomas were included in the study.

Results: Six female and two male patients with chorioretinal coloboma were tested. Average age was 25.75 years (SD= 14.02). Average testing time was 10 minutes 47 seconds per eye (SD= 90.27 seconds). Average number of tested points inside colobomas was 12.08 (SD= 11.74) with an average sensitivity of 7.36 dB (SD= 7.72). Average number of tested points surrounding colobomas was 12.08 (SD= 5.89) with an average sensitivity of 12.71 dB (SD= 5.67). The sensitivities both in and adjacent to the colobomas ranged from 0 to 20 dB. Areas at the edge of even large colobomas often had normal thresholds. When the sensitivity of areas inside the coloboma was compared to that of areas adjacent to it the most significant difference was observed in patients who had large colobomas (r20.04, p<0.01) in forme fruste patients.

Conclusions: MP1 microperimetry seems to show that the area surrounding the coloboma has relatively good sensitivity. Application of the same testing process to other retinal lesions may offer us additional glimpses of structure-function relationships.

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1038 - A601
Association Between Structural Parameters and Visual Function in Different Stages of Glaucoma

Purpose: To determine the association between visual function, as measured by Humphrey visual field (VF), and structural parameters of lamina cribrosa (LC), peripapillary retinal nerve fiber layer (pRNFL) and ganglion cell complex (GCC) thickness, as measured by optical coherence tomography (OCT) at different stages of glaucoma.

Methods: Forty one eyes of 24 glaucoma patients were classified as pre-perimetric (glaucomatous optic neuropathy with normal HVF), early, and advanced glaucoma were 98 ± 14, 77 ± 11 and 70 ± 6 microns, respectively. GCC thickness measurements in pre-perimetric, early, and advanced glaucoma were 262 ± 29, 193 ± 27 and 107 ± 16 microns, respectively. pRNFL thickness measurements in pre-perimetric, early, and advanced glaucoma were 89 ± 10, 72 ± 9 and 71 ± 8 microns, respectively. There was a statistically significant difference in LC, pRNFL and GCC thickness among patients with pre-perimetric (MD = 0.66 ± 0.28 dB, N=13), early (MD = 2.9 ± 1.6 dB, N=14) and advanced glaucoma (MD = 12.1 ± 7.0 dB, N=14) (p < 0.001). In the pre-perimetric group, pRNFL and GCC thickness significantly correlated with MD (r=0.75, p=0.003 and r=0.84, p=0.003, respectively). In the early group, LC and pRNFL thickness significantly correlated with MD (r=0.96, p=0.0008). Conclusions: An overall association between visual function and structural parameters of LC, pRNFL, and GCC thickness was found. The results suggest that LC thickness may be a better parameter for monitoring patients with advanced stage glaucoma.

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1040 - A603
Structure-Function Correlation of the Human Central Retina
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Purpose: To precisely correlate high resolution structural and functional maps of the human macula.

Methods: A custom-made software tool (MultiModalMapper) allowed for co-registration of fundus-mapped micropointer (MP, Nidek) and spectral domain optical coherence tomography (SD-OCT) (Heidelberg Engineering) datasets. The transformation model features mapping of 2D micropointer data on 3D-OCT datasets using corresponding landmarks on both fundus images. The software accounts for different radial lens distortion of both systems. Well-defined features of structural and functional correlations are exemplified in macular telangiectasia (MacTel) type 2. Longitudinal data were analyzed from the RAMA-trial (ranibizumab for MacTel type 2; ClinicalTrials identifier: NCT00544400). The study received ethical approval by the local committee and each patient gave written informed consent to participate.

Results: While damage to the outer retina (photoreceptors) was accompanied by a loss of retinal sensitivity as measured by micropointer, similar changes to the inner retina usually showed a normal corresponding function. There was a significant correlation between thickness of outer retina and retinal sensitivity (r=-0.8, p<0.001, two-tailed Pearson correlation coefficient). Longitudinal data from the RAMA-trial revealed that small lesions affecting the outermost neurosensory retina typically preclude functional detection but later cause severe loss of light sensitivity.

Conclusions: There can be remarkable functional compensation if the macular pathology spares the outer neurosensory retina. There is a general need for surrogate endpoints to diagnose disease in its early stages, when treatment is most effective and irreversible (functional) damage can be prevented or delayed. Since SD-OCT is becoming more widely available, surrogate endpoints derived from structure-function correlation may become highly relevant in future clinical trials.

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1039 - A602
Fixation Pattern and Macular Sensitivity in Eyes With Uveitic Macular Edema

Purpose: Persistent macular edema often leads to visual loss in uveitis and ocular inflammatory diseases. We investigate the effects of uveitic macular edema (UME) on macular functional parameters quantified with an automatic micropointer and correlated with retinal thickness.

Methods: 20 eyes of 14 patients with UME were evaluated with spectral optical coherence tomography / scanning laser ophthalmoscope (Spectral OCT/SLO™, OPKO/OTTI, Toronto, Canada) by the same operator. Spectral OCT was used to characterize the type of macular edema. Micropointerometry together with retinal thickness map were used to quantify fixation pattern (location and stability), macular sensitivity, and corresponding retinal thickness at 28 test points. Multiple linear regression model with generalized estimation equation was used to evaluate relationship between macular sensitivity and thickness, duration, and type of UME.

Results: Of 14 patients, the mean age was 52.8±18.8 years, range 23-86 years. Associated uveitic diseases include: intermediate uveitis (8 eyes), idiopathic posterior uveitis (5), sarcoidosis-associated panuveitis (2), multifocal choroiditis (2), birdshot chorioretinopathy (2), and Lyme disease-associated posterior uveitis (1). The mean duration of UME was 8.1±4.2 months, range 3-18 months. Spectral OCT revealed 7 eyes (35%) with cystoid macular edema (CME) and 13 eyes (65%) with diffuse macular edema. There was a significant negative correlation between fixation pattern and pRNFL thickness (r=0.75, p=0.003 and r=0.84, p=0.0003, respectively). In the early group, LC and pRNFL thickness significantly correlated with MD (r=0.86, p<0.001 and r=0.75, p=0.002, respectively). In the advanced group, only LC thickness significantly correlated with MD (r=0.67, p=0.008).

Conclusions: Microperimetry quantification of macular sensitivity and fixation patterns may offer novel information regarding the impact of visual impairment on eyes with UME. Further and larger systematic evaluations are indicated to enhance the functional assessment of UME.

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1041 - A604
Correlation of Visual Acuity to Outer Retinal Morphology in Spectral Domain OCT Images of Retinal Diseases

Purpose: To assess the relationship between visual acuity (VA) and outer retinal morphology evaluated from spectral domain optical coherence tomography (SD OCT) images in various retinal diseases.

Methods: A series of 73 patients (136 eyes) requiring SD-OCT for standard of care assessment of retinal disease were recruited for this study. All subjects were scanned using the Topcon 3D OCT-1000 with the cube scan protocol (6 x 6 mm area; 128 B-scans/512 A-scans / B scan) The evaluation was limited to the 20 B scans passing through the central subfield (CSF). It included integrity of the external limiting membrane (ELM), inner retinal layer (IS-OS) and photoreceptor inner segment-outter segment (IS-Os) function of minimal angle of resolution (MAR) units for statistical analysis.

Results: All scans obtained were of gradable quality for outer retinal integrity. The percentage agreement and kappa statistics was 69 % (0.53) for grading of the ELM, and 72 % (0.54) for IS-Os. The mean logMAR VA was 0.8 (n=39) for eyes with absent ELM, 0.3 (n=33) for abnormal ELM and 0.2 (n=61) for normal ELM (p value<0.001). For IS-Os status, the mean logMAR VA was 0.9 (n=30) for absent IS-Os, 0.4 (n=38) for abnormal IS-Os and 0.2 (n=65) for normal IS-Os (p value <0.001). The trend in distribution of VA along the 3 step scale of ELM and IS-Os junction in the CSF were graded as absent, abnormal and normal. VA was measured on a Snellen chart with the patient’s habitual refraction and converted to logarithmic units of minimal angle of resolution (MAR) units for statistical analysis.

Conclusions: A statistically significant association between ELM, IS-Os integrity and VA suggests that outer retinal morphology evaluation by SD OCT may provide useful variables for clinical research and care.

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1042 - A605
Correlation of SD-OCT Morphology and Retinal Function in Neovascular Age-Related Macular Degeneration (nAMD)

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**Purpose:** To correlate the retinal function in patients with neovascular age-related macular degeneration (nAMD) to specific characteristics of retinal morphology after exactly superposing the retinal sensitivity map to OCT data using Spectralis-OCT and the MP-1 micrometer.

**Methods:** Thirty eyes showing untreated nAMD (10 classic, 9 minimally classic, 11 occult) were examined with the Heidelberg Spectralis-OCT and the NIDEK HM1 octomicroscope (MD). The fundusphoto (FP) of the MP was exactly matched with the infrared OCT image of the Spectralis-OCT using virtualDub (Ver.1.8.6) and Paint.NET (Ver.3.36) software. Each test point of light sensitivity in the FP was transmitted to the corresponding location on Spectralis-OCT using Image J software and subsequently the microparameters were evaluated with respect to the following OCT-findings: neovascular complex (NVC), pigment epithelium detachment (PED), subretinal fluid (SRF), intraretinal fluid (IRF), drusen and intraretinal hard exsudates.

**Results:** Mean retinal sensitivity was worst directly over the NVC at 1.45 ± 2.4 dB. If SRF or a PED were present at the site of the NVC, mean retinal sensitivity was 1.26 dB, 0.11 dB and 0.64 dB, respectively. Further functional deficiency was caused by retinal fluid whereas IFR was associated with an inferior retinal sensitivity of 4.4 ± 3.5 dB compared to SRF with a mean of 6.3 ± 4.5 dB. PED was associated with a retinal sensitivity of 6.7 ± 4.5 dB, additional SRF resulted in a similar mean value of 6.4 ± 3.6 dB, whereas additional IFR resulted in worse retinal sensitivity of 2.4 ± 3.4 dB. Drusenoid retinal epithelium irregularities resulted in a decreased light perception value of 9.7 ± 4.6 dB, whereas exsudates were associated with a value of 8.4 dB.

**Conclusion:** In nAMD, severe macular function loss was detected especially at sites showing an NVC. Fluid or PED alone cause a rather similar functional deficiency, whereas a combination of both results in worse outcomes. Drusen and exsudates are associated with only moderate loss of macular function.

**Support:** None

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1045 - A606
Relationship Between Fundus Image Quantity and Visual Field Status in Age-Related Macular Degeneration


**Purpose:** To relate structural change to functional change in age-related macular degeneration (AMD) in a cross-sectional population using fundus imaging and the visual field status.

**Methods:** 10 degree standard and SWAP visual fields and other standard functional clinical measures were acquired in 44 eyes of 27 patients at various stages of AMD, as well as fundus photographs. Retro-mode SLO images were captured in a subset of 29 eyes of 19 of the patients. Drusen area, measured by automated drusen segmentation software (Smith et al. 2005) was correlated with visual field data. Visual field defect position was compared to the position of the imaged drusen and deposits using custom software.

**Results:** The effect of AMD stage on drusen area within the 6000 µm was significant (One-way ANOVA: F = 17.231, p < 0.001), however the trend was not strong across all stages. There were significant linear relationships between visual field parameters and drusen areas. The main deviation (MD) declined by 3.04 dB and 3.92 dB per each % drusen area for standard perimeter and SWAP, respectively. The visual field parameters of focal loss displayed the strongest correlations with drusen area. The number of pattern deviation (PD) defects increased by 9.30 and 9.68 defects per log % drusen area for standard perimeter and SWAP, respectively. Weaker correlations were found between drusen area and visual acuity, contrast sensitivity, colour reading speed and reading speed. 72.6% of standard PD defects and 65.2% of SWAP PD defects coincided with retinal signs on fundus photography. 67.5% of standard PD defects and 65.9% of SWAP PD defects coincided with deposits on retro-mode images.

**Conclusions:** Perimetry exhibited a stronger relationship with drusen area than other measures of visual function. The structure-function relationship between visual field parameters and drusen area was linear. Overall the indices of focal loss had a stronger correlation with drusen area within a group where AMD in SWAP visual field defects had a high coincidence proportion with retinal manifestations of AMD. Smith R.T. et al. (2005) Arch Ophthalmol 123:201-206.

**Support:** None

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1044 - A607
Coupling Retinal Imaging With Psychophysics to Assess Perceptual Consequences of AMD

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**Purpose:** Retinal imaging does not necessarily provide a complete picture of expected vision loss for macular disease. We use a psychophysics test coupled with computational modeling to relate pathologies, found via fundus imaging, to expected perceptual function for a group of AMD patients.

**Methods:** We investigated 10 low vision patients with mild yet progressive AMD, as well as 10 age-matched healthy controls at the Edward Harkness Eye Institute, Columbia Presbyterian Medical Center. Both patients and controls, whose ages ranged from 65 to 84, were corrected to 20/20 to 20/50 visual acuity. All the subjects participated in a 2-APC perceptual task, where they were required to discriminate face and car images in the presence of variable noise. Color fundus photographs were collected using a Zeiss FF 450 Plus camera. Fundus images were segmented using a robust and automated algorithm to quantify disease-specific pathologies on the retina.

We mapped each patient’s retinal pathology to cortical activity and neurometric curves using a computational model of V1 and a decoding framework. We compared the psychometric curves between controls and patients, and investigated the quality of the neurometric predictions. We further analyzed the correlation between the neurometric curves with statistics of drusen in the masks.

**Results:** AMD patients had substantially lower discrimination accuracies compared to controls. Moreover, the degradation in the discrimination accuracy of AMD patients was much more pronounced at higher signal-to-noise (SNR) levels of the stimulus. We observed a positive correlation (r = 0.67) between the fraction of drusen-free area on the mask with the predicted perceptual discrimination at the highest SNR level for the stimulus.

**Conclusions:** The psychophysics and modeling framework we developed provides a quantitative assessment for the perceptual consequences of AMD and can potentially serve as a method for relating clinical findings in retinal imaging to perceptual function.

**CR:** J. Shi, inventor on a patent application, P. J. Wielarda, inventor on a patent application, P. R. Smith, inventor on a patent application, P. P. Saaja, inventor on a patent application, P.

**Support:** NEI R01 EY015520, NGA NURI Grant H1M1582-071-2012 and New York Community Trust
1046 - A609
The Relationship Between Macular Sensitivity and Retinal Thickness in Eyes With Diabetic Macular Edema
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Purpose: To investigate relationship between macular sensitivity and retinal thickness in diabetic macular edema (DME) quantified with an automatic fundus perimeter/topography system (Scanning laser ophthalmoscope/ Spectral domain optical coherence tomography (SLO/OCT)/ OPKO/OTI, Toronto, Canada).

Methods: Fourteen eyes of 9 patients (mean age = 69 years; range 35 - 88 years) with DME (mean BCVA = 0.85 ± 0.20; range 0.5 - 1.0; 9 between 1-5 years and 1 with more than 5 years in duration) were evaluated with SLO/OCT™ device by same operator. Macular perimeter (fundus-related perimeter together with retinal thickness map) was used to quantify macular sensitivity, fixation pattern (location and stability), and relationship between macular sensitivity and thickness. Multiple linear regression model with a generalized estimation equation (GEE) was used to evaluate relationship between macular sensitivity and thickness. GEE model counted for correlation within repeated measures of thickness and sensitivity for same macular area.

Results: Fixation pattern revealed that 9 eyes (64.29%) had central (greater than 50% of fixation point within 0.5mm of foveal center), 30I (43%) peri-central (between 25% - 50% within 0.5mm of foveal center); and 2 eyes (14.29%) eccentric (less than 25% of fixation point within 0.5mm of foveal center) fixation pattern. Fixation stability revealed that 12 eyes (85.71%) had stable (more than 75% with central 2º of point of fixation), (2.14 2º) relatively unstable (less than 75% of fixation points located within 2º, but more than 75% located within 4º of point of fixation); none had unstable fixation (less than 25% of fixation points located within 4º). We measured macular sensitivity and corresponding thickness in 91 points of 14 study eyes. We regressed macular sensitivity against its thickness, distance from fovea (3 circles with radius of 0.5, 3, 6 mm from fovea center), duration of DME (< 1 year, 1 to 5, > 5 years), visual acuity in LOGMAR, age, and gender. Macular sensitivity decreased 0.01 dB (% 0.05) and 0.02 DB (% 0.01) with every 1µm increase in macular thickness. It decreased 0.13 dB (% 0.13) CL, -0.2, -0.05 with every 1 year of increase in age. There was an increase of 1.90 dB (% 0.05) CL, 1.90, 2.71) moving from foveal center to second and third circles.

Conclusions: Fixation quantification of macular sensitivity and retinal thickness, in association with other factors such as age, may offer novel information regarding impact of DME on retinal function.

CR: E. Hafit Naimi, None; R. Channa, None; J. Wang, None; M. Ibrahim, None; P. Turcuoglu, None; Z. Rentiya, None; A. Rashid, None; A. Khwaja, None; D.V. Do, None; Q.D. Nguyen, OPKO/OTI, Toronto, Canada, F.

Support: None

1048 - A611
Computer-Assisted Volumetric Sub-Analysis of Intraarticular Cysts Using Optical Coherence Tomography and Correlation With Visual Acuity
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Purpose: Cystoid macular edema (CME) represents a common pathological appearance of the retina in various ocular diseases. Currently Spectral Domain Optical Coherence Tomography (OCT) allows measurement of central foveal thickness and macular volume. We describe a novel automated method for measuring intraretinal cystic volumes and total macular volume. In this study we used Spectral-Domain OCT (SD-OCT) imaging to quantify the CME volume.

Methods: We developed the software called “Cystometer” that can automatically delineate retinal tissue and intraretinal cystic borders and compute macular tissue volume and cystic volume. These volumes were determined by examining OCT movies (Audio Video Interleave files, each representing 128 X 128 OCT scans of a single examination). We computed the retinal thicknesses with LogMar visual acuity (VA) in patients with CME secondary to diabetic retinopathy (DR), branch retinal vein occlusion (BVO) and pseudophakia (PK). Generalized Estimating Equation regression, which accounts for correlated data, was used for statistical analysis.

Results: Analysis of 113 movies representing 16 eyes of 13 patients with CME showed 14 eye and 1 eye with macular pucker with pucker and 8 eyes with CME. The cystic volumes correlated strongly with the macular volume. The largest cystic volume was 72 µm3 in 1 eye with BVO. Macular volume was 5.79 µm3 in 1 eye with DR.

Conclusions: Analysis of OCT images using this software can provide reliable quantitative information that can be useful in the follow-up of patients with CME and allows correlation with VA. Increasing cystic tissue volumes have a deleterious effect on visual acuity, the former to a lesser extent in BVO than in DR and PK CME.

CR: D. Weinberger, None; T.R. Burke, None; Y. Nahum, None; B. Levant, None; A. Levant, None; S.D. Smith, None; S. Chang, None.

Support: None

1047 - A610
Spectral-Domain Optical Coherence Tomography in Resolved Uveitic Cystoid Macular Edema: Features Associated With Permanent Vision Loss
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Purpose: Cystoid macular edema (CME) is a common complication of uveitis, resulting in significant vision loss. Vision typically recovers with the resolution of CME. However, a subset of patients experience permanent decrease of central vision despite resolution of CME and absence of pathology in other ocular structures. Using spectral-domain optical coherence tomography (OCT) imaging technology, we attempted to identify retinal features that may be associated with the vision loss.

Methods: This is a case-control retrospective comparative series. We reviewed medical records of patients with uveitic CME and identified two groups of patients: 1) Study group consisted of patients who failed to regain pre-CME BCVA following resolution of CME, and the vision loss could not be accounted for by other ocular pathologies; 2) Control group consisted of patients who regained their pre-CME BCVA following resolution of CME. Once all patients were identified, we reviewed the OCT scans obtained from the RTVue (Optovue Inc, Fremont, CA) of each patient. Patients were excluded if macular cystic space, epiretinal membrane, or distorted macular anatomy was noted. Two variables were then assessed in the qualified subjects: 1) Photoreceptor inner/outer segment (IS/OS) junction, hypothesized to be represented by the highly reflective band immediately inner to the retinal pigment epithelium, is graded as intact, partial, or absent; 2) Foveal thickness, as calculated by the software program included with the RTVue.

Results: We identified 7 subjects (eyes) in Study and 8 subjects (eyes) in Control. The mean pre-CME BCVA were 20/25 in Study and 20/20 in Control. The mean post-CME BCVA were 20/75 in Study and 20/20 in Control. The mean foveal thickness were 170µm in Study and 232µm in Control, with a difference of 62µm (p<0.001). IS/OS junction was graded as intact in 2, partially intact in 4, and absent in 2 of the Study eyes, while it was graded as intact in all 8 Control eyes. All Study eyes had a foveal thickness of less than 180µm, an intact IS/OS junction, or a combination of both. Conclusions: This preliminary study suggests that reduced foveal thickness and intact IS/OS junction may be important in the prediction of permanent vision loss following CME resolution in uveitic patients.

CR: P.Y. Chang, None; V. Diao, None; D.M. Hankle, None; J. Mauri, None; C.S. Foster, None; C.M. Samson, None.

Support: None

1049 - A612
Microperimetry and Spectral-Domain Optical Coherence Tomography in Patients With Retinal Vein Occlusion
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Purpose: The aim of the study was to investigate the correlation between the retinal sensitivity tested by Microperimetry (MP) and structural abnormalities of the outer retina assessed by Spectral-Domain Optical Coherence Tomography (SD-OCT) in patients with retinal vein occlusion.

Methods: Thirty patients with retinal vein occlusion were included in the study. Six patients had a branch vein occlusion and 7 had a central retinal vein occlusion. All patients underwent MP and SD-OCT imaging. Microperimetry results were superimposed on retinal topography maps (SD-OCT). Point-to-point analysis between microperimetric retinal sensitivity and underlying integrity of Inner segment-Outer segment (IS-OS) junctional layer was performed. Nine patients had a fluorescein angiogram (FA) and these findings were correlated with the MP and SD-OCT results.

Results: Decreased mean retinal sensitivity weakly correlated with the disruption of the IS-OS layer both in branch and central retinal vein occlusion (correlation coefficient (r) -0.2, weak inverse correlation). Ischemia on FA correlated positively with decreased macular sensitivity (r=0.69, p<0.001). SD-OCT results showed that retinal layers may not be seen as observed in this study. A larger study to evaluate the functional and structural changes in the retinal layers in central and branch retinal vein occlusion is warranted.

CR: M. Kurth, None; G. Lande, None; E. Su, None; P.M. Garcia, None; R.B. Rosen, None.

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1050 - A613
Polarization Maintaining Fiber Based Ultra-High Resolution Spectral Domain Polarization Sensitive Optical Coherence Tomography of the Human Retina
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**Purpose:** To measure the polarization properties of the fovea and nerve head region with a fiber based ultra high resolution polarization sensitive OCT (PS-OCT) system.

**Methods:** We present a new ultra high resolution spectral domain polarization sensitive optical coherence tomography (PS-OCT) system based on polarization maintaining (PM) fibers. The method transfers the principles of our previous bulk optic PS-OCT system to a fiberized setup. Thereby, the main advantage of our bulk optics setups, i.e. the use of only a single input polarization state to simultaneously acquire reflectivity, retardation, optic axis orientation, and Stokes vector, is maintained.

**Results:** We measured the fovea and the nerve head of healthy volunteers with our system. The polarization sensitive images of the macula show, that most of the retinal layers in this area do not alter the polarization state. However, the RPE changes the polarization state of backscattered light in a random way. This polarization scrambling indicates depolarization. The retardation images of the nerve head region show increased retardation in the superior and inferior nerve fiber bundles and decreased retardation in the nasal and temporal nerve fiber layer. The optic axis orientation image shows a 360° rotation around the nerve head, in good agreement with the radial orientation of the nerve fiber bundles around the optic nerve head.

**Conclusions:** The flexibility and simple alignment of fiber optics based systems is an important step towards the development of commercial PS-OCT systems. In addition the use of a broadband light source with a bandwidth of 110 nm results in a smaller speckle size. This increases the density of independent sampling points, leading to improved resolution of PS measurements, which is especially important for measurements of the thinner part of the retinal nerve fiber layer. In addition, the smaller speckle size allows a better resolution of depolarization measurements, leading to improved spatial resolution of RPE segmentation.

CR: E. Gotzinger, None; B. Baumann, None; M. Pircher, None; C.K. Hitzenberger, None.

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1052 - A615
Influence of Blood Inhomogeneity on Doppler OCT Signals in Retinal Capillary System

**Purpose:** To demonstrate applicability of Doppler Optical Tomography (DOT) technique for 3-D analysis of blood flow in retinal vascular system. An influence of optical inhomogeneity of human blood on Doppler measurement in retinal capillaries will be addressed.

**Methods:** Using high resolution and high speed (230,000 Ascans/sec) Spectral OCT system was used for in vivo imaging of retinal vasculature in 3-D. In vivo studies were performed in healthy and pathologic eyes enabling to visualize net capillaries distributed densely in macular region (outside from avascular zone). Specialized scanning protocols were applied to measure low-frequency Doppler signals caused by almost perpendicular orientation of vesseles in the central retina. Measurement protocols and signal processing were based on the joint spectral and time domain OCT. To test applicability of the method additional in vitro studies of the human blood flow were conducted.

**Results:** Detailed analysis of velocity data demonstrates that we are able to see Doppler signal coming from the steady scattering medium under capillary while the blood is flowing. This effect is present in both in-vivo and in-vitro studies. Such signal is present due to optical inhomogeneity of blood causing time dependent phase variation similar to Doppler signal. It also affects the velocity readout from blood vesseles introducing additional broadening of velocity profiles. We will demonstrate our calculations and experimental data showing how strong this effect can influence the velocily imaging in retinal blood vasculature especially in the case of small retinal capillaries.

**Conclusions:** Measurements of Doppler data from retinal vasculature in 2-D and 3-D obtained with high resolution and high speed Spectral OCT system are demonstrated. We have shown that is possible to enhance visualization of retinal capillaries using joint spectral and time domain OCT. However, the direct retrieval of blood flow velocity in small capillaries is limited due to orientation of capillaries and strong influence of optical inhomogeneity of the medium. In this contribution we will demonstrate optimal conditions for measuring blood flow in small retinal vesseles to enhance their visibility and calculate the flow rate.

CR: D. Bukowska, None; I. Grulkowski, None; S. Tamborski, None; I. Gorczynska, None; M. Szulmowski, None; A. Kowalczyk, Optopol Technology SA, C. M. Wojtkowski, None.

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1053 - A616
Three-Dimensional Real-Time Flow Visualization Using Spectral and Time Domain Optical Coherence Tomography

**Purpose:** To demonstrate the capability of joint spectral and time domain optical coherence tomography to visualize in real-time three-dimensional vascular structure along with quantitative blood flow in the retina of the human eye in-vivo. To demonstrate measurement protocols that allow for velocity distribution assessment with high sensitivity at high acquisition speeds needed for three-dimensional real-time observation of retinal blood flow.

**Methods:** The specialized measurement protocols and advanced data-processing techniques that base on Spectral and Time domain Optical Coherence Tomography have been developed and applied to data obtained from healthy volunteers. Novel methods of analysis and visualization of the segmented vascular structure has been introduced. All data presented in this contribution are obtained with the prototype high-resolution, high-speed Spectral OCT system acquiring 120 000 ascans/s, constructed at the Nicolaus Copernicus University.

**Results:** In-vivo real-time, ultrahigh resolution OCT imaging has been performed in 10 eyes of 5 healthy volunteers. In all cases the blood flow in three-dimensional vascular net in the macular region of the retina as well as in the proximity of the optic disk is observed in real-time. We also present two-dimensional fundus-like maps indicating the direction and velocity value of blood flow.

**Conclusions:** Using three-dimensional joint spectral and time domain OCT and novel analysis tools we were able to visualize three-dimensional blood flow in real-time. We believe that the novel technology can provide a better understanding of retinal functions as well as facilitate aiming OCT system at diagnostically important points in retinal diseases connected with blood flow disorders. Our method enables significantly better visualization of three-dimensional vascular structure than was previously possible.

CR: M. Szulmowski, None; D. Szlag, Optopol Technology SA, C. S. Orlowski, Optopol Technology SA, C. M. Sylwestrak, None; A. Szulmowska, None; A. Kowalczyk, Optopol Technology SA, C. M. Wojtkowski, None.

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1051 - A614
Cilioretinal Arteries in Diabetic Eyes Are Associated With Increased Retinal Blood Flow Velocity and Occurrence of Diabetic Macular Edema

**Purpose:** To analyze retinal blood flow characteristics of diabetic eyes using the Retinal Functional Image (RFI) and standard imaging techniques including fundus photography, fluorescein angiography (FA), and Spectral Domain OCT/SLO (SD-OCT) to evaluate the relationship between occurrence of cilioretinal arteries and macular edema in diabetic retinopathy.

**Methods:** Patients with a diagnosis of diabetic retinopathy were included. All patients underwent fundus photography, FA, SD-OCT and RFI imaging. The presence of cilioretinal artery (CilRA) was established using color/red-free fundus photos, FA and RFI. Two groups of eyes were created according to the presence (CilRA group) or absence (NoCilRA group) of cilioretinal artery or arteries in the studied eye. Cilioretinal arteries were defined as vessels which originate at the optic disc without evidence of communication with the central retinal artery, loop over the margin of the disc and fill with fluorescein dye along with the choroid.

**Results:** Thirty nine eyes with diabetic retinopathy were included. Cilioretinal artery was identified in 15 eyes (38,4%). In the CilRA Group, SD-OCT evidence of macular edema was observed in 86,7% (13 out of 15 eyes), whereas macular edema was observed on SD-OCT in 29,2% (7 out of 24 eyes) in the NoCilRA group. Mean blood flow velocities in retinal arterries and veins were significantly higher in diabetic eyes with cilioretinal artery (p = 0.04 and p = 0.005, respectively). Mean velocity in cilioretinal arteries was significantly higher in comparison to the mean arterial blood velocity (p = 0.03). In CilRA group, cilioretinal-retinal collaterals, assessed by RFI, were detected in 4 (26,7%) out of 15 eyes with cilioretinal arteries. Mean velocity in retinal veins was significantly lower when cilioretinal-retinal collaterals were present (p = 0.008).

**Conclusions:** Using the RFI in conjunction with standard fundus imaging techniques, the presence of cilioretinal artery in diabetic eyes was found to be associated with increased retinal blood flow velocity and increased occurrence of diabetic macular edema. The occurrence of cilioretinal-retinal collaterals was also noted, however, the pathophysiological significance of this finding requires further investigation.

CR: A. Ponce, None; G. Landa, None; W. Ameli, None; R.B. Rosen, OPKO/OTI, C.

Support: Support from Bendlund-Lowenstein Retinal Fund and the Gladys Brooks Foundation
High Reproducibility of Retinal Blood Flow Velocity Measurements Using the Retinal Function Imager


Purpose: To assess the inter-session and inter-session reproducibility of blood flow velocity measurements in the perifoveal vessels using the Retinal Function Imager (RFI).

Methods: Twenty six eyes of 20 healthy subjects free from eye disease and with no history of ocular trauma were recruited for this study. All patients were imaged by the RFI (Optical Imaging, Ltd) with analysis of blood flow velocity of secondary vessels. Six eyes of each subject were imaged on three separate occasions, days 1,4 and 7. Intra-session variability was assessed by the coefficient of variance (standard deviation divided by the mean) of all measured segments between each repeated scan. Five eyes of 5 subjects were re-imaged on a different occasion, days 10 to 14 months apart from the first measurement. Inter-variability was calculated using intraclass correlation.

Results: The average venous velocity was 3.3 ± 0.6 mm/sec; the average arterial velocity was 4.3 ± 0.9 mm/sec. On average, 159 ± 58 arterial segments and 162 ± 54 venous segments were measured in each eye. The average coefficient of variance between measurements in the same day was 8.5 ± 4.9 % for all vessels; 8.5 ± 5.2 % for venules and 8.4 ± 4.8 % for arterioles. When comparing the measurements on different days the same subjects the average interclass correlation was r = 0.964.

Conclusion: The RFI showed low intra-session and inter-session variability in a group of healthy subjects. These highly reproducible measurements might serve as an important tool for assessing both physiological and pathological processes affecting retinal blood flow velocity.


Support: None

1054 - A619

Increased Foveal Avascular Zone in Diabetic Retinopathy Patients Detected Non-Invasively by the Retinal Function Imager

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Purpose: To non-invasively measure and compare the foveal avascular zone (FAZ) in healthy subjects and diabetic retinopathy (DR) patients.

Methods: Fourteen eyes of 11 DR patients and 22 eyes of 18 healthy subjects were acquired from each subject. Following registration, pixel values were analyzed to locate blood motion, thus obtaining non-invasive capillary perfusion maps (nCPM) of healthy subjects. These highly reproducible measurements might serve as an important tool for assessing both physiological and pathological processes affecting retinal blood flow velocity.

Results: The average FAZ area in patients with DR was significantly larger compared to controls 0.21 ± 0.07 vs 0.13 ± 0.06 mm², p<0.001, as was the FAZ diameter 0.65 ± 0.72 vs 0.48 ± 0.95 µm, p<0.001 (Fig.1).

Conclusion: Using the RFI we detected a significantly enlarged FAZ area in patients with DR, which represents the ischemic process in the diabetic eye. Non-invasive and safe monitoring of the FAZ dimensions may provide an important tool for early diagnosis, follow-up and tailoring treatment in diabetic patients.

CR: D.A. Nelson, Optical Imaging Ltd, E. H. Barash, Optical Imaging Ltd, E. A. Ruf, Optical Imaging Ltd, E. Z. Burgansky-Eliash, Optical Imaging Ltd, E. D. Izhaky, Optical Imaging Ltd, E. A. Barak, None; A. Lowenstein, None; T. Rock, None; E. Bartov, None; A. Grinvald, Optical Imaging Ltd, I; Optical Imaging Ltd, P.

Support: None

1055 - A618

Retinal Functional Imaging of Peri-Foveal Blood Flow Velocities in Diabetic Retinopathy


Purpose: Diabetes mellitus (DM) is a micro-angiopathic disease that has been associated with decreased arterial and venous retinal blood flow velocities (RBFV). This study investigates the use of a novel non-contrast angiographic imaging device, the Retinal Functional Imager (RFI), to measure RBFV in patients with both non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

Methods: Prospective, cross-sectional study. The RFI device was used to quantitatively measure peri-foveal blood flow velocities in patients with NPDR and PDR. Control data was extrapolated from a recently published study using the same device.

Results: The study included patients with NPDR (n=10, 20 eyes) and PDR (n=10, 20 eyes). The mean age was 58 ± 9.3 years, 45% were male, 55% were non-insulin dependent. 45% of eyes had clinically significant macular edema (CSME). Mean duration of DM diagnosis was 12.3 years. Mean arterial RBFV (mm/sec) = 4.19 ± 0.99 (Control), 3.83 ± 0.53 (NPDR), and 3.36 ± 0.33 (PDR). The mean venous velocities were 3.03 ± 0.59 (Control), 2.78 ± 0.55 (NPDR), and 2.43 ± 0.35 (PDR). Compared to control eyes, PDR eyes had a lower arterial (p<0.001) and venous (p<0.001) velocities. When compared to NPDR eyes, PDR eyes had a lower arterial (p<0.01) and venous (p<0.05) velocities. Pearson’s correlation coefficient analysis showed that RBFV were not closely correlated with age, gender, visual acuity, insulin use, presence of CSME, years of DM diagnosis, or history of pan-retinal or focal laser.

Conclusions: Eyes with PDR were shown to have a slower peri-foveal arterial and venous blood velocities compared to healthy controls and NPDR.

CR: K. Mukkamala, None; L. Spielberg, None; G. Land1, None; S. Balasubramanian, None; R.B. Rosen, None.

Support: None

1057 - A620

Retinopathy

Retrobulbar Blood Flow Changes in Eyes With Diabetic Retinopathy - A 10-Year Follow-Up Study

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Purpose: To assess long-term changes in flow parameters of the retrobulbar vessels in diabetic patients.

Methods: This was a historical prospective study of 136 eyes that were evaluated in our institution between 1994-1995, 36 were re-evaluated between 2004-2008 and formed the study group. They were divided into four groups for comparison: eyes of diabetic patients without diabetic retinopathy (DR), eyes with nonproliferative DR (NPDR), eyes with PDR and eyes of non-diabetic patients (controls). Color Doppler imaging was used to access the retrobulbar circulation. Flow velocity in the three major retro-bulbar vessels was measured, and the resistive index (RI) was calculated and compared between the groups and the two time periods.

Results: There was a similar increase in the RI of the ophthalmic artery (OA) in all patient groups. RI values of the central retinal artery (CRA) and posterior ciliary artery (PCA) had increased in the two non-DR groups and in the NPDR group, with a surprising decrease measured in eyes with PDR (P=NS). Combining the NPDR and PDR groups resulted in a milder increase of the RI of the CRA and the PCA in the DR group compared to the other groups.

Conclusions: We showed that there was a decrease of the resistance in two retrobulbar vessels in patients with PDR during a long-term follow-up. The finding of a milder increase of the RI in patients with DR compared to the non-DR controls was, significant for the CRA. These results demonstrate that an increase of the resistance in the retrobulbar vessels, as a part of DR, can lessen over time and even be reversed. These results are unexpected given the direct statistical relationship between the duration of the diabetes and the severity of the retinopathy that was reported in several studies. They are, however, in line with the results of follow-up studies that were carried out using laser Doppler velocimetry. Further studies are needed in order to verify these findings and their contribution to better understanding of the pathophysiology of DR.

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Organizing Section: MOI Contributing Section: VI, CO

1767 - A516
Automated Intra-retinal Layer Segmentation of 3-D Macular OCT Scans Using a Multiscale Graph Search
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Purpose: Intra-retinal layer segmentation is of paramount importance to monitor the progression of retinal diseases such as the variation of the nerve fiber layer and macular edema formation. The purpose of this study is to develop and validate a method that can automatically segment 10 intra-retinal layers in 3-D macular OCT scans.

Methods: 100 macular scans (200 x 200 x 1024 voxels, 6 x 6 x 2 mm) were obtained from the right eye of 14 normal subjects using a Cirrus® HD-OCT machine (Carl Zeiss Meditec, Inc., Dublin, CA). The 3-D graph search method hierarchically detected 11 retinal surfaces in 5 multiscale OCT volumes using gradient magnitudes of the OCT volumes. Retinal reference standards were created by averaging in the z-direction the manual tracings obtained from 2 retina specialists in 10 randomly selected X-Z images for each OCT scan. The accuracy of computer segmentation results was estimated by comparing to the reference standards in terms of unsigned border positioning error and layer thickness difference between the computer segmentations and the reference standards were compared to the inter-observer variability between the two manual tracings.

Results: The overall mean unsigned border positioning error of 11 retinal surfaces was 5.75 ± 5.1 mm (2.88 ± 2.55 mm). While the unsigned border positioning errors of 9 retinal surfaces were significantly smaller than the unsigned border positioning differences between the 2 manual tracings (< 0.01, 95% CI), those of 2 retinal surfaces were not significantly different (> 0.01, 95% CI). In 9 out of 10 intra-retinal layers, the absolute layer thickness differences between the computer segmentations and the reference standards were significantly smaller than those between the 2 manual tracings (< 0.01, 95% CI).

Conclusions: The proposed method consistently and automatically segmented 10 intra-retinal layers from 3-D macular OCT scans and performs comparably to a retina specialist on this dataset in terms of unsigned border positioning error and layer thickness.

CR: K. Lee, None; M.K. Garvin, The University of Iowa, P; S. Russell, None; M. Sonka, The University of Iowa, P; M.D. Abramoff, The University of Iowa, P.

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1768 - A517
Automated Ten Boundary Detection in Intra- and Outer Retinal Area of Three-Dimensional Optical Coherence Tomography
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Purpose: To present an automatic OCT image segmentation algorithm and evaluate the repeatability of outer retinal boundary detection for exploring possible choroid structure change in diseases.

Methods: A fast and fully automated segmentation method has been developed based on a customized edge detector, in which an edge refinement scheme utilizes the shortest-path search. The introduced edge refinement scheme suppresses the false edges by integrating both intensity and edge information. The algorithm is capable of segmenting up to 10 boundaries, including the inner sclera border, in retinal images. Three-dimensional (3D) macular scans of 20 eyes were utilized to evaluate outer retinal boundary repeatability. Each scan had three repetitions. The 3D scans were preprocessed with a proper scaling approach and averaging algorithm to get corresponding 3D scan images with improved signal-to-noise ratio.

Results: 10 boundaries were detected with the automated segmentation algorithm. The standard deviation and correlation coefficient of the thickness from the outer border of the retinal pigment epithelium to the inner sclera border were calculated to evaluate the repeatability. The newly developed segmentation method was capable of reliably segment intra- and outer retinal boundaries with good repeatability. The segmented boundaries were found to be in agreement with the known anatomical boundaries.

Conclusions: The proposed segmentation method utilizes the unique edge information and incorporates intensity information to produce robust results. The automated segmentation algorithm was able to produce reliable results for the segmentation of 10 boundaries including the outer retinal area, which is promising towards further investigation of the intra- and outer retinal structure changes in diseased eyes.

CR: Q. Yang, Topcon Medical Systems, Inc., E; C.A. Reisman, Topcon Medical Systems, Inc., E; Z. Wang, Topcon Medical Systems, Inc., E; A. Tomidokoro, None; M. Araie, None; M. Hangai, None; N. Yoshimura, None; Y. Fukuma, Topcon Medical Systems, Inc., E; K. Chan, Topcon Medical Systems, Inc., E.

Support: None

1767 - A518
Automated Segmentation of Seven Retinal Layers in SD OCT Congruent With Expert Manual Segmentation
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Purpose: Spectral Domain Optical Coherence Tomography enables depth-resolved imaging of the retina which is critical for the quantification of retinal layer thicknesses. Manual segmentation of these layers is labor intensive. A fully automated method to segment and quantify retinal layers would reduce labor and time costs and provide an objective evaluation of the retinal structures of interest.

Methods: Our graph cut-based algorithm associates each pixel in retinal images with all other pixels by weights which we have customized based on prior anatomical information, such as proximity to the fovea, scan orientation, and nerve fiber layer brightness. Dijkstra’s algorithm utilizes this weighting matrix to find the shortest weighted paths across an image, thus effectively segmenting the retinal layers. A total of 108 macular B-scans from 10 normal adult subjects were segmented manually by one grader and automatically using our software. To estimate inter-expert-observer variability, a subset of 29 B-scans was graded manually by two experts.

Results: We measured the average thickness of 7 retinal layers in each B-scan. We calculated the absolute value difference of the average layer thicknesses between the manual and automatic estimates and likewise between the two manual expert graders. The mean and standard deviation of these differences across all B-scans are compared in Table 1.

Conclusions: The automatic algorithm accurately segmented 7 retinal layers, with consistent results better or equal to the observed inter-expert-variability. This automated approach may significantly reduce the resources and time necessary to conduct large-scale ophthalmic studies.

CR: S.J. Chiu, None; X. Li, None; P. Nicholas, None; C.A. Toth, Biotigen, Genentech, Alcon, F; Genentech, Alcon, C; Genentech, Alcon, R; J.A. Izatt, None; S. Farsiu, Genentech, F.

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1770 - A519
Normative Values for Foveolar, Macular and Peripheral Retinal Thickness by Spectral-Domain Optical Coherence Tomography
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Purpose: To describe normative data for the foveolar, macular and peripheral retinal thickness with spectral-domain optical coherence tomography (SD-OCT) in Japanese normal subjects.

Methods: A total of 30 healthy eyes from 30 subjects, age ranging 12 to 80 years (48 ± 22, mean ± SD) were included in this study. Inclusion criteria were best corrected visual acuity of 20/20 or better, refractive error from -5.0 to +3.0 diopter, no ocular diseases and normal intracocular pressure. We measured retinal thickness at a central fovea and retinal regions 1, 3, and 9 mm from fovea in 8 directions of nasal, superior nasal, superior, superior temporal, temporal, inferior temporal, inferior and inferior nasal using SD-OCT (Cirrus, Carl Zeiss Meditec).

Results: The mean foveolar thickness was 193.3 ± 59.9 µm. The retinal thickness at 1 mm nasal of fovea in 8 directions of nasal, temporal, superior nasal, superior, superior temporal, temporal, inferior temporal, inferior and inferior nasal was 328.4 ± 18.4, 320.7 ± 15.1, 319.8 ± 22.1 and 319.7 µm, respectively. The thickness differences were presented. Since racial differences of OCT measurement have been reported, our data proposes the guidelines for normative retinal thickness in Asian normal subjects.

CR: H. Omata, None; K. Morii, None; D. Imai, None; S. Yoneya. None.

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Assessment of Macular and Intraretinal Thickness Measurements in Eyes of Healthy Volunteers and Subjects With Type 1 Diabetes Using Optical Coherence Tomography

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Purpose: To assess the thickness measurements of the macula and intraretinal layers in patients with type 1 diabetes mellitus and no retinopathy using optical coherence tomography (OCT); and to compare these findings with those of age-matched healthy volunteers.

Methods: Standard macular mapping by Stratus OCT was performed in 74 healthy eyes (34±16 yrs, 51 female, 23 male) and 39 eyes with type 1 diabetes mellitus (DM) with no retinopathy (6±10 yrs, 19 female, 20 male) on biomicroscopy. Automatic layer segmentation was performed using a custom-built software for OCT retinal image analysis (OCTRA) which identifies the retinal thickness of the layers. The mean RNFL, GCL+IPL, INL, OPL, IS/OS and IS/OS/RPE junction were measured in healthy volunteers and DM eyes compared using Mann-Whitney U test. Because of the number of statistical comparisons made in the study, a modified p-value of <0.001 was considered statistically significant. Missing values (n=30±0.001) was also recorded.

Results: Stratus OCT-measured thickness of the total retina in the central subfield (R1) of DM eyes was higher than those from healthy volunteers (242±23 versus 232±24, p<0.001). Intraretinal thickness was significantly different between DM and healthy eyes for R2, R3, and R5, p<0.001 and R5 and p<0.001. Although this was thinner in the pericentral regions in DM eyes (R2, R3, R4 and R5, p<0.001 and R5 and p<0.001), GCL+IPL complex in R3, R4, R5, and R8, which was also thinner in DM eyes; INL in R2 and R3 thicker in DM eyes; OPL only in R8 (thicker in both DM eyes and IS/OS/RPE junction in R1, R4, R5, R8 and R8/thicker in DM eyes). Our study also showed no significant differences in macular and intraretinal layer thickness measurements within regions between females and males in the DM group.

Conclusions: Our study reveals significant differences in macular and intraretinal thickness measurements in DM eyes. It is not limited to thickness measurements obtained from age-matched healthy subjects without diabetes. In addition, the differences of the intraretinal layer thickness measurements between R4 and R5 in the DM group were not significant. These results are not consistent with past reports which could be due to analyzing data composed of mixed diabetic groups (i.e. type 1 and type 2; and minimal and no DR). Caution should be taken when preparing future studies involving diabetic subjects.

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Automated Macular Pathology Diagnosis in Three-Dimensional (3D) Spectral Domain Optical Coherence Tomography (SD-OCT) Images

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Purpose: To develop an automated method to identify the normal macula and four macular pathologies (macular hole (MH), macular edema (ME), retinal pigment epithelium (RPE), age-related macular degeneration (AMD)) in SD-OCT images.

Methods: 202 eyes of 58 healthy volunteers and 144 macular disease patients (68 M, 17 M, 116 ERM, and 52 AMD eyes) were scanned using SD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Inc., Dublin, CA) with Macular Cube 256x256 scan protocol. A holistic data-driven approach, in which 3D OCT data were encoded using a rich set of dense, spatially-distributed features, is proposed. Machine learning algorithms were used to identify the most discriminative features automatically from our training dataset. For ground truth, one ophthalmologist labeled each scan with the pathologies it contained. A two-class non-linear support vector machine (SVM) was trained using leave-one-patient-out cross validation. For performance evaluation, areas under the receiver operating characteristics curve (AUC) were computed for classifications of healthy and four pathologies separately.

Conclusions: We have developed an automated method for macular pathology diagnosis in OCT images and have obtained promising results, particularly in the cases of identifying the normal macula and identifying macular edema (AUC >0.9 for both). Our results demonstrate that the proposed holistic image representation along with a data-driven learning framework can identify effective features without relying on a potentially error-prone segmentation module.

CR: Y.-Y. Liu, None; M. Chen, None; H. Ishikawa, Biopigtions; G. Wellstein, Carl Zeiss Meditec, Meditec; J. Schuman, Heidelberg Engineering, R. Pfizer, R. Carl Zeiss Meditec; P. Biopigtions; Carl Zeiss Meditec; R. Rehg, None. Support: NIH RO1-EY11378, P30-EY08098; Eye and Ear Foundation, Research to Prevent Blindness, Insts Budget.

Automated Measurement of Optic Nerve Head Shape From Stereo Color Photographs of the Optic Disc: Validation With Spectral Domain Optical Coherence Tomography Measurements

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Purpose: To develop an automated method to identify the normal macula and four pathologies separately.

Methods: The retinal segmentation algorithm uses a graph theoretic approach to find optimal surfaces. The surface segmentation problem is transformed into computing a minimal s-t cut in a derived arc-weighted directed graph. For each layer individualized cost functions are used and optimized. We are using cost functions based on edge information and on shape information. The system is able to segment 5 individual layers (retinal nerve fiber layer; ganglion cell layer; inner plexiform/inner nuclear layer; outer nuclear layer; interface of the inner and outer segments/retinal pigment epithelium/bruch membrane) by identifying 6 boundaries. Each slice stack contains 49 slices with a resolution of 512x496 pixels for each slice. This results in rather complex graph setups. To handle this care has been taken to reduce the memory complexity and the computational complexity of the segmentation. The algorithm maintains individual sub-regions of the slice stack with different spatial resolutions at the particular steps of the segmentation procedure. To evaluate the algorithm performance 14 OCT slice stacks have been used, seven healthy retinas and seven retinas showing symptoms of retinitis pigmentosa. Within this work we focused on the segmentation performance of the retinal layer between the interface of the inner and outer segments and Bruch membrane. The segmentation results have been compared with manual segmentation results performed by two senior Ophthalmologists.

Results: The algorithm revealed ca. 96% conformity in the healthy group and ca. 89% conformity of the segmented layer in the group with pathologic slice stacks. An average segmentation took ca. 2.39 min on a regular desktop PC.

Conclusions: The algorithm demonstrated both satisfying segmentation performance and structural results of the retinal layers. The method would be suitable for clinical setup.

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Automated Classification of Papilledema Using Frisen Grading and OCT Measurements


Purpose: To develop and test a computer-based algorithm to assess digital images of the optic disc for signs of papilledema. Based on reported observations by neuro-ophthalmologists, one of the earliest signs of disc edema is the change in sharpness or contrast especially in the superior and inferior regions of the disc margins. Our hypothesis is that region-based analysis of disc images allows classifying different stages of the disease.

Methods: A retrospective set of 28 retinal images, 1024x1024 pixels, 75% with papilledema, was used to train and test this algorithm. The ground truth consisted of the grading by three ophthalmologists using the Frisen scale for each image. The Average Total Retinal Thickness and the Average Retinal Nerve Fiber Layer Thickness measured by OCT were also provided. The algorithm extracts features from a number of regions of interest (ROIs) in each image. These ROIs were defined as annuli of pixels centered on the optic disc and four quadrants corresponding to superior, inferior, nasal, and temporal regions with respect to the optic disc. This allows the algorithm to detect quadrant-based intensity changes at different distances from the disc margins. These images were analyzed in three colorspaces: RGB, LAB, and YCBr. Features include mean, variance, median, maximum change of intensity, and mean rate of intensity change (slope). A classification model was built by combining the features that best predicted OCT measurements individually.

Results: The best model for classifying the images into two classes, “normal-early” and “advanced”, in terms of sensitivity 0.92, specificity 0.93, and area under the ROC curve 0.989, combined 28 features from the YCBr color space that measure the speed of intensity changes away from the disc margins. The top 2 features were from the superior region, followed by two nasal. The top temporal region feature was ranked 27 in its contribution to the model.

Conclusions: These results show that correct classification of papilledema stage is possible using region-based features from optic disc images. This algorithm could be used for rapid screening of papilledema in clinical, intensive care, and emergency response settings.

Support: None

Wavelet Denoising of Multiple-Frame OCT Data Enhanced by a Correlation Analysis

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Purpose: Speckle noise suppression on OCT images is currently performed by averaging multiple frames. In contrast to this common approach we propose a novel wavelet based method that utilizes the structural properties of the actual image content to better differentiate between speckle and relevant tissue information.

Methods: Each of the recorded single B-Scans is decomposed by a wavelet analysis. The wavelet coefficients representing a local frequency analysis of the images are then adapted by weights computed out of a statistical analysis. For each coefficient on every frame individual weights are calculated. They are constructed out of a statistical analysis. For each coefficient on every frame individual weights are calculated. They are constructed out of a statistical analysis. For each coefficient on every frame individual weights are calculated. They are constructed out of a statistical analysis.

Results: The best model for classifying the images into two classes, “normal-early” and “advanced”, in terms of sensitivity 0.92, specificity 0.93, and area under the ROC curve 0.989, combined 28 features from the YCBr color space that measure the speed of intensity changes away from the disc margins. The top 2 features were from the superior region, followed by two nasal. The top temporal region feature was ranked 27 in its contribution to the model.

Conclusions: These results show that correct classification of papilledema stage is possible using region-based features from optic disc images. This algorithm could be used for rapid screening of papilledema in clinical, intensive care, and emergency response settings.

Support: None
Clinical Significance of Frame Averaging With Spectral Domain OCT


Purpose: The ability to average multiple scans and suppress speckle noise artifact is a potentially important advantage of spectral domain optical coherence tomography (SDOCT), but the requirements to produce clinically significant benefits has not been established. In this study, we evaluate the benefits of SDOCT averaging by assessing the visualization of outer retinal structures of interest.

Methods: We collected OCT data from the Cirrus HD-OCT (ver 4.3) from 35 eyes of 35 consecutive patients referred to the imaging unit for retinal disease. All patients underwent 3-scan acquisitions: (a) 1024 x 5 high-definition (HD) B-scan raster without averaging, (b) 1024 x 5 with 4x averaging, and (c) a single B-scan (1024 x 1) through the foveal center but with 20x averaging. For each patient, the central B-scan was used to assess visualization of four outer retinal features of clinical value: (a) external limiting membrane (ELM), (b) inner segment - outer segment (IS-OS) junction, (c) retinal pigment epithelium (RPE), and (d) choroid. Quality of visualization of each feature was graded in a masked fashion (1 scan to scan type) according to three parameters (ability to identify, brightness, and continuity), each of which were rated on a 0-3 qualitative scale (0 being worst and 3 best). Quality Scores (QS) for the three scan types were compared using Chi square test for difference.

Results: Quality scores are shown in Table 1. QS consistently improved with 4x averaging and improved slightly further with 20x. The most significant benefits were observed for brightness scores. For ELM identification, 91.4% of 20x cases achieved the highest QS score (c"v) on all parameters compared with 92.9% of 4x cases and only 54.3% of non-averaged cases. Amongst the various structures, averaging appeared to have the least beneficial effect for assessment of the RPE and IS-OS junction.

Conclusions: The presence of outer retinal structures is often thought to be the result of a number of factors such as the corneal curvature, motion of the eye, and the positioning of the camera. Flattening the dataset makes visualization of these structures easier by bringing the dataset into a more consistent shape, which also allows for easier by bringing the dataset into a more consistent shape, which also allows for the efficient truncation of the dataset. Here, we present a quantitative comparison of two automated methods that eliminate distortions characteristic to optical coherence tomography imaging.

Methods: First, the retinal surfaces are detected through an automated 3-D graph-theoretic approach. A surface is then selected and used to determine the flattening plane through two consecutive thin-plate spline fits. The first spline-fit uses a smoothing regularization term and an equal number of control points in both axial directions along the retinal surface. The second spline-fit uses a smaller regularization term and a larger number of points in the directions of the slice acquisition is used to approximate the ripping seen in C-scans. In both stages, points within the neural canal are avoided using a circular mask to approximate the region. This two-stage approach is compared with the method that uses a single spline-fit. The method is quantitatively validated using depth maps of the optic nerve head constructed from fundus photographs (Tang '10, SPIE) taken at two slightly different angles. Since the depth images approximate the shape of the optic nerve head, they can be compared with the top surface of the flattened dataset. The normalized depth map is registered to the OCT dataset and the mean unsigned difference is computed over 30 glaucomatous datasets, the mean unsigned difference between the depth maps and the top surface from the datasets flattened (which are also normalized consistently) by the two-spline flattening approach was significantly smaller than the single-spline flattening approach by 20.2% (p < 0.001).

Conclusions: Although various methods exist for flattening OCT datasets, thus far, none have been quantitatively validated. The presented two-spline flattening method was compared quantitatively with a single-spline approach and found to be more robust.

CR: B. J. Antony, None; L. Tang, None; M. Abramoff, Patent application; P. K. Lee, None; M. Sonka, Patent application; P. M. Garvin, Patent application, P. Support: R01 EY108553, R01 EB004460, NIH Grant EY17066, VA Center for Prevention and Treatment of Vision Loss

Assessment of Frames Averaging Algorithms for Optical Coherence Tomography

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Purpose: Averaging several frames of optical coherence tomography (OCT) images can improve image quality by suppressing background and speckle noise, but can also introduce artifact if the registration of frames does not adequately remove motion error. The purpose of this study is to evaluate two commercially available frame-averaging algorithms, by post processing, in two RTVue software versions (Version 4.0.1.143 and Version 4.0.7.4).

Methods: A Fourier domain OCT system (RTVue, Optovue, Inc. Fremont, CA), was used to scan 40 human subjects (20 normal and 20 glaucoma) with line scans (centered at fovea, scan length = 6mm). The RTVue postprocessing software registers and averages 16 consecutive frames for each line scan. Two versions of RTVue software (4.0.1.143 and 4.0.7.4) were evaluated. Three parameters were used to assess image quality. The noise variance evaluates noise suppression (smaller value better). The edge width evaluates edge blurring due to misregistration (smaller value better). The contrast to noise ratio (CNR) evaluates contrast enhancement (larger value better). The Wilcoxon rank sum test was used to evaluate the significance of differences in image quality.

Results: The noise variance, edge width, and CNR of frame-averaged images (both software versions) were significantly better than single frames (p < 0.001, Table 1). Frame averaging by software version 4.0.7.4 was significantly better than version 4.0.1.143 in terms of edge width (p = 0.04), but not the other 2 parameters (Table 1). The edge width parameter correlated with subjective assessment of image quality.

Conclusions: Both version of frame-averaging software dramatically suppressed noise and increased contrast. Software version 4.0.7.4 preserves edge sharpness better than version 4.0.1.143, indicating better registration of image frames. Registration of image frames is critical to image quality and edge width is a good parameter for its evaluation.

CR: W. Wu, None; O. Tan, Optovue, Inc; P. Optovue, Inc; P. D. Huang, Optovue, Inc; J. Lammer, Optovue, Inc; I. Optovue, Inc.; C. Optovue, Inc.; P. Carl Zeiss Meditec, Inc.; P. Optovue, Inc.; R.

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Segmentation of Retinal Lesions by Polarization Sensitive Optical Coherence Tomography

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Purpose: To demonstrate new algorithms based on polarization sensitive optical coherence tomography (PS-OCT) for segmenting retinal lesions like retinal pigment epithelial (RPE) atrophies, macular hole, macular holes and intraretinal fluid by PS-OCT based algorithms are an interesting alternative to conventional algorithms based on OCT intensity data. The segmentation of the RPE by the tissue specific DOPU parameter provides a reliable backbone for segmentation of adjacent structures. PS-OCT might improve diagnosis and precise follow-up of these diseases.

Methods: An experimental spectral domain PS-OCT system was used that allows to simultaneously record 2- and 3-D data sets of backscattered intensity and various polarization parameters in the human retina. We previously have shown that the RPE depolarizes backscattered light; this effect can be used to segment the RPE based on the parameter “degree of polarization uniformity” (DOPU). We demonstrate the use of this method to segment and quantify RPE atrophies. Furthermore, we expand on this method and developed new algorithms that use the segmented RPE as a direct mask for locating hard exudates, like Bruch’s membrane or the photoreceptors by intensity based segmentation methods. These layers are then used to quantify area and volume of drusen and subretinal fluid. Hard exudates are also segmented by their depolarizing properties. Data sets of 60 patients with geographic atrophies, drusen, hard exudates, or intraretinal fluid are analyzed.

Results: Segmentation of RPE atrophies worked well and showed a good correlation with autofluorescence images. Drusen segmentation worked well in most cases, with some exceptions in large, confluent drusen. Segmentation of hard exudates in patients with diabetic retinopathy showed a good correlation with fundus photography. First results in two patients with subretinal fluid demonstrate the potential of the method for quantifying fluid volume.

Conclusions: Segmentation of retinal lesions like RPE atrophies, drusen, hard exudates, and intraretinal fluid by PS-OCT based algorithms are an interesting alternative to conventional algorithms based on OCT intensity data. The segmentation of the RPE can be achieved with a specific DOPU parameter that provides a reliable backbone for segmentation of adjacent structures.

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1783 - A532
Automatic Delineation of Drusen With Polarization-Sensitive Optical Coherence Tomography
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Purpose: To date the assessment of optical coherence tomography (OCT) images of the retina requires considerable manual interaction. We evaluated the ability of a novel fully automated technique to segment cystoid and subretinal fluid spaces in high quality optical coherence tomography (OCT) images.
Methods: Regions of hyporeflectivity (e.g. cyst, vitreous space or retinal tissue) were first segmented from the original OCT FD OCT image (zoom-in view in Fig. A) by a fast globally convex segmentation algorithm without necessitating initialisation. Those regions detected outside the retina were then automatically removed by considering their relative locations to the inner limiting membrane and retinal pigment epithelium estimated by curve fitting technique. Falsely detected regions within the retina were also automatically eliminated by using differentiating features (e.g. size, intensity and shape).
Results: 20 B-scan images (one from each volume scan of the Heidelberg Spectralis OCT) were studied. Mean processing time for a B-scan was 5.3 seconds. The performance of the program was validated by comparing the areas automatically detected (Fig. B) with those manually delineated by medical retina specialists (Fig. C). Results showed no statistical difference (p=0.2).
Conclusions: A fast, fully automated segmentation approach showed promising results for segmentation of cystoid and subretinal fluid spaces in OCT images and has the potential to aid treatment and management of eye disease.

1784 - A533
Fast Automated Segmentation of Fluid Spaces in Fourier-Domain OCT Images of the Retina
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Purpose: To date the assessment of optical coherence tomography (OCT) images of the retina requires considerable manual interaction. We evaluated the ability of a novel fully automated technique to segment cystoid and subretinal fluid spaces in high quality optical coherence tomography (OCT) images.
Methods: Regions of hyporeflectivity (e.g. cyst, vitreous space or retinal tissue) were first segmented from the original OCT FD OCT image (zoom-in view in Fig. A) by a fast globally convex segmentation algorithm without necessitating initialisation. Those regions detected outside the retina were then automatically removed by considering their relative locations to the inner limiting membrane and retinal pigment epithelium estimated by curve fitting technique. Falsely detected regions within the retina were also automatically eliminated by using differentiating features (e.g. size, intensity and shape).
Results: 20 B-scan images (one from each volume scan of the Heidelberg Spectralis OCT) were studied. Mean processing time for a B-scan was 5.3 seconds. The performance of the program was validated by comparing the areas automatically detected (Fig. B) with those manually delineated by medical retina specialists (Fig. C). Results showed no statistical difference (p=0.2).
Conclusions: A fast, fully automated segmentation approach showed promising results for segmentation of cystoid and subretinal fluid spaces in OCT images and has the potential to aid treatment and management of eye disease.
1787 - A536
Image Extraction and Advanced Visualization of OCT Retinal Images
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Purpose: To design and validate computer algorithms and create software for image extraction archiving and advanced visualization of retinal images acquired with spectral domain optical coherence tomography (OCT). The application is aimed to increase effectiveness in the clinical practice and to assist OCT image reading centers for clinical trials.

Methods: Fast programming languages were used to design algorithms for rapid image retrieval, segmentation and display. The platform consists of multiple tiers. On the front-end there are two modes: 1) for automatic and 2) for manual insertion of demographic data and images. The core of the program consists of image presentation and clinical data comparison module. A friendly graphical user interface was created to display the OCT images and data together. Information for the right and left eye is presented separately. Selection menu for desired type of visualization with image presentation filters is also incorporated. The back-end of the platform contains fast database for image and clinical data archiving. Advanced searching capabilities allow for data mining.

Results: The platform was tested on computer with Intel processor: Core 2 Duo, 2.5 GHz, 4 GB RAM under Microsoft Vista 32-bit operating system. One hundred sham test images with the same resolution as the original OCT images were used to test the platform. The results show very robust and instantaneous loading and display of the image sets from multiple visits (average less than 1 sec. from 5 visits with 6 images per visit) when archived on the local hard drive. The images from left and right eye are loaded simultaneously and remain in the memory, so that flipping back and forth between the eyes does not require more loading time. The visits are chronologically presented and can be filtered based on multiple criteria. During the test the software reliably filtered visits with intraocular procedure from follow-up visits without procedure.

Conclusions: Robust, reliable software platform for OCT image extraction, visualization and archiving was designed and validated for the purposes of clinical evaluation and OCT image reading centers.
CR: B. Madow. None.
Support: None.

1788 - A537
Distance Measurement Between an Electrode and the Retina Using OCT Images

Purpose: To investigate the correlation between electrical impedance of an intraretinal microelectrode and the electrode retina distance measured by optical coherence tomography (OCT).

Methods: Experiments were done in normal rats (n=2). Baseline OCT images were acquired prior to insertion of the micro electrode in the rat eye. Electrode insertion was made with a 75 um diameter platinum electrode. The electrode was advanced until it was visible in the fundus view of the OCT system. The scan line was adjusted to be along the length of the microelectrode to allow simultaneous scanning of the electrode tip and the retina. Electrical impedance was measured using a 10mV sine wave at 100kHz. Impedance and OCT data were acquired as the electrode was advanced towards the retina, under micromanipulator control.

Results: The impedance increased consistently as the electrode was advanced towards the retina. This is illustrated in the graph below; values of impedance and distance have been normalized to the starting value of each. Distance equals zero represents the electrode tip in contact with the retina. Data represented as mean ± s.s.d

Conclusions: Increasing electrical impedance is proportional to how close the electrode is to the retina. Electrical impedance can be used to sense proximity to the retina.

1789 - A538
System for Modeling and Localizing Metamorphopsia in OCT images
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Purpose: To model patterns of visual distortion caused by metamorphopsia in a patient, by use of a deformable Amsler grid, based on cubic B-splines; and to localize the affected area in macular OCT images for further analysis.

Methods: In order to model distorted vision, we display in a computer monitor an interactively deformable Amsler Grid to the patient at a distance of 30 cm. One eye is covered and the other fixes the grid center. The perceived distorted lines will be deformed in the opposite direction of patient’s distortion until vision is corrected and the lines are seen straight again. The grid is based on cubic B-splines in order to have a smooth deformation. Once the metamorphopsia model is acquired, we align it with the corresponding OCT images of the patient’s macula for further analysis. This was tested on seven patients with macular disease.

Results: Five patients could reliably fulfill the task. The system provides the model of distorted vision in a range of 47.5º horizontal and 31.3º vertical visual angles. The grid lines are placed every 5.52º horizontal and 3.62º vertical visual angle. The perceived distorted vision was modeled and the affected area was localized in macular OCT and fundus images (see figure). The pathology matched the location of the distortion as graded by an experienced ophthalmologist. The system provides a measurement of the deformation seen in the grid (i.e., the average displacement of pixels) in order to have an estimation of the size of the affected area in the macula (in mm) according to the patients’ visual perception, which helps to evaluate the progression of the disease.

Conclusions: A deformable Amsler grid based system provides a simple and useful method for modeling distorted vision in patients with metamorphopsia. By aligning the model with macular OCT images, we can identify macular features, which could help in the development of an automatic method to model metamorphopsia.

CR: A. Martin-Gonzalez, None; I.M. Lanzl, None; R. Khoramnia, None; N. Navab, None.
Support: Supported partly by Bayerische Forschungsstiftung (BfS) and Secretaria de Educacion Publica de Mexico (SEP)

1790 - A539
Reading OCT Pseudo-Images: Humans vs. Bayesian Ideal Observer
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Purpose: Optical coherence tomography (OCT) has recently become one of the primary methods for non-invasive probing of the human retina. The pseudo-image formed by OCT (the so-called B-scan) varies probabilistically across pixels due to complexities in the measurement technique. It was shown that the distribution of pixels intensity can be well described by a stretched exponential density function such as P(β)≈(1/β)Γ(β)/Γ(βλ)dβ, where Γ(β) is the gamma function, and β and λ are the parameters of the distribution. In this work, we present a psychophysical experiment in which we study the ability of human subjects to detect a patch in pseudo-images and compare its performance with a Bayesian ideal observer algorithm.

Methods: The images used in this experiment were simulated and patches were created through a Gaussian modulation of parameter β in the distribution. The size of the patch was defined by the standard deviation of the Gaussian. In a 4AFC experiment we measured the threshold of d’ necessary to discriminate the location of the patch in the image as a function of size and β, which is the parameter that controls the size of the distribution’s tail. The experiment was performed by displaying the range of intensities with both linear and logarithmic scales. Ten naive observers took part in this experiment.

Results: Results of the psychophysical experiment show that threshold decreases with increasing size in an exponential fashion for all βs varying from 0.6 to 1. Only for the logarithmic presentation the parameter β had an effect on the threshold. Simulations of the ideal observer show thresholds behaving in the same way as human’s data but two orders of magnitude smaller. This would show that the algorithm integrates spatial information more efficiently than humans, based on the optimal use of the knowledge it has about the stimulus.

Conclusions: We think this type of algorithm would be an alternative to develop systems to automatically detect anomalies in these images and then use them to help physicians during the diagnosis.
CR: J.F. Barraza, None; J. Cormensana, None; N.M. Grzywacz, None.
Support: PICT 2002 ANPCYT, Argentina
Taking the Machine Out of the Equation: Measuring Macular Thickness From Different OCT Capture Systems in a Reading Centre

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**Purpose:** To compare manually-assessed retinal thickness measurements on OCT in a reading centre in healthy and diseased eyes captured by different commercially available OCT instruments.

**Methods:** Three different OCT instruments (Stratus OCT [Carl Zeiss Meditec, Inc, Dublin, CA], RTVue [Optovue Corp., Fremont, CA], Spectralis HRA OCT [Heidelberg Engineering, Inc., Heidelberg, Germany]), were used to capture radial line scans (or equivalents in healthy or diseased eyes. The scans from each system were exported into a JPEG format and imported into custom reading centre software, iPath Reading Centre (Digital Healthcare, Cambridge UK). Scans were calibrated in the vertical plane and scrutinised side by side to identify common features. A single scan from each of the different capture systems was chosen at the same orientation and manual measurements were taken from the inner limiting membrane to the visible pathology or the RPE-choriocapillaris complex, whichever was more pronounced.

**Results:** Two eyes were included in the study. Using each patient-eye as a block effect test each device, a 2-way ANOVA showed that there were no significant differences between the machine mean measurements of retinal thickness across the three OCT capture systems. The mean thickness measurements for Spectralis, Stratus and RTVue were 0.150, 0.149 and 0.136 respectively.

**Conclusions:** The three OCT systems provided similar results for retinal thickness measurements. This has important consequences for reading centres and their approach to perform manual measurements for OCT thickness rather than relying on computer software. This study has several limitations. Although the scan orientation chosen was the same for each system, there can be no guarantee that the same location was used in each image to perform the measurement, or that the scan intersects the same anatomical region in all systems. However, the images were scrutinised in advance to determine common features and the thickness lines were drawn on all scans before the measurements were known. The sample size is also quite small which may result in a type II error and thus the study will be extended to a larger set of patients and will include reproducibility assessments.

CR: W.P. Patton, None; K.A. Muldrew; None; M. Stevenson; None; U. Chakravarthy, None.
Support: None

### Automatic Computer-Based Grading for Age-Related Maculopathy

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**Purpose:** To develop and test a system that detects drusen and pigment abnormalities in Age-related maculopathy (ARM) patients, replicating the simplified 5-year risk of development of advanced stages of AMD.

**Methods:** We developed a system that detects the two characteristic features of ARM which were identified in the AREDS study: Drusen and pigment abnormalities. First, by using Amplitude Modulation-Frequency Modulation (AM-FM) methods, we obtained mathematical features that characterize drusen. Using morphology-based filters we extract the drusen features from the background and automatically detect, classify and quantify the pathologies in order to be used in statistical analysis applied to agree or disagree, alter or add annotations. Once a visit review is complete, they can to be automatically determined, mapped and color coded accordingly to the baseline and alter any previously made annotation in order to seal the final diagnosis.

**Results:** The algorithm was tested on a set of 100 images from the AREDS database, using a single image of the central field eye per subject. For images with drusen, we obtained a rate of correct classification greater that 90%. For images with pigment abnormalities, we obtained a rate of detection of 75%. These results compare well with published results of human grading for ARM and AMD, which achieved sensitivities of 61% for ARM and 86% for AMD.

**Conclusions:** Age-related maculopathy degeneration (AMD) is the most common cause of visual loss in the United States and is a growing public health problem. The ultimate goal of the system is to provide biomarkers to identify patients at risk of developing advanced stages of AMD and to improve outcomes by identifying more specific interventions. In this manner one will be able to select the best treatment earlier in the disease, which will lead to improved therapeutic outcomes.

CR: E. Barriga, VisionQuest Biomedical, E. V. Murray, University of New Mexico, F. C. Agurto, University of New Mexico, F. M. Pattichis, University of New Mexico, F. S.R. Russell, University of Iowa, F. P. Soliz, VisionQuest Biomedical, LLC, I.
Support: None

### An Annotation Software to Help in Early Detection of AMD

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**Purpose:** ADCIS, in partnership with experts in Ophthalmology and Pfizer Inc., developed a software using imaging tools to track the evolution of pathologies during the Age-Related Macula Degeneration conversion.

**Methods:** 100 patients with high risk of conversion were enrolled in a clinical trial at 3 different sites and are examined every 6 months over a period of 2 years. At each visit, color fundus, infrared, red free and autofluorescence images, 3D OCT, fluorescein and indocyanin green angiographies are acquired with the HRA II Spectralis. Then, these images are exported from the Heidelberg Eye Explorer database and uploaded to a remote database accessible from all sites.

**Results:** For each image on the follow-up resulting in a sequence of difference-images. These images are processed to correct non-uniform illumination and normalize brightness. Vessel centers are detected from the retinal vascular tree were segmented and used for image registration, based on a proprietary technique, to allow comparing any gray-scale image to the respective baseline and to compute differences. The process repeats for each image on the follow-up resulting in a sequence of difference-images. These differences can be added, after a specific colorization, and mapped, showing the progression of the detected changes over time accordingly to the defined color scheme.

**Conclusions:** The proposed method allows changes from color fundus photographs to be automatically determined, mapped and color coded accordingly to the baseline and was successfully applied to AMD patients’ eyes. CR: T. Santos, None; C. Maduro, None; J. G. Cunha-Vaz, Critical Health, C.
Support: POFC-QREN-UE/FEDER-Ver+Saúde-3512

### Macular Changes Follow-Up in Dry AMD Using the RetMarker

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**Purpose:** To automatically compute differences over time from color fundus photography sequences in AMD patients’ eyes.

**Methods:** Color fundus photographs, 30º field-of-view centered on the fovea, were taken every 6 months during a 2-year follow-up period from 52 eyes of 52 patients. Images were converted to gray-scale through principal component analysis to capture the highest level of contrast from each color channel. Gray-scale images were thereafter processed to correct non-uniform illumination and normalize brightness. Vessel centerlines were extracted from the retinal vascular tree were segmented and used for image registration, based on a proprietary technique, to allow comparing any gray-scale image to the respective baseline and to compute differences. The process repeats for each image on the follow-up resulting in a sequence of difference-images. These differences can be added, after a specific colorization, and mapped, showing the progression of the detected changes over time accordingly to the defined color scheme.

**Results:** This fully-automated procedure allows determine and to map changes detected over a time sequence of color fundus images. Specifically to these AMD patients’ eyes, this allowed to detect drusen size and confluence indicating turn over among other retinal changes from the difference-images.

**Conclusions:** The proposed method allows changes from color fundus photographs to be automatically determined, mapped and color coded accordingly to the baseline and was successfully applied to AMD patients’ eyes. CR: T. Santos, None; C. Maduro, None; J. G. Cunha-Vaz, Critical Health, C.
Support: POFC-QREN-UE/FEDER-Ver+Saúde-3512

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1791-1794
1996 - A545

An Evaluation for Automated Cup-Disc-Ratio Assessment System for Digital Fundus Images

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Purpose: To evaluate the performance of an automatic system for cup-to-disc ratio (ICDR) measurement from non-stereoscopic digital fundus images

Methods: We developed an enhanced version of our previously reported automatic system (Wong et al, ARVO 2009). The vertical optic cup and disc heights were detected from points in the inferior (5 o’clock to 7 o’clock) and superior (11 o’clock to 1 o’clock) of the disc. The system is tested on a study sample of 71 retinal fundus images (S072 x 2048, Field 2) from the Singapore Malay Eye Study (SiMES) study. Clinical CDR was defined by an ophthalmologist.

Results: The mean clinical CDR was 0.61 and the mean CDR from the automated system was 0.63. Compared with the clinical reference, the automatic system had a vertical disc error of 10μm (95% CI, 93.8 - 143.1) and a vertical cup error of 14μm (95% CI, 117.5 - 174.4). The CDR of the automatic system had an unsigned error of 0.08 CDR units (95% CI, 0.061 - 0.090), with 94.4% of the images having a CDR error of less than 0.2 CDR units.


1979 - A546

Statistical Deformation Modeling of the Optic Disk

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Purpose: Generation of dense statistical deformation models (SDM) capturing the optic nerve head (ONH) variability to indicate relevant differences between healthy and glaucomatous cases from color fundus images.

Methods: While ONH variability is commonly captured by sparse geometric measurements, we represent it by dense deformation fields between one single reference image and images of a sample set calculated by non-rigid image registration. The reference image is not a simple average, but is indicated by the minimal residual deformations. For both, glaucomatous (N=90) and controls (N=90), a SDM is generated by Principal Component Analysis. The gold standard diagnosis was given by a glaucoma specialist based on an elaborate ophthalmological examination with ophthalmoscopy, visual field, IOP, FDT, and HRT II. Eliminating the control variation modes from glaucoma SDM, the glaucomatous variations exclusively remain. Figure 1 (right) exemplifies a glaucomatous rim changes in the nasal sector (9 o’clock) of the ONH.

Conclusions: The proposed SDM approach allows a dense and detailed representation of common and idiopathic glaucomatous ONH variations. We expect that these models provide new insights to the glaucoma disease and can be potentially applied for automated glaucoma detection.

Support: German Research Foundation (DFG SFB-539), Erlangen Graduate School in Advanced Optical Technologies (SAdOT)

1978 - A547

Automatic Detection of Peripapillary Atrophy in Digital Fundus Photographs

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Purpose: To determine the performance of an automatic system for the detection of peripapillary atrophy in digital fundus photographs

Methods: We tested the performance of a proposed approach for the detection of peripapillary atrophy (PPA) using a sample of digital fundus photographs from the SCORM study (Saw et al, IOVS 2006). The optic nerve head is first detected using an approach similar to our previously reported method (Wong et al, ARVO 2009). Subsequently, an entropy transform is applied on the peripapillary area, the output of which is divided into sections corresponding to the inferior, superior, nasal and temporal regions. Principle component analysis is used to determine the variables which best describe the data. These variables are then used as inputs in a naive Bayesian classifier to determine the presence of PPA in the fundus photographs.

Results: The sample consisted of 40 photographs with PPA and 40 without PPA, clinically assessed by an ophthalmologist. Using the described approach, 86.3% of the photographs were correctly classified (sensitivity: 0.83; specificity 0.90). Cross-validation was performed using a leave-one-out approach, attaining an average accuracy of 83.8%.

Conclusions: We have tested an approach proposed for the automatic detection of peripapillary atrophy. The test results are promising for the further development of this approach into an automated tool to aid in the detection of early glaucomatous damage in digital fundus images.


CR: R. Bock, None; J. Horninger, None; G. Michelson, None.

1976 - A544

Using Am-Fm to Automatically Detect Glaucoma

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Purpose: To validate a classification algorithm for the detection of glaucoma in color fundus digital photographs using amplitude modulation-frequency modulation (AM-FM) as feature extraction technique and Partial Least Squares (PLS) as a classification method.

Methods: A DR screening algorithm has been tested on 2 different databases. The first dataset consisted of 1200 images from MESSIDOR, and 500 images from the University of Iowa department of Ophthalmology provided by Dr. Michael Abramoff. The images were categorized by ophthalmologists into 4 levels of DR severity. Multiscale AM-FM, a mathematical technique that extracts features from images in different frequency bands, was applied to each image. Images are further subdivided in regions of interest (ROIs). A total of 39 features are extracted for each region, corresponding to the 3 estimates produced by AM-FM and 13 combinations of bandpass filters. An unsupervised clustering method (k-means) is used to group similarities in the ROIs prior to computer classification. Testing is done using the cross validation method, where the training and testing sets of images are chosen randomly from our dataset.

Results: The MESSIDOR database is divided in three sets of 400 images each. The results obtained for each of the 3 sets are: AUC1=0.86, AUC2=0.84, and AUC3=0.85, corresponding best sensitivity and specificity values were 98%/67%, 92%/66%, and 95%/70%. For the U of Iowa database, we obtained an AUC of 0.82, with 91%/65% sensitivity/specifity. An additional test was performed for the classification of images containing Threatening DR. An AUC=0.99 and sensitivity/specifity of 100%/88% was obtained for this case.

Conclusions: The classification results obtained with our algorithm are comparable to the results obtained in the classification of DR. As opposed to other methods, ours is a top-down approach not requiring manual segmentation of lesions. In addition, the feature extraction using AM-FM is proven to be robust since different sizes of images and different places of acquisition for the database are used in this implementation without significant variation in the results.

CR: C. Aguero Rios, University of New Mexico, F. V. Murray, University of New Mexico; P. S. Barriga, VisionQuest Biomedical, E. M. S. Pattieh, University of New Mexico; F. W. Bauman, Jr.; None; P. Soliz, VisionQuest Biomedical, I.
Validation of Automated Fundus Image Analysis of Arteriovenous Ratios

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Purpose: Current methodology for the extraction of arteriovenous ratios (AVR), a metric for hypertensive retinopathy, from fundus images requires time intensive, manual identification and measurement of vascular features. We have developed a set of image processing algorithms able to perform such analyses automatically on large databases of fundus images, offering significant diagnostic and screening potential. However the validity of our automated measurements is yet to be verified. Here we compare AVRs obtained by the automated software to manual calculations.

Methods: 98 fundus images from the eyes of 49 patients were randomly selected from a database of hypertensive and non hypertensive patients. Vessels were classified as either artery or vein, vessel thickness measured, and AVRs calculated by the software and by a human observer. Paired t-test was performed to evaluate differences in manual and automated measurements.

Results: 98 fundus images were analyzed. Between 34 and 76 vessels per eye were identified and measured, with strong agreement demonstrated between automated and manual results. There was no statistically significant difference in AVRs calculated by the software and human observers.

Conclusions: AVRs obtained from fundus photographs by automated software were shown to be strongly concordant with manual measurements. Automated AVR analysis of fundus photographs is a valid technology with promising applications.

Support: Unrestricted Grant from Research to Prevent Blindness

Boundary Detection of Optic Disc and Parapapillary Atrophy From Color Fundus Images Using Dual-Channel Color Morphology and Snakes

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Purpose: The presence of parapapillary atrophy (PPA) representing chorio-retinal atrophy around the optic disc (OD) has been associated with certain relatively common eye conditions (eg, Glaucoma and myopia). However, the significance of its development and extent has not been fully established. Although often detected in color fundus photography, there is to date no computer-aided measuring tool available for its accurate detection and measurement. We describe a novel approach to automatically segment the OD and PPA and compare this against the performance by an ophthalmologist.

Methods: Pre-processing techniques were initially applied to color fundus images on the red and blue channels separately in order to segment the OD and the OD-plus-PPA respectively. Average filtering was performed within an initial mask to create an enclosed homogeneous area. The OD and OD-plus-PPA boundaries were then further segmented by using a frequency de-convoluted model called ‘snakes without edges’, based on techniques of curve evolution, level sets and ‘Mumford-Shah functional’. We carefully selected the step size of the energy function to ensure that our snakes stopped at the desired boundaries. PPA was then derived from the subtraction of the OD from the OD-plus-PPA. We applied this technique on fundus images taken from a database of a well-characterized cohort and compared the accuracy of boundary detection against the manually-labeled ground truth information drawn by an ophthalmologist.

Results: Of the 33 randomly selected images of 25 subjects with PPA, 27 were of sufficient quality for analysis. Our proposed algorithm achieved a mean accuracy level of 86.6% (S.D.=5.9) in detecting OD, 87.1% (S.D.=6.5) in detecting OD-plus-PPA and 73.5% (S.D.=12.8) in detecting PPA.

Conclusions: Our proposed algorithm achieved good accuracy compared to the gold standard of a human expert. Further work to test this algorithm in a larger sample is indicated. Possible application includes semi-automated screening systems for diagnosis of eye conditions associated with PPA in the community.

Support: Tan Tock Seng Scholarship

A Content-Based Image Retrieval Approach for Image Quality and Alignment Evaluation

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Purpose: To create an automated system for evaluating image quality, including alignment according to ETDRS protocol.

Methods: One hundred images were extracted from a database of 500 patients (1000 eyes). A reference image was selected based on a visual interpretation of acceptable alignment of ETDRS field 2. Each of the remaining 99 images was compared to the reference image using two metrics: cross-correlation and mutual information. These two metrics were compared to a calculated difference in optic disc location for each image to the reference image. A function that estimates disc alignment from either metric was calculated using polynomial curve fitting. This analysis was done in two different ways. First, it was applied to images that were not manipulated. Second, it was applied to images for which the reference image was matched to that of the standard image.

Results: The normalized cross-correlation between images showed an inverse relationship with optic disc distance (R2=0.7) in the red channel. The mutual information metric also showed an inverse relationship with optic disc distance (R2=0.65) in the green channel with histogram equalization. Higher errors were produced by images with uneven illumination.

Conclusions: Finding reliable metrics to match images is essential in being able to index a set of standard images by objective measures of content. Our results show that it is feasible to build a catalog of image alignment that can be mined automatically using metrics of information content. Uses include stand alone, real time, assessment of image quality and automatic building of reference datasets.

Support: None
1805 - A552
Low-Cost Super Resolution Retinal Imaging With Embedded Denoising: Quantitative and Qualitative Assessment of Reconstructed Images From a Scanning Laser Ophthalmoscope
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Purpose: To assess the applicability of a Super Resolution (SR) algorithm for increasing image quality and enhancing the visualization of physiologically significant landmarks by generating SR images of the retina from multiple low resolution pictures of the same scene.

Methods: The dataset consisted of 32 retina video sequences from normal subjects taken with a low-cost SLO. Each video consisted of 20 frames, each of size 1024x1024 pixels with a footprint of 10 um and acquired at 10 frames per second. Regions of interest (512x512 pixels) from 4 to 16 frames were used to test a SR algorithm that uses a Total Variation (TV) functional to increase image resolution by factors of 2X to 4X. The functional contains an embedded denoising term that corrects for acquisition artifacts introduced by the SLO. Quantitative metrics of information content and image quality were applied to the original and SR images to assess changes introduced by the algorithm. Qualitative assessment of utility in discerning four physiologically salient features on the retina (disc margins, major and minor vessels, and macula) was performed by three highly experienced individuals in a masked, pair-wise comparison experiment of the original image to the SR version. Inter-grader agreement (kappa) in the choice of preferred image was calculated.

Results: There were no statistically significant differences in the quantitative metrics between the original and SR images (p>0.01), i.e. all original and SR image pairs had essentially the same contrast, brightness, and entropy. In the qualitative assessment, all graders chose the SR images over their original counterparts in all cases resulting in perfect inter-grader agreement (kappa=1).

Conclusions: The video frames contributed with sub-pixel information to reconstruct SR images. The quantitative metrics remained unchanged indicating that SR does not create information. Rather it combines the information of all the observations into a single image of increased pixel detail aiding the clinician into making a better evaluation of the retinal features. The results demonstrate that more useful images can be obtained without incurring higher acquisition costs through an efficient algorithm that combines the non-redundant information contained in images of the same scene.

CR: J.W. Warnick1, R.T. Smith1, None; R. Allikmits1, None; L. Lee1, None; J. Shi1, None.
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1806 - A555
Fast Fourier Transform of Retinal Blood Vessel Structure as a Methodology for Detection of Structural Change in Smokers and Individuals With Coronary Artery Disease
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Purpose: To test the hypotheses that micro-irregularities in retinal vessel structure using Fast Fourier Transform (FFT) analysis of continuous retinal vessel diameter recordings is firstly different in subjects with coronary artery disease (CAD) compared to smokers and normals, and secondly varies with age.

Methods: Two groups comprised of 21 smokers (mean age 32 yrs, ±9) and 30 CAD patients (mean age 56 yrs, ±16) were compared with age-matched controls (mean age 56 yrs, ±16). All individuals underwent dynamic retinal arterial recordings using the retiopsychometer X (RMS Instruments, UK). FFTs along retinal arteries and veins were obtained at 3 different points using 30 second baseline recordings of retinal artery diameter (RAD) and retinal vein diameter (RVD).

Results: There was no difference in RAD between the smokers, 122µm ±15 and age-matched controls, 120µm ±20 (p=0.369). Similarly no difference was found between CAD (group 2) patients and controls (118µm ±16 and 114µm ±18). The RVD was increased in smokers and CAD patients compared their controls; smokers: 161µm ±16, versus controls 149µm ±17 and CAD: 157µm ±22 versus controls 147µm ±17. The increase in RVD in smokers was significant (p=0.004). No defined frequency calculated by FFT was detectable in either retinal arteries or veins in participants who smoked or who had CAD compared to their respective control groups.

Conclusions: The lack of detectable pulsation frequency would indicate changes in retinal blood vessel wall properties and their dynamic behaviour in the regulation of blood flow. This could be explained by a loss of endothelial function occurring with age, smoking and the presence of CAD. These changes may be a surrogate marker for vascular pathologies.

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Validation of a Registration Algorithm for the Multimodal Spatial Alignment Between an Initial Retina Video Frame and a Retina Composite Image

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Purpose: Accurate placement of lesions is crucial for the effectiveness and safety of a retinal laser photocoagulation treatment. Computer assistance provides the capability for improvements to treatment accuracy and execution time. One possible solution for compensating retinal motion is to register the frames of a live retina video stream on a retina composite image potentially containing a treatment plan. We developed and validated a method for the multimodal registration of the initial frame of a video sequence on a retina composite image.

Methods: The general concept of the multimodal registration procedure is the following. Points on the vessel centerline and the optic disc are detected in both modalities. In a first step the initial video frame and the composite image are spatially pre-aligned using the determined optic disc parameter. Subsequently, the detected points on the vasculature from both images are iteratively matched starting in a small region around the optic disc and then expanding the matching region until the entire video frame is registered. The transformation model changes from affine to quadratic. For the optic disc detection we introduced a new approach, which calculates the highest local mean intensity variance at detected vessel centerline points to set up a region of interest for applying the Hough transform. The presented registration procedure is designed for a computer assisted retinal laser photocoagulation system. It initializes our real-time registration procedure that makes use of the spatial alignment information from the registered initial frame and the features of the segmented composite image to register subsequent frames of the video sequence.

Results: The presented registration procedure was applied to 35 pairs of composite images and initial video frames acquired with a scanning digital ophthalmoscope (SDO). The recorded data cover a wide range of image quality and reveal diverse retinal pathologies. For 31 of the 35 registered composite image/SDO video frame pairs the vasculature of both images appeared well aligned when presented in checkerboard overlay and were hence considered successfully registered. The average registration error obtained was 2.68 pixels.

Conclusions: The algorithm demonstrated its capability to register various pairs of initial SDO video frames and composite images acquired from patients with respectable accuracy.

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Adaptive Optics Scanning Laser Ophthalmoscopy for Imaging Retina Using A Single Liquid Crystal Spatial Light Modulator

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Purpose: To develop an adaptive optics confocal scanning laser ophthalmoscope (AO-SLO) system for high resolution retinal imaging which uses a single liquid crystal spatial light modulator (LC-SLM) as a wavefront corrector and is combined with a standard resolution confocal scanning laser ophthalmoscope (SLO) capable of acquiring wide field of view retinal images and across which the retinal region to be imaged with AO-SLO can be shifted rapidly.

Methods: We developed an AO-SLO system using one LC-SLM device as a wavefront corrector. The accumulated astigmatism resulting from the sequence of the off-axis refraction on concave mirrors is cancelled by introducing a counter astigmatism, which enables the RMS wavefront error intrinsic to the optical system to be lower than 0.1 wave at the subject's pupil without AO correction. It has a basal system to correct subjects' defocus and the residual astigmatism and high-order aberration including subjects' eye and the optics is corrected by LC-SLM. The AO-SLO retinal images are acquired at 10 frames per second and its rate is 1.5 degree by 1.5 degree. It is combined with a standard resolution SLO for a large field of view retinal imaging across which the retinal region to be observed with AO-SLO can be shifted by an operator's mouse-operation. The light source is 480 nm superluminescent diode with its bandwidth of 50 nm for high resolution imaging, 780 nm laser diode for wavefront sensing, and 980 nm superluminescent diode for wide field imaging. The power into the eye is 230 mW, 70 mW, 350 mW, respectively.

Results: Nearly diffraction limited resolution was confirmed experimentally using a monkey eye with resolution chart at its back surface and photoreceptors of healthy eyes have been observed with this AO-SLO system.

Conclusions: High resolution AO-SLO retinal imaging system was realized with a single LC-SLM based adaptive optics. It is combined with a standard resolution SLO for wide field of view imaging across which multiple view of the AO-SLO retinal imaging can be easily obtained by changing the angle of the beam at the pupil.

2313 - A561
High-Speed Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO)
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Purpose: To develop a new generation AOSLO for in-vivo study of retinal structure and function at the cellular level and improve retina image fidelity.

Methods: A fast and sensitive Shack-Hartmann wavefront sensor was developed with a CMOS camera (MicroStab-NIR, Intevac Inc. CA); its spectral response was optimized for both visible and near infrared light; it is able to capture the wavefront at the frame rate $120$ Hz when the light power is $0.5$ mW which was estimated a typical level for wavefront detection in AOSLO setting. This sensor was used to measure the wavefront and supply the feedback control information in the adaptive optics (AO) system for ocular aberration real time compensation. An electromagnetic deformable mirror (DM) (mirror™-S, Imagineeyes, France) was adopted as the wavefront corrector in the AO-system. This DM is driven by 32 actuators with maximum stroke up to 50 micrometers. The AO system was integrated with the scanning optics to form the AOSLO. Low coherence light sources were employed for high fidelity retinal imaging.

Results: The updating frequency of the AO loop is greater than 70 Hz in the human eye, while most previously reported AO for retinal imaging run under 30 Hz. For a 6 mm diameter pupil, after AO correction, the root-mean-square wave aberration was reduced to less than 0.1 micrometers.

Conclusions: We have implemented a new generation AOSLO that is highlighted with robust AO correction for the ocular aberration. The wavefront sensor developed in this study can not only facilitate a fast AO system but also be used as an independent instrument for measuring the ocular aberration dynamics during certain visual process. In-vivo study of retinal diseases and basic research with this AOSLO are underway.

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2313 - A563
Improved Adaptive Optics Control System Using Pupil Tracking for High-Resolution Retinal Imaging
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Purpose: Adaptive Optics (AO) which is used to correct the aberrations of the eye for high resolution retinal imaging needs to be fast enough to accommodate rapid eye movements. Here we evaluate a method that integrates pupil tracking into the AO system of the AO-Flood Illumination Fundus Camera (AO-FIFC) to enhance the temporal and spatial resolution of the AO system and improve the retinal image quality.

Methods: The AO loop of AO-FIFC includes HASO 32-eye wavefront (WF) sensor (10Hz), mirror 52-deformable mirror (DM)1,4,5 (85 Hz), both from Imagine Eyes, France), and a pupil tracking system (65 Hz). Between two WF gradient measurements, the aberration to be corrected is calculated by adding the latest measured WF aberration and an estimated change in aberration due to pupil movement. The change of aberration is estimated as the product between the pupil displacement and the second derivative of the WF. New algorithm updates the DM according to each new pupil position. The method is tested by simulations and experimentally with an artificial eye of 7 mm pupil mounted on a translation stage and the AO-FIFC. Simulations are done with ten in vivo aberration measurements; they are shifted on y axis by a few units and the same shift is produced using the method.

Results: The difference of the wavefronts represent the error of the method, which was 40% ± 20% RMS in average for a 400 µm shift. Experiments done (Imagine Eyes, France) resulted in 83% ± 20% RMS and 90% ± 20% RMS error for 50 µm and 300 µm shift respectively.

Conclusions: The method provides a satisfying correction of the aberration produced by shift for 50µm which is the most probable eye shift statistically-according to the survey done using the pupil tracking system. The experimental result for the 300 µm shift being less likely to occur, is slightly higher than simulations, pointing an experimental error due to the set-up which shall be corrected.

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2312 - A562
High-Resolution Retinal Imaging With Dual-Deformable-Mirror Adaptive Optics Scanning Laser Ophthalmoscope
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Purpose: To further develop and test our system for controlling a dual deforma-

Methods: A Lagrange-Multiplier(L-M)-based damped Least-Squares (DLS) algorithm was implemented in our dual-DM AOSLO. Starting from the Shack-Hartmann wavefront measurements, the algorithm enables the system to simultaneously correct large-amplitude-low-order aberrations by a Woofer DM (Imagine Eyes), and the small-amplitude high-order aberrations by a Tweeter DM (Boston Micromachines). The L-M method integrates the two DMs to form a single “imaginary” monolithic DM, and the DLS method was used to suppress the correlation between the two DMs, providing reasonable actuator commands for each DM. The damping factor used for each DM is the median of all eigenvalues of the normal influence matrix of that DM, because that value is good for balancing the error damping for all actuators, yielding efficient wavefront correction. By adjusting the damping factors, the new control allows us to change the weight of each DM to yield either a Woofer-dominated or a Tweeter-dominated AO correction. The control was tested by comparing imaging performance in both artificial and real eyes. The performance of sequential control (one DM then the next) was compared to the simultaneously operating dual DM control.

Results: The Woofer-Tweeter dual-DM AOSLO system works well. For artificial eyes, the wavefront correction accuracy with the L-M-based DLS algorithm can be steadily controlled around 0.035 micron (RMS) for small static aberrations, equivalent to the best sequential control where the BIC correction is held while the Mirao DM correction was running. In vivo, both techniques gave good results. Using the gradient of cone sizes near the fovea as a resolution target, both techniques yield resolution very close to the diffraction limit. The dual-DM control was at least as good as the sequential control, and occasionally its images were better.

Conclusions: It is important to notice that the DLS-control-based dual DM AOSLO is more convenient for the operator. It is stable, robust, and requires little operator interaction, yielding a truly real-time AO correction for retinal imaging in a Woofer-Tweeter system. Thus, for a subject with large refractive errors, the L-M-based DLS dual-DM control can simultaneously correct the refractive errors and higher order aberrations.

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2314 - A564
Performance of a Content-Adaptive Filtering Method for Photoreceptor Cell Counting
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Purpose: Measurement of photoreceptor cell density may potentially become an important parameter for screening and diagnosis of diseases that affect human vision. A method was developed to automatically count the number of photoreceptor cells by using content-adaptive filtering (CAF). The performance of the CAF method was evaluated using simulated images with various photoreceptor cell densities and blur levels.

Methods: AO retinal imaging was performed in a visually normal subject. From an original image of the photoreceptor cell mosaic, images with various photoreceptor cell densities were simulated by scaling the original image by factors of 1.25, 1.5, 1.75, and 2. Blurred images were generated by applying Gaussian filters with σ = 2 and 3 pixels to the original and scaled images. The CAF method consisted of a customized bandpass filter using the McCollan transformation, a threshold-based image binarization process and cell count estimation. The error of the CAF method was determined by comparing the number of photoreceptor cells counted by the CAF method to those manually counted by 2 independent observers.

Results: The variation in the number of photoreceptor cells manually counted on 15 images by 2 independent observers was on average 7%. As anticipated, photoreceptor cells counted both by the automated CAF method and manually decreased as the photoreceptor cell spacing or blur level increased. Errors of the CAF method for the small scaling factors were 12%, 13%, 21%, and 3% for scaling factors of 1, 1.25, 1.5, 1.75, and 2, respectively. Errors of the CAF method were 12%, 7%, and 1% for original, σ = 2 blurred, and σ = 3 blurred images, respectively. For the original image scaled by a factor of 2, the errors of the CAF method were 16%, 5%, and 3% for σ = 2 blurred, and σ = 3 blurred images, respectively.

Conclusion: Photoreceptor cell counts derived by the CAF method were in agreement with manual counting and the agreement improved with blur, which may be attributed to reduced image noise. This cell counting method may be useful for estimating changes in photoreceptor cell density due to retinal diseases that degrade image quality.

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Visualization of Retinal Microstructures by Adaptive Optics Scanning Laser Ophthalmoscopy With One-Micrometer Probe

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Purpose: Adaptive optics (AO) is known to provide high-resolution image of in vivo human retina with the resolution around a few micrometers. AO retinal imaging systems with several wavelength probe light up to 985 nm have been demonstrated, and it was found that the retinal microstructure possesses different contrast with different probe wavelength. This study aims at demonstrating AO scanning laser ophthalmoscopy (SLO) with further longer wavelength of one micrometer for the visualization of retinal microstructures.

Methods: 3 eyes of 3 normal subjects examined by AO-SLO with 1 um probe. The AO-SLO is capable of dynamic aberration correction by using an AO subsystem consisting of a 840 nm beacon, a magnetic deformable mirror (Mira52), and a Shack-Hartmann wavefront sensor. The AO operates at 15 Hz closed loop, and reduces the residual root-mean-squared aberration to less than 0.1 μm. The depth of focus was 77 μm. In addition to the AO, large stroke defocus was corrected by a Badal optometer. The SLO subsystem uses ASE light source with 1.04 μm center wavelength for imaging. The optical power on the cornea was 1.1 mW. The eyes were scanned with a 1 degree by 1 degree field of view at the eccentricity of 7 degree. The retinal images were qualitatively accessed by two observers.

Results: Clear photoreceptor mosaic was observed for 3 of the 3 eyes, where the depth position of the focus (DPF) was aligned to be close to the photoreceptor layer (figure (a)). When the DPF is set to a nerve fiber layer (NFL), several dark spots were observed with 2 of the 3 eyes (arrowheads in figure (b)).

Conclusions: The visibility of photoreceptors of this 1um AO-SLO was comparable to that reported by AO-SLO with shorter wavelength. The dark spots on the NFL were rarely reported by short wavelength AO systems. This may be contrasted specifically by the long wavelength imaging. The presence of hot spots may be due to possible differential reflectivity of the photodetector and the non-uniformity of the illumination. Further analysis is required to identify the cause of the dark spots.

Support: Research Grant from Japan Science and Technology Agency

Segmentation-Based Registration of Volumetric Images Acquired With Adaptive Optics Optical Coherence Tomography

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Purpose: Optical coherence tomography (OCT) with adaptive optics (AO) provides unprecedented 3D resolution of the microscopic retina in vivo. The high resolution and high magnification, however, result in substantial eye motion artifacts that are difficult to remove using conventional OCT registration algorithms. Here we develop a new feature-based algorithm that is tailored for AO-OCT imaging and consists of a two step process of layer segmentation and rigid registration.

Methods: A multi-resolution scheme followed by multi-scale directional edge detection and dynamic programming estimates the location of the major retinal layers for segmentation. Individual B-scans are next registered axially and rotationally using similarity transformation, assuming a locally flat retinal pigment epithelium (RPE). To evaluate the method, retinal volumes were acquired on several subjects with no pathology using the AO-OCT instrument described in Cense et al.[1] 12 volumes, each consisting of 100 voxels (width x height x depth with voxel size: 0.9x1.1x9.0 μm³), were collected within the central retina, segmented, and then registered. Effectiveness of the algorithm was qualitatively assessed by viewing fly-through videos of the processed volumes and projected B-scans in the slow scan direction, and quantified by measuring residual axial deviations of the segmented RPE layer.

Results: The algorithm was found to correct eye motion artifacts substantially in all volumes processed. The visibly apparent axial motion in the original projected B-scan (left figure) is noticeably reduced (center figure). Across the 12 volumes, the residual mean-square error of the RPE layer before and after processing is 81.6±57.7 and 3.2±4.7 pixels respectively. Segmentation of a B-scan from the same volume is shown in the rightmost image.

Conclusions: A method to remove motion artifacts from AO-OCT volumes is presented and demonstrated effective on normal retinas. The proposed method is implemented as a plug-in for ImageJ and will be publicly available.

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Liquid Crystal Adaptive-Optics Combined Spectral-Domain Optical Coherence Tomography for Retinal Imaging

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Purpose: In order to improve the quality of retinal image, we propose an adaptive optics (AO) system with a liquid crystal (LC) spatial light modulator (SLM) and its application on the spectral-domain optical coherence tomography (SD-OCT) is described. The AO system uses LC SLM as the corrector to compensate large ocular aberrations of the subject's eye, and was combined with the retinal imaging OCT.

Results: Based on this system, a clear retinal image with high lateral resolution was obtained.

Conclusions: The result suggests that LC SLM can effectively correct the wavefront error of eye, and the LC based AO has potential application on the OCT system for retinal imaging.

Support: None
High Penetration and High Resolution Adaptive Optics Spectral Domain Optical Coherence Tomography With One-Micrometer Probe

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Purpose: Adaptive optics spectral domain optical coherence tomography (AO-SD-OCT) enabled high resolution imaging (0.6 μm × 2 μm per 3 μm in vivo retinal imaging). We enhance the penetration depth of AO-SD-OCT by using one-micrometer probe and demonstrated high penetration and high resolution imaging of retina and choroid.

Methods: Seven eyes of 7 normal subjects were examined by AO-SD-OCT. A broadband 1.03 μm SLD light source (a band-width of 150 nm was used) was used as a probing beam providing a depth resolution of 3.4 μm in tissue. An InGaAs line-scan camera acquired 47,000 depth-scans/s. The AO system was configured with a single magnetic deformable mirror (Mira60, Imagine Eyes) and a Shack-Hartmann wavefront sensor. The AO closed loop operates at 7 Hz and the measured residual RMS wavefront error was less than 0.1 μm which provided a transversal resolution of 3.6 μm on the retina. Seven eyes of 7 normal subjects were involved in this study. The field-of-view was 4.5 degrees. The patch of retina at an eccentricity of about 6 degrees nasal was scanned iteratively and 5 frames are averaged to reduce speckles.

Results: The wave interface between a nerve fiber layer (NFL) and a ganglion cell layer (GCL) was observed for 6 of the 7 subjects. This wave appearing may reflect the cross-sectional structure of nerve fiber bundles. The interface between GCL and inner plexiform layer was observed for 7 of the 7 subjects. The chorio-scleral interface was observed for 5 of the 7 subjects. This implies high penetration of the one-micrometer probe.

Conclusions: The detailed visualization of NFL, GCL and choroid makes the AO-SD-OCT useful not only for the investigation of photoreceptors but also for glaucoma.

single cell, in-vivo Imaging of Chick Retina With Adaptive Optics

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Purpose: Previous studies have shown disaggregation in photoreceptor density at different retinal locations in the chick eye. These results are based on in vitro measurements on excised retina, with possible artifacts caused by tissue drying and/or shrinkage during histological preparation. Through the use of adaptive optics (AO) technology, it is now possible to image and directly count cells in living eyes.

Our experiment uses high resolution AO reflected imaging to determine if there are regional variations in cell density in the chick eye.

Methods: The current New England College of Optometry AO fundus camera was modified to allow high resolution imaging of the chick retina. The AO system consisted of a Hartmann-Shack wavefront sensor and a 37 element Iris AO Inc MEMS deformable mirror. A wavelength of 550 ± 20 nm was used for imaging over a 2.5° field of view. Relay optics were added to de-magnify the 6.2mm pupil used for human imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. Retinal imaging to a 2mm pupil for the chick. The bird was anesthetized and mounted in a prone position on a goniometer stage to allow for tip / tilt adjustment. However, the AO system was modified to allow high resolution imaging of the chick retina. The AO system consisted of a Hartmann-Shack wavefront sensor and a 37 element Iris AO Inc MEMS deformable mirror. A wavelength of 550 ± 20 nm was used for imaging over a 2.5° field of view.

Results: The wave interface between a nerve fiber layer (NFL) and a ganglion cell layer (GCL) was observed for 6 of the 7 subjects. This wave interface may reflect the cross-sectional structure of nerve fiber bundles. The interface between GCL and inner plexiform layer was observed for 7 of the 7 subjects. The chorio-scleral interface was observed for 5 of the 7 subjects. This implies high penetration of the one-micrometer probe.

Conclusions: The detailed visualization of NFL, GCL and choroid makes the AO-SD-OCT useful not only for the investigation of photoreceptors but also for glaucoma.
2323 - A575
Marmoset Cone Photoreceptor Imaging Using a Compact Adaptive Optics
Ophthalmoscope

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Purpose: To enhance electrophysiological and anatomical studies of retinal and central pathways serving color vision, we undertook to image the cone photoreceptor mosaic of a common marmoset (Callithrix jacchus) during routine ophthalmology-recording experiments.

Methods: We designed and built a compact Adaptive Optics (AO) flood-illuminated ophthalmoscope. The instrument is portable (16.7 kg) and can be transported and attached to an electrophysiology-recording rig. The instrument is optimized for imaging marmoset eyes, with wide field of view (5.2° in diameter) projecting onto a non-cooled 2048 x 2048 pixel CCD camera (Megaplus ES4020). Shack-Hartmann aberrometry drives a pupil-conjugate Mirao 524 deformable mirror to correct wavefront error over a 3.2 mm dilated pupil (tropicamide 0.5%). Retinal images from one anaesthetized marmoset were collected at 15 Hz, using 5 ms pulses of light delivered via 400 m of 400 μm optical fiber from a 671 nm multimode diode laser. At the end of the experiment, the animal was overdosed with sodium pentobarbitone then perfused with 4% paraformaldehyde in 0.1M phosphate buffer for 10 min. Eyes were removed, cut open and fixed in the same solution for 20 or 30 min. Retinas were dissected and prepared as whole-mounts.

Results: Adaptive optics corrected image quality was sufficient to resolve cone photoreceptors across the horizontal meridian from 13° temporal to 16° nasal retina, including the optic nerve head. Recovered cone density profiles over the measured field are in agreement with established figures from histological data, peaking at 120,000 cones/square mm within 0.5 mm of the fovea and declining to 4,000 cones/square mm at 13° eccentricity.

Conclusions: Cone-resolved retinal imaging using a portable AO ophthalmoscope is a viable adjunct to electrophysiological and anatomical investigations of color vision.

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2324 - A574
High Resolution in vivo Imaging in Patients With Stargard Disease

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Purpose: To explore the macular cone photoreceptor structure and correlate with the photoreceptor layer in Optical Coherence Tomography (OCT) and a conservative examination of VA in patients with stargard disease.

Methods: High resolution images of the macula were obtained with Adaptive Optics in patients with stargard disease between 12 and 40 years old, they underwent controlled ophthalmic examination including best corrected visual acuity (BCVA), ETDRS, hard sill, autofluorescence, fluorescein angiography (HRA2 Heidelberg, Germany), Spectral Domain Optical Coherence (SD-OCT) and strabismus. The device corrects ocular wavefront aberrations (OWA) in a closed-loop operation at 10 Hz, based on a 52-μm electromagnetic deformable mirror and a 1024 lenslet Shack–Hartmann sensor (Imagine Eyes, France). Each acquisition provides 20 consecutive images. Ten of them were averaged and digitized to produce an enhanced final image. AO images were then analyzed and compared with visual function, autofluorescence images and spectral optical coherence tomography scans.

Results: Most of AO images revealed increased cone spacing with irregular packing centrally in macular area and preserved in periphery and near the optic nerve. we distinguished 2 different aspects. Aspect 1 showed central atrophy area in autofluorescence and this was also associated with disorientation or loss of the reflective band at the photoreceptor layer in inner segment and outer segment junction in SD-OCT, correlated with the de loss VA (1/10) and the absence of the overlying typical cone mosaic in AO. Therefore the second aspect showed central atrophy in autofluorescence in young patient with 12 years of optic nerve disease and the retinal layer had disappeared on OCT when VA was still fair (8/10) and cones mosaic in this area were visualized but abnormally large and spaced from each other.

Conclusions: As a new technology, AO allows more precision of structural alterations observed in young patient with 12 years of optic nerve disease and it enables to improve the assessment of visual function at the corresponding retinal locations.

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2325 - A576
Diseases as Revealed by Adaptive Optics - OCT Images

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Purpose: Adaptive optics - OCT (AO-OCT) provides a 5-fold increase in lateral resolution compared to Fourier-domain (Fd) OCT. This permits cellular level investigation of retinal changes in living eyes of patients. The goals of this study were (1) to evaluate inner and outer segments of cone photoreceptors in patients with retinal and optic nerve diseases and (2) to compare them with visual function at the corresponding retinal locations.

Methods: Twenty one patients with various types of retinal and optic nerve diseases were enrolled. Fd-OCT imaging was performed using the high-resolution imaging module of a spectral domain OCT (Cirrus, Carl Zeiss). AO was performed with the AI-DIO device (Imagine Eyes, France). Each acquisition provides a 20 consecutive images. Ten of them were averaged and digitized to produce an enhanced final image. AO images were then analyzed and compared with visual function at the corresponding retinal locations.

Results: Inner and outer segments of cone photoreceptors were measured from AO-OCT images and compared between retinal locations of different visual sensitivities. Functional tests included visual field maps and mFERG. Length of inner and outer segments of cone photoreceptors was also shorter at the affected retinal locations, however, in optic nerve disease patients, there was no statistically significant difference in the inner segment length between the affected and unaffected areas. Unlike outer segments, the changes in inner segment length, when observed, was more stable within the same retina.

Conclusions: This study demonstrated that outer segment length of cone photoreceptors provide a reliable measure correlated with visual function in both retinal and optic nerve disease patients.

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2327 - A577
In-vivo High-Resolution Imaging of Retinal Nerve Fiber Layer Using Adaptive Optics Scanning Laser Ophthalmoscope

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Purpose: To test the ability of an adaptive optics scanning laser ophthalmoscope (AOSLO) to image the human nerve fiber layer, and construct a large scale map of the nerve fiber layer. To better understand how the nerve fiber layer is formed by imaging regions with sparse nerve fibers at high resolution.

Methods: The nerve fiber layer of three human eyes was imaged by a dual deformable mirror AOSLO. This system incorporates both a BMC MEMS DM and a magnetic Mirao 52D DM as well as a Shack Hartmann sensor. Illumination for imaging and wavefront sensing was obtained from a supercontinuum laser (Fianium) with an 840 nm filter used in the imaging beam and a 740 nm filter used for the wavefront beacon. The system allows rapid acquisition of small field images across the eye by using displacement mirrors which can place the imaging field of 2.0°by1.5° within a 30 degrees region of the retina. The traversal-resolution of the system was approximately 7 microns depending on the exact field size of the subject.

Results: A montage of the nerve fiber layer 13 by 10 area was constructed, starting from the nasal side to the temporal side including both superior and inferior retinas. Similar but smaller fields were imaged for the other subjects. The data shows that while the nerve fibers are well demarcated and have a side-by-side structure near the optic nerve, they are less well ordered as the nerve fiber layer emerges from the horizontal raphe. Near the raphe we were able to see fiber bundles smaller than 10 microns. In numerous places smaller bundles could be imaged separating from one bundle, crossing a gap where there were not nerve fiber bundles, then joining a separate bundle (see Figure 1). The capillaries supplying the nerve fiber layer were also readily imaged.

Conclusions: The AOSLO allows detailed mapping of the human nerve fiber layer, and can produce high magnification scans of the NFL over significant regions of the retina. The wide-field system has the ability to get the large scale montage without changing the fixation target position during the experiment.

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2329 - A579
Leukocyte Dynamics in Parafoveal Capillaries Using AOSLO

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Purpose: To investigate leukocyte dynamics in parafoveal retinal capillaries, using noninvasive, in vivo video microscopy in humans.

Methods: An adaptive optics scanning laser ophthalmoscope (AOSLO) was used to acquire videos of parafoveal capillaries, showing leukocytes flowing in a single-file manner. Videos were acquired at 840 nm and 60 Hz at overlapping locations near the fovea, for one normal subject with no ocular or systemic conditions. Motion contrast methods were used to enhance visualization of capillaries and leukocytes. We selected capillary segments near the foveal avascular zone (FAZ), where the capillary network was single-layered and planar. Spatiotemporal plots were generated for each capillary segment, and traces on the plots were extracted for analysis. Extracted traces were used to determine leukocyte frequencies; speeds and flow directions were also computed in selected vessels. The computed flow directions were compared to expected flow directions by identifying the arterial and venous ends of capillaries.

Results: The parafoveal capillaries, revealed after motion contrast enhancement on AOSLO videos, were used to guide the selection of capillary segments for spatiotemporal plot analysis. There was considerable variation in the appearance of traces on spatiotemporal plots, but we could identify the traces on the plots that were due to moving leukocytes, which had a characteristic appearance. By comparing leukocyte frequencies between capillaries near the FAZ, we identified four distinct patterns of connected capillary segments that accounted for a clear majority of the leukocytes found, which we labeled as leukocyte preferred paths (LPPs). In general, the LPPs were a collection of capillaries that provided the most direct path connecting arteries to veins. For the LPPs, the average leukocyte speed was 1.57 mm/s, and the computed flow directions matched the expected flow directions.

Conclusions: The distribution of leukocytes varied across the parafoveal capillary network. In particular, we confirmed the existence of leukocyte-preferred-paths in retinal capillaries. These methods can be used to investigate leukocyte dynamics in situ.

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2328 - A578
High-Resolution Blood Flow Imaging for Mild Non-Proliferative Diabetic Retinopathy by Adaptive Optics Scanning Laser Ophthalmoscope

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Purpose: To determine pathologic changes in the blood flow in eyes with mild nonproliferative diabetic retinopathy (NPDR) by using high-resolution imaging by adaptive optics scanning laser ophthalmoscope (AOSLO).

Methods: Six eyes of six patients with mild NPDR and 20 normal eyes of 20 volunteers were examined. All the subjects underwent a complete ophthalmologic examination, spectral-domain optical coherence tomography, and imaging with an original prototype of the AO-SLO system fabricated using liquid crystal-on-silicon technology. The AOSLO system has a transverse resolution of 3 μm and can be used to observe retinal pathology at the cellular level, including direct visualization of the cone photoreceptors and the flow of white blood cells. Fluorescein angiography (FA) was performed in all patients with mild NPDR to compare the pathologic changes observed on AO-SLO with the FA findings.

Results: In the cases of normal eyes, AO-SLO images showed a regular blood flow pattern. In the cases of eyes with mild NPDR, many highly reflective spots (about 10 μm in diameter) were seen on the inner walls of vessels on AO-SLO images, even in areas where FA showed no abnormalities; this may indicate the adhesion of leukocytes to the inner wall of the retinal vessels or leukocyte entrapment in retinal microcirculation. In some eyes, several bumps were observed in the blood flow images on AO-SLO, and FA showed the presence of microaneurysms in these areas. These bumps may indicate leukocyte entrapment in microaneurysms. These findings were not observed in normal eyes.

Conclusions: AO-SLO images showed abnormal blood flow patterns in eyes with mild NPDR and compared with the FA, showed the entrapment or adhesion of leukocytes to the retinal vessels; these findings have been shown to be involved in the pathogenesis of various pathogenic conditions, including diabetes, only in animal models. Thus, AO-SLO may be a useful modality to study the abnormalities in microcirculation that are associated with the pathogenesis of diabetic retinopathy.

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2330 - A580
Counting Cones in Eyes With Subtle Defects in the Retinal Pigment Epithelium by Autofluorescence or Scattered Light Imaging

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Purpose: To determine for middle-aged subjects the structural integrity and distribution of cones that overlie subtle, changes to the retinal pigment epithelium. To assess the guiding of light by cones in region of patchy autofluorescence, retinal pigment epithelial (RPE) defects, or small drusen. The fundus changes were documented with wavefront autophuorescence and scattered light images using scanning laser polarimetry.

Method: Four subjects, 2 females and 2 males aged 52 - 97 yr who had not had previous cone count measurements, were recruited based on fundus status. The RPE was assessed using widefield autofluorescence imaging measurements performed with an AOSLO using 594 nm at 92 microwatts over a 27 x 23 deg field, with 750 x 456 pixels. The RPE was further assessed by computing the depolarized light image, using confocal scanning laser polarimetry using 780 nm at 2-3 milliwatts over a 15 x 15 deg field with 256 x 256 pixels. Regions of interest were analyzed for contrast or color changes, including patchy autofluorescence, RPE defects. Control areas at similar eccentricities were selected. Cones were assessed using a second generation Adaptive Optics Scanning Laser Ophthalmoscope at 840 nm +/- 6 nm at 185 microwatts covering 530 x 550 microns of the retina. Cones were measured outside the central fovea where the density with eccentricity varies gradually, allowing better comparison to control regions.

Results: Clear-cut guiding of light by cones, allowing cone counting, was clearly visible in all eyes, with two subjects tested without mydriatics. There were individual differences in the distribution of cones, and also the strength of light return from cones, both among subjects and within an eye. The regions of RPE defects had entire patches of either missing or poorly guiding cones, with control patches having densely packed, more uniformly distributed cones. In the subjects with visible RPE defects, the ratio of average cone densities was 1.14 and 1.02 for control, abnormal, but more important the distribution of the cones was nonuniform in affected regions. In one region of about 90 x 100 microns, there were few cones visible. The lateral resolution of the AOSLO, also demonstrated smaller patchy changes near the target regions, not apparent on imaging with widefield autofluorescence.

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Macular Telangiectasia Evaluated by Spectral-Domain Optical Coherence Tomography and Adaptive Optics Imaging

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Purpose: Two different systems, Adaptive-Optics (AO) Retinal Camera and Spectral Domain Optical Coherence Tomography (SD-OCT) were used to visualize cones in six eyes from 9 patients diagnosed with macular telangiectasia focusing especially on the outer neurosensory macula layers.

Methods: Best corrected visual acuity, fundus examination, fundus autofluorescence and pre-injection frames, fluorescein, ICG angiographies and SD-OCT (HR-A2 Heidelberg, Germany) were performed and compared to AO images. We used a compact AO camera that corrects ocular aberrations in closed-loop operation at 10Hz, based on a 52-actuator electromagnetic deformable mirror and a 1024 lenslet Shack-Hartmann sensor (Imagine Eyes, Orsay, France). The retina is illuminated by a pulsed infrared LED. Each acquisition provides 20 consecutive images. Ten of them are averaged and digitized to produce an enhanced final image. The AO images are then compared with SD-OCT.

Results: The highly reflective photoreceptor inner/outer segment junction (IS/OS) can be used as a pattern of photoreceptors integrity in SD-OCT images. In areas where the IS/OS junction is absent on SD-OCT, no cones are visualized in registered AO images. Regions where intact IS/OS are present correlate with areas where cones are unambiguously visualized using the AO camera. Furthermore, distinct transition zones between intact and absent IS/OS are correlated with AO images. Endly, the subfoveal area is coneless on AO images when there is a hyporeflective hole on SD-OCT; if the IS/OS junction is irregular, the normal cone mosaic is disturbed.

Conclusions: SD-OCT analysis of eyes with macular telangiectasia (MacTel) demonstrates regions of apparent photoreceptor disruption which are highly correlated with regions where cones are not visualized using AO. This study shows the synergistic nature of these high-resolution retinal imaging systems.

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Comparison of Anterior Segment Time Domain Optical Coherence Tomography and High Frequency Ultrasound Biomicroscopy for the Anterior Segment


Purpose: To compare anterior segment parameters using quantitative imaging by anterior segment time domain optical coherence tomography (TD-OCT) and high frequency ultrasound biomicroscopy (HF-UBM).

Methods: At Department of Ophthalmology at Bari University 63 eyes of 39 subjects had anterior segment evaluation by TD-OCT (Stratus OCT, ver. 6, CarlZeiss Inc) and HF-UBM (OTI-Scan HF35-50). Central corneal thickness (CCT), anterior chamber depth (ACD) (measured from the central corneal endothelium to the anterior lens capsule), and the peripheral iridocorneal angles (temporal and nasal) were assessed and compared.

Results: There was an excellent correlation between TD-OCT and HF-UBM measurements for the nasal angle (r=0.81, P<.0001), temporal angle (r=0.84, P<.0001), ACD (r=0.95, P<.0001), and CCT (r=0.94, P<.0001). There was no significant difference (paired t test) between the mean ACD, CCT, and angle parameters measured by TD-OCT or HF-UBM. The TM-OCT images showed sharper definition of the scleral spur than the HF-UBM images.

Conclusions: Anterior segment TD-OCT and HF-UBM can both be used for anterior segment measurements with comparable results.

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4363 - A196
Birefringence of the Peripapillary Retinal Nerve Fibre Layer
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Purpose: To measure the birefringence of the peripapillary retinal nerve fiber layer (RNFL) in normal subjects and glaucoma patients using the results of scanning laser polarimetry (SLP) and spectral domain optical coherence tomography (SOCT). Using an ex vivo polarized sensitive OCT, it was shown that birefringence is reduced in glaucoma before the RNFL thickness is reduced [Gottlinger et al ARVO 2009].

Methods: Birefringence B of the RNFL can be calculated from phase retardation P measured by SLP and thickness T measured by SOCT: B = P/T. In 185 subjects (77 normal, 49 ocular hypertensive, 35 preperimetric, and 24 perimetric glaucoma patients) retardation maps (GDxVCC) and RNFL thickness at circular B-scans (diameter 3.4 mm, 768 A-scans) around the optic nerve head (ONH) (Spectralis HRA&OCT, Heidelberg Engineering) were measured. For all subjects the GDxVCC typical scan consisted of 250 A-scans with a scan rate of 2.8. Raw data from both instruments were exported for further analysis. Using SLP-IR images, phase retardation maps were aligned to SOCT-IR images (Image, Turborex). In the aligned images, phase retardation values were extracted from the retardation maps at exactly the position of the circular OCT B-scans. Relative birefringence was calculated for 768 positions around the ONH, averaged to 32 sectors (11.25° each) and to peripapillary total mean. Positions with retinal vessels were excluded from the calculation. As the calibration factor for the phase retardation maps was unknown, only relative birefringence could be calculated.

Results: In normal subjects, relative birefringence showed a variation around the ONH with relative maxima superior and inferior and relative minima temporal and nasal to the ONH, as shown previously [Huang et al 2004]. In our study the birefringence increases in glaucoma patients. Assuming a mean relative birefringence of 1 in normal subjects, the mean relative birefrigence (± SD) for the patient groups is (1.04 ± 0.13) in ocular hypertensive, (1.07 ± 0.10) in preperimetric, and (1.40 ± 0.14) in preperimetric glaucoma patients.

Conclusions: Using a combination of commercially available SLP and SOCT, in our study the characteristics of described reduced birefringence in glaucoma could not be confirmed. This might be due to artifacts of the GDxVCC phase retardation results caused by phase retardation introduced by the sclera and/or not completely confirmed. This might be due to artifacts of the GDxVCC phase retardation results caused by phase retardation introduced by the sclera and/or not completely confirmed. Using a combination of commercially available SLP and SOCT, in our study the characteristics of described reduced birefringence in glaucoma could not be confirmed. This might be due to artifacts of the GDxVCC phase retardation results caused by phase retardation introduced by the sclera and/or not completely confirmed.
4365 - A198

Prenatal Ultrasonographic Detection of Ophthalmic Diseases

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Purpose: To describe the utility of prenatal ultrasonography as a tool in early detection of fetal ocular abnormalities.

Methods: A non-comparative, retrospective review of four neonates with abnormal intracranial sonograms suggestive of ocular or orbital pathology.

Results: In all four patients, echographic findings suggestive of ophthalmic pathology were detected but without diagnostic certainty. A large heterogeneous orbital mass detected in a fetus at 34 weeks of gestation was revealed to be infantile fibrosarcoma on postnatal excision of the tumor. A retrolental fibrovascular stalk detected at 23 weeks gestation that failed to regress on serial ultrasonic ultrasound was confirmed on ophthalmic exam as persistent hyperplastic primary vitreous/persistent fetal vasculature. An ultrasound at 13 weeks revealing hypoplastic eyes and later malformed extremities was confirmed on autopsy to be Fraser syndrome. Glove size asymmetry noted by prenatal ultrasound at 23 weeks gestation was found on postnatal sonograms to be microphthalmia with coloboma and retrolubar cyst.

Conclusions: High resolution antenatal ultrasonography permits early detection of fetal ophthalmic abnormalities but does not yield definitive diagnoses. These early findings could influence the obstetrician’s approach to delivery and serve to mobilize pediatricians and ophthalmologists to provide timely intervention upon delivery.

CR: E.H. Leung, None; A.M. Berrocal, None.
Support: None.

4366 - A199

Retinal Screening in Pediatric Patients


Purpose: Retinal screening has proven effective in reducing or preventing visual loss from sight-threatening posterior segment eye disease. Diagnostically conclusive retinal imaging relays to a considerable extent upon the adequate positioning of the patient. It is desirable to detect posterior segment pathologies at an early stage of life. The objective is to photograph anatomic structures of the posterior eye segment with enough detail to make diagnostic decisions.

Methods: A total of 528 children were examined. Three different non-myrdaticfundus cameras (Nidek, HRC, Iview) were compared with regard to their practicality and reliability of image analysis.

Results: The duration of examination per subject ranged from 3.8 minutes to 7.5 minutes. Hand-held devices were unexpectedly hard to handle, so these measurements were discontinued. A chin rest was used where possible.

Conclusions: In pediatric patients, fast image acquisition is often necessary. Therefore, non-myrdaticfundus imaging can be used for suitable children. The non-flash camera was tolerated better in general. To optimize adequate patient positioning, support elements as in self tonometry are conceivable.

CR: Y. Hauessler-Sinangin, None; H. Swyter, None; M. Koss, None; P. Singh, None; S. Scholtz, None; F. Koch, None.
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4367 - A201

The Optos Imaging System as an Ophthalmoscope: Fundus Assessment of Problem Eyes Where Conventional Examination Techniques Fail


Purpose: To investigate the utility of Optos P200 (Dunfermline, Scotland) imaging to evaluate the fundi of patient eyes where tiny pupils or media opacities made conventional ophthalmoscopy and biomicroscopy impossible to perform.

Methods: In a 12-month retrospective case analysis, we reviewed 8 patients [12 eyes] with extremely limited or no views to the posterior segment due to very small pupil diameters, dense nuclear cataracts, extensive posterior synechiae, or other media opacities, alone or in combination. These eyes were unable to be satisfactorily examined by standard slit lamp biomicroscopy using any standard contact or hand-held lenses lenses, or by indirect ophthalmoscopy. The examinations were attempted by two retina specialists, each with more than 25 years experience as subspecialists. The patients were then sent for imaging using the Optos P200 device and B-scan ultrasonography if no fundus images could be obtained.

Results: Of the 12 eyes that were imaged in our study, the cause of the poor view to the posterior pole included extensive posterior synechiae (3 eyes), anterior or posterior lenticulass capsule fibrosis (3 eyes), pupils less than 3mm in diameter (5 eyes), and dense nuclear sclerotic cataract (3 eyes). Imaging quality was deemed adequate to make a clinically relevant assessment in all cases except 3 eyes, two of which had pupils less than 2 mm in diameter, and one that had dense vitritis. In all, Optos P200 images were clinically useful and allowed appropriate diagnoses to be made in 9/12 cases studied. Diagnoses included uveitis/parasplasitits, proliferative diabetic retinopathy, vascularproliferative tumor, necrotizing retinitis, Vogt-Koyanagi-Harada Syndrome, and fungal endophthalmitis.

Conclusion: In many eyes with tiny pupils or media opacities, retinal examinations using the Optos P200 ultrawidefield imaging system can often be conducted where conventional examination techniques yield virtually no view of the retina. Such eyes would typically be deemed impossible to examine with light, and would be assessed with B-scan ultrasonography only. In this setting, the Optos P200 system can be considered a specialized ophthalmoscope capable of documenting the retina findings very quickly.

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4368 - A201

Retinal Imaging by Automatic Composition of Slit Lamp Images

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Purpose: Slit lamp composites can serve as a powerful retinal imaging modality; however, the technology has not yet been developed to its full potential. A previously proposed algorithm attempts to create the mosaic by means of a frame to frame alignment, minimizing the squared sum of differences (SSD) between pixel values. As this approach appears to be highly susceptible to noise, we suggest an image enhancement step before image alignment in order make it more suitable for retinal images. Furthermore, small alignment errors lead to a “drifting” of the stitched sequence over time due to the high temporal locality of the frame to frame matching. This is particularly problematic in cases where the slit lamp is moved back and forth. We propose a multi-frame alignment algorithm to overcome this limitation.

Methods: Image sequences have been acquired using a LSI 532s slit lamp (Carl Zeiss Meditec, Jena, Germany). In order to automatically extract the actual slit lamp image from the video frame, the left and right edges are detected by means of a Hough transform run directly on the gradient image. The video image is then cropped accordingly. Reflections are eliminated by masking very bright pixels. Subsequently, the extracted images are filtered using a laplacian of gaussian kernel. Because of their specific anatomy, blood vessels are considerably emphasized by an edge detection kernel. The frames are then aligned by minimizing the SSD between the filtered images. Currently, a pure translational registration is established. During the composite construction process, the system keeps a list of all frames and their orientations with respect to the global coordinate system. Instead of aligning the current frame with the last one only, the algorithm selects N previously processed frames and aligns the current frame with the N reference frames simultaneously. The references are chosen based on an overlap criterion. After registration the mosaic is constructed by blending all frames together using an appropriate image fusion algorithm. Currently, this is achieved using laplacian pyramids.

Results: Experiments on test sequences demonstrated high accuracy under visual inspection. The drifting problem was successfully eliminated.

Conclusions: The suggested multi-frame alignment algorithm substantially advances previous work and thereby increases the potential of automatic slit lamp compositing.

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Comparison of Fundus Autofluorescence Between Fundus Camera (Topcon) and Confocal Scanning Laser Ophthalmoscope (HRA) in Various Pathologies

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**Purpose:** To investigate the differences between the Fundus Camera (Topcon TRC-50X) and Confocal Scanning Laser Ophthalmoscope (Heidelberg retina angiogram (HRA)) on the fundus autofluorescence (FAF) imaging (resolution and FAF characteristics).

**Methods:** Eighty-nine eyes of 46 patients with various retinal diseases underwent FAF imaging with HRA (488nm exciter / 500nm barrier filter) before fluorescein angiography (FA) and Topcon imaging (580nm exciter / 460nm barrier filter) before and after FFA. The quality of the FAF images was estimated, compared for their resolution and analysed for the influence of fixation stability and cataracts. Hypo- and hyper-FAF behaviour was analysed for the healthy disc, healthy fovea, and a variety of pathological features.

**Results:** HRA images were found to be of superior quality in 18 eyes, while Topcon images were estimated superior in 21 eyes. No difference was found in 50 eyes. Both poor fixation (p=0.009) and more advanced cataract (p=0.013) were found to strongly increase the likelihood of better image quality by Topcon. Images acquired by Topcon before and after FFA were identical (100%). The healthy disc was usually dark on HRA (71%), but showed mild autofluorescence on Topcon (88%). The healthy fovea showed in 100% Hypo-FAF on HRA, while Topcon showed in 52% Iso-FAF, in 43% mild Hypo-FAF, and in 5% Hypo-FAF as on HRA. No difference of FAF was found for geographic atrophy, pigment changes, and drusen, although Topcon images were often more detailed. Hyper-FAF due to exudation showed better on HRA. Pigment epithelium detachment showed identical FAF behaviour on the border, but reduced FAF with Topcon in the center. Cystic edema was visible only on HRA in a petaloid pattern. Hard-exsudates caused Hypo-FAF only on HRA, hardly visible on Topcon. Baclelgon phenomenon by blood however was identical.

**Conclusions:** The filter set of Topcon and the single image acquisition appear to be an advantage for patients with cataract or poor fixation. Preceding FFA does not alter the Topcon FAF image. Regarding the FAF behaviour, there are differences between the two systems which need to be taken into account when interpreting the images.

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Arteriovenous Crossings Are More Sensitive Than Microalbuminuria for the Detection of Early Vascular Changes in Arterial Hypertension

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Purpose: Arterial hypertension (AHT) is an important cardiovascular risk factor. The eye is the only organ where vascular changes due to AHT can be examined directly. Microalbuminuria has been introduced as a marker of vascular changes in the kidney. We compared these two markers in a working population.

Methods: 526 voluntary members of the staff of the University Hospital Erlangen (mean age 47±8 years, 45 male, 181 female) underwent a thorough examination with extensive history, measurement of blood pressure (BP) and laboratory testing of blood and urinary samples. Fundus photographs were examined by an experienced ophthalmologist.

Results: 36 participants had a history of AHT. At the time of examination, 42 participants had an elevated systolic BP (>140 mmHg). Arteriovenous crossings were present in 37 participants. They were found in 20% of participants with elevated systolic BP at the time of examination and in 5% of the other participants (p=0.005). Elevated urinary albumine to creatinine ratios (UACR) were measured in 22 participants. 10% of participants with elevated systolic BP and 9% of those with normal systolic BP had an elevated UACR (p=0.94, not significant).

Conclusions: Arteriovenous crossings were found in 14% of participants with a history of AHT and in 6% of the other participants (p=0.095, not significant). 11% of individuals with a history of AHT and 9% of the others had elevated UACR (p=0.08, not significant).

Support: None.


CR: C.R. Huchzermeyer, None; R.E. Schmieder, None; K. Schmid, None; G. Michelson, None.

Supported by: New England Retina Foundation.

Anatomic Outcomes Using Spectral Domain OCT Following Treatment for Exudative Age Related Macular Degeneration

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Purpose: To assess anatomic differences in the photoreceptor layer and subretinal space using spectral domain OCT between patients undergoing monotherapy with ranibizumab versus combination therapy with verteporfin (reduced fluence PDT) plus ranibizumab.

Methods: This was a prospective study of 15 eyes with choroidal neovascularization secondary to age-related macular degeneration undergoing either three monthly ranibizumab injections (Group M) or reduced-fluence PDT plus preranibizumab. Spectral domain OCT was performed at 1 day, 1 week, weeks 2, 4, 8 and 12 weeks. Anatomic features were assessed by a masked reader at each of these time points.

Results: At baseline, photoreceptor inner segment/out segment junction (IS/OS) was visible in 40% of patients (Group C: 38%, Group M: 43%) and at final visit the IS/OS junction was visible in 40% overall but higher in the combination group (Group C: 50%, Group M: 29%; p=0.05). 50% of eyes in the combination group had an increase in subretinal fluid or intraretinal fluid at day 1 versus 0% in the monotherapy group (p=0.05). At week 1, 25% of eyes in Group C had subretinal or intraretinal fluid which resolved fully in each case by week 4. Average baseline visual acuity was 20/200 with a final visual acuity of 20/150 at three months. The average baseline vision of patients in Group C was 20/300 with a final vision of 20/200. The baseline vision of patients in Group M was 20/150 with a vision of 20/100 at the three month time point average. Average number of ranibizumab injections in the combination group was 1.125 (range 1-2). All patients in the monotherapy group received three injections as scheduled.

Conclusions: Photoreceptor structure assessed by spectral domain OCT at 12 weeks was not significantly different between the monotherapy and combination group. Reduced-fluence PDT may decrease possible deleterious effects to photoreceptors seen in the past. Combination therapy with Verteporfin plus ranibizumab may be associated with transient increase in subretinal and intraretinal fluid within 1 week therapy that resolves within 3-4 weeks.

CR: J. Jonisch, None; K. Blinder, None; G.K. Shah, None; A.C. Walsh, None.

Support: None.

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4377 - A210
A Comparison of Optical Coherence Tomography With Fundus Fluorescein Angiography for Monitoring Recurrence of Choroidal Neovascularization During Treatment of Exudative Age-Related Macular Degeneration
Purpose: The purpose of this trial was to compare the accuracy of optical coherence tomography (OCT) with fundus fluorescein angiography (FFA) in detecting active leakage from choroidal neovascularization (CNV) in age-related macular degeneration (AMD).
Methods: This was a post-hoc analysis of data from a prospective trial in which 19 patients with exudative AMD and treated with photodynamic therapy (PDT) combined with lucentis intravitreal injections had 6 weekly OCT and FFA for 12 months. A retinal specialist masked to any additional clinical information analysed the OCT and FFA images independently from each other to assess for signs of active disease. OCT images were said to be positive for active disease if there was subretinal or intraretinal fluid, thickening greater than 300 μm or an increase of greater than 50 μm from the previous scan. FFA was considered positive for signs of active CNV if there was fluorescein leakage and/or an increase in CNV size.
Results: Of the 19 patients that completed the study, 9 were male, 10 were female. 9 had predominantly classic  and 5 had minimally classic or occult CNV. All patients received one session of PDT at the beginning of the trial and an average of 5.4 injections of Lucentis over the 12 month follow-up. There were 160 assessments in which good quality OCT and FFA images were obtained on the same day. In 32 of these assessments there were signs of active CNV. 103 (78%) had OCT and 121 (92%) had FFA evidence of active leakage (p<0.005).
Conclusions: OCT alone is likely to miss 22% of active CNV recurrence compared with FFA combined with OCT when monitoring patients being treated for exudative AMD.
CR: G. Raymond, Novartis, F.T.L. Gray, Novartis, F.S.N. Sinkar, None; J.S. Muecke, None; J.S. Gilhotra, Novartis, F. Support: None CT: www.anzctr.org.au, 00082363

4378 - A211
Optical Coherence Tomography Pattern of Fluid Recurrence in AMD Patients Treated With Ranibizumab
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Purpose: To evaluate OCT patterns of retinal fluid presenting as sign of leakage recurrence following 3 injection of ranibizumab in patients with AMD.
Methods: 23 eyes of 23 patients (15 female, 8 male, mean age 75 years, 5 predominantly classic, 3 minimally classic and 15 occult NVM) received 3 consecutive monthly intravitreal injection of ranibizumab 0.5 mg. In the case of visual acuity (VA) loss of at least 5 letters with OCT evidence of retinal fluid or fluorescein angiography (FA) evidence of leakage patients were re-injected. Patients underwent ETDRS VA, FA and OCT (Spectralis, Heidelberg) examination at baseline and at monthly interval for 6 months. Four patterns of retinal fluid were identified: diffuse retinal edema (DE), subretinal fluid (SRF), intraretinal cysts (RC) and sub-RPE fluid (SRPF). Horizontal and vertical scans at the fovea and in correspondence of FA leakage, star-shaped and volume scans were acquired by means of OCT.
Results: At baseline 18 eyes showed RC, 15 DE, 17 SRF and 19 eye SRPF. At month 3 (one month post third injection) only 4 eyes showed residual RC and SRF; stable VA, that declined at month 4 (1 eye, 4.3%) and month 5 (3 eyes, 13%) and were re-injected. At month 4 three eyes (13%) showed SR and three (13%) RC or DE; at month 5 five eyes (21.7%) showed SRF and three (13.9%) SRF and RC and at months 5 and 6, (7.7%) showed SRF and DE or RC and two (6.6%) SRF. At month 6 two eyes (8.4%) with SRF at month 3 and one (4.3%) with SR at month 5 showed an increase of SR and developed DE and RC and A VA decrease >5 letters and needed a retreatment. SRP showed increased in all 19 eyes, but disappeared in only 10. At months 15 eyes (75.1%) showed a fluid-free retina and in total 10 eyes (43.4%) were re-injected during follow up. In 5 eyes (21.7%) during follow up SRF recurrence were detected before at CNV boundaries and subsequently fluid increased at boundaries and in macular region causing VA decrease.
Conclusions: Subretinal fluid at the CNV boundaries was the early and sole sign of recurrent retinal fluid in 21.7%. Interesting small SR fluid appearance showing subtle disease activity was detectable at the outer edge of 21.7% CNVM and temporarily preceding macular RC and DE appearance. This early sign of recurrence could be a novel sign to value disease progression and reinjection decision.
CR: L. Migliavacca, None; L. Rossetti, None; S. De Cilla, None; N. Orzalesi, None. Support: None

4379 - A212
Predictors for Visual Outcome Prior to Anti-VEGF Therapy in Vascular Occlusive Diseases
L.E. Wolf-Schnurrbusch, C. Franne, S.P. Rothenbuchler, S. Wolf, Universitätsklinik für Augenheilkunde, University of Bern, Bern, Switzerland; Universitätsklinik für Augenheilkunde, Bern Photographic Reading Center, Bern, Switzerland.
Purpose: With high resolution SD-OCT it’s possible to distinguish the outer retina layer with the external limiting membrane (ELM), the inner/outer segment junction, and the RPE very well. Purpose of our study was to identify features as predictors for favorable visual outcome prior to Anti-VEGF therapy in patients with clinical significant macular edema (CSME) due to Central Retinal Vein Occlusion (CRVO) and Branch Retinal Vein Occlusion (BRVO).
Methods: Patients with CSME due to CRVO and BRVO were examined at BL (best corrected visual acuity (BCVA), biomicroscopy, fluorescein angiography and Spectralis OCT). If both eyes were eligible, one was randomly chosen as the study eye. Patients with intact ELM in the SL-OCT images were included into group 1, whereas patients with disturbances in the ELM were included into group 2. In addition size and configuration of cystoid spaces were assessed. BCVA was analysed 4 weeks after the initial intravitreal anti-VEGF therapy in respect to the layer integrity and to findings like the configuration, size and localisation of the cystoid spaces.
Results: BRVO (n= 32): We distributed 28 eyes with BRVO to group 1 and 24 eyes to group 2. On average patients with intact ELM experienced a gain in BCVA of 8±3 letters, but patients with disturbances in ELM gained only 2±3 letters. CRVO (n= 32): We distribute 17 eyes with CRVO to group 1 and 15 eyes to group 2. On average the patients with the intact ELM experienced a visual gain of 7±4 letters, but patients with disturbances in ELM gained only 2±1 letters. The size of cystoid spaces was not related to BCVA, but there are differences regarding the configuration of those cystoid spaces.
Conclusions: Analysis of SD-OCT provides predictors for BCVA in patients with vascular occlusive diseases for a better selection prior to therapy.
CR: L.E. Wolf-Schnurrbusch, None; C. Franne, None; S.P. Rothenbuchler, None; S. Wolf, None. Support: None CT: www.clinicaltrials.gov, NCT00564291

4380 - A213
Objective Assessment of Visual Function in Patients Receiving Anti-Angiogenic Treatment for Wet Macular Degeneration: A Longitudinal Study
Purpose: To use functional MRI as an objective, fixation-independent measure of topographic visual function and assess cortical responsivity in patients undergoing anti-angiogenic treatment for wet age-related macular degeneration (AMD).
Methods: Patients with bilateral neovascular AMD were scanned using functional MRI before and at regular intervals while undergoing treatment with intravitreal anti-angiogenic injections (primarily LucentisTM). Blood oxygenation level-dependent (BOLD) signals were measured in the brain while patients viewed a visual stimulus consisting of a full-field flickering (6 Hz) white light alternating with a uniform gray background (18 sec on, 18 sec off). Topographic distribution and magnitude of activation in visual cortex were compared within individuals longitudinally throughout the treatment period (up to 1 year) and with control patients not currently undergoing treatment.
Results: The area of visual cortex activated increased significantly after the first treatment to include more posterior cortex that normally receives inputs from lesioned parts of the retina. Subsequent treatments yielded no significant further increase in activation area; however, activation magnitude continued to increase. Untreated patients showed a consistent lack of significant response in the cortex representing retinal lesions.
Conclusions: Retinal treatments may improve vision but also result in a concomitant improvement in fixation stability. Current clinical behavioural measures (e.g. acuity, perimetry) are largely dependent on fixation stability, and therefore cannot separate improvements of visual function from fixation improvements. Functional MRI, which provides an objective and sensitive measure of visual function independent of fixation, reveals a significant increase in visual cortical responses in wet AMD patients following treatment with anti-angiogenic injections. Despite recent evidence that visual cortex degenerates subsequent to retinal lesions, our results indicate that it remains responsive as its inputs are restored.
CR: H.A. Baseler, None; A. Gouws, None; M. Crossland, None; C. Leung, None; A. Tufail, None; G.S. Rubin, None; A.B. Molord, None. Support: Medical Research Council, UK
Spectral-Domain Optical Coherence Tomography and Fundus Autofluorescence in Patients With Pattern Dystrophy


Purpose: Pattern macular dystrophy is a group of rare inherited retinal diseases in which there is abnormal accumulation of lipofuscin-like material at the level of retinal pigment epithelium (RPE). There is a wide spectrum of macular findings described in literature ranging from flecks to a more typical butterfly-shaped lesion. There are isolated reports in literature describing histopathological findings in such patients. The advent of spectral-domain optical coherence tomodraphy (SD-OCT) has enhanced our understanding of retinal dystrophies. The present study describes the OCT and fundus autofluorescence (FAF) features in patients with pattern dystrophy to possibly provide more insight into the pathophysiology of this disease.

Methods: Ten eyes of five patients clinically diagnosed with pattern macular dystrophy were included in the study. Their ages ranged from 43 to 81 years and there were three men and two women in the cohort. All patients underwent a complete ophthalmological examination including Snellen visual acuity and color vision testing. Color fundus photography, SD-OCT, FAF and infrared videography were performed on all patients. Fluorescein angiography, microperimetry (MP-1) and electrophysiological testing were performed, wherever appropriate.

Results: The Snellen visual acuity in the five patients with pattern dystrophy ranged from 20/20 to 20/70. The clinical features ranged from yellowish flecks in the macular area to pigmented lesions in all patients with some showing patches of atrophy. SD-OCT showed localized areas of RPE changes corresponding to the yellowish lesions with an intact photoreceptor layer. There were areas of hyperautofluorescence on FAF corresponding to areas of lipofuscin-like deposits and hypoautofluorescence in areas of RPE atrophy. Retinal function, as measured by visual acuity and MP-1 correlated well with the presence of normal photoreceptor layer.

Discussion: The characteristic changes in patients with pattern dystrophy, as defined by the evolving technology of SD-OCT and FAF and the retinal functional correlation helps us to better understand the pathophysiological mechanisms involved in the disease. Future studies evaluating long-term follow-up of these patients will help to better define the course of the disease.

CR: R. Cappelli, None; K.V. Chalam, None; S. Grover, None.
Support: None

Spectral-Domain Optical Coherence Tomography and Fundus Autofluorescence in Patients With Pattern Dystrophy


Purpose: To report a novel association of reticular pseudodrusen and adult vitelliform detachment and evaluate the clinical findings of these patients using multi-modal imaging.

Methods: A retrospective review was done of five cases of adult vitelliform detachment secondary to reticular pseudodrusen. Clinical examination, color and red-free fundus photography, fundus autofluorescence (FAF) and spectral domain optical coherence tomography (SD-OCT) data were retrospectively reviewed for the five patients. Reticular pseudodrusen were observed to be subretinal drusenoid deposits above the level of the retinal pigment epithelium (RPE) with a predilection for the superior paramacular. Adult vitelliform detachments were hyperautofluorescent accumulations of vitelliform material in the subretinal space between the IS/OS junction and RPE. The time interval for follow-up examination varied from three to twenty one months.

Results: Five patients with this distinct subretinal drusenoid pattern were found to have an accumulation of vitelliform material in the subretinal space. All five patients maintained stable visual acuity over the follow-up interval. These patients all had preservation of the function of the fovea and outer photoreceptor segments (IS/OS) and external limiting membrane (ELM). There was no associated outer nuclear layer (ONL) thinning observed in these patients.

Conclusions: We utilized multi-modal imaging to document the novel finding of adult vitelliform detachment associated with subretinal drusenoid deposits commonly referred to as reticular pseudodrusen in five patients. These subretinal drusenoid deposits may be mistaken for basal laminar cuticular drusen but can be easily distinguished with multi-modal imaging. Multi-modal imaging served as an essential adjunct to clinical examination in the diagnosis and follow-up of patients with adult vitelliform detachment and reticular pseudodrusen. All patients with this new finding maintained stable visual outcomes over follow up period without any therapeutic intervention.

CR: K. Laud, None; S.A. Zweifel, None; R.F. Spaid, None.
Support: None

Therapeutic Efficacy Using Retinal Pigment Epithelium Elevation Maps in Retinal Angiomatous Proliferation

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Purpose: To investigate the therapeutic efficacy of combined anti-vascular endothelial growth factor and photodynamic therapy (PDT) in retinal angiomatous proliferation (RAP) using a retinal pigment epithelium (RPE) elevation map (REM) with Spectral Domain Optical Coherence Tomography (OCT).

Methods: Subjects comprised 4 eyes in 4 patients (2 men, 2 women; mean age, 81.3 years) with stage 2 RAP examined in the Department of Ophthalmology at Osaka University in whom REM measurement was possible. All subjects have received prior treatment for the condition. Combined intravitreal bevacizumab and PDT were administered to patients 1 and 2, while combined intravitreal ranibizumab and PDT were administered to patients 3 and 4. Visual acuity (logMAR) assessment, fluorescein and indocyanine green angiography (FA and IA) and OCT were performed preoperatively and 3 months postoperatively. REM was generated using an RTVue® (Optovue Inc, Fremont, CA) MMS protocol and the mean and standard deviation of RPE elevation height (μm) were investigated. If automatic analysis of the REM was insufficient, it was manually adjusted.

Results: Mean visual acuity improved from 0.52 preoperatively to 0.27 postoperatively. Postoperatively, neovascularization disappeared on IA and leakage decreased in FA, and there was a marked reduction in macular edema and RPE detachment on OCT. Decrease of mean and standard deviation of RPE elevation height: from 19.2 to 0.9 and from 38.0 to 2.7 in patient 1, from 168.3 to 16.5 and from 122.5 to 26.5 in patient 2, from 9.3 to 2.3 and from 26.5 to 5.1 in patient 3 from 11.3 to 0.1 and from 35.4 to 2.6 in patient 4, respectively.

Conclusions: REM enabled to evaluate RPE elevation height objectively, suggesting the usefulness of REM in investigating therapeutic efficacy in RAP.

CR: H. Iwami, None; M. Yamamoto, None; T. Kohno, None; M. Kaida, None; N. Miki, None; M. Horiyashiki, None; A. Hamaguchi, None; K. Shiraki, None.
Support: None
4385 - A218
Bilateral Papillomacular Folds in Nanophthalmos: Advanced Retinal Imaging
Ophthalmology, New York Eye and Ear Infirmary, New York, NY.

Purpose: To report the results of the retinal imaging of a rare case of bilateral partial-thickness papillomacular retinal folds in pediatric nanophthalmos.

Methods: A patient referred for nanophthalmos underwent advanced retinal imaging, including fundus exam, color fundus photography (CFP), scanning laser ophthalmoscopy and spectral-domain optical coherence tomography (SLO/OCT), non-contrast angiography (NCA), autofluorescence (AF) and perimacular retinal blood flow (RBF) velocity using the retinal functional imager (RFI).

Results: Imaging report of a 9-year-old female with axial lengths of 18.2mm OD and 18.3mm OS, best-corrected visual acuity (VA) of 20/30 OD and 20/50 OS and refractive error of +14 OD and +15 OS. Fundus exam revealed bilateral papillomacular retinal folds and absent foveal light reflexes. CFP showed crowded optic discs and a normal macular pigment distribution. SLO/OCT revealed bilateral partial-thickness retinal folds and bilateral absence of the foveal depression. NCA showed a rudimentary foveal avascular zone (FAZ) OS and an unusually small FAZ OD. AF and RBF velocity were normal bilaterally.

Conclusions: This is the first report of comprehensive imaging of bilateral papillomacular retinal folds in nanophthalmos. OCT revealed that the retinal folds are in fact partial-thickness and exclude the inner segment/outer segment junction. NCA confirmed previous reports of a rudimentary FAZ in nanophthalmos that, along with an absent foveal depression, may be the main limitation to obtaining an optimal VA. In contrast to previous reports, the macula is not hyperpigmented. This report also highlights the utility of NCA in unusual situations in which the patient is unable to get FA due to fear of allergic complications.

CR: A. Hong, None; L. Spielberg, None; S. Rao, None; J. Panarelli, None; K. Mukkamala, None; G. Landa, None; R. Rosen, OPKO, C; A. Ponce, None.
Support: None
**Assessing Reproducibility and Variation Between Time-Domain versus Spectral-Domain Optical Coherence Tomography in Patients With Diabetic Macular Edema**


**Purpose:** To evaluate retinal thickness, agreement in macular thickness measurement and the intra-class reproducibility of images across one time domain (TD) and two spectral domain (SD) optical coherence tomography (OCT) machines, in patients with diabetic macular edema (DME).

**Methods:** 61 eyes with DME were scanned with Stratus™ (TD; Carl Zeiss Meditec, Dublin, CA) and Spectralis™ (SD) OCT devices. The same operator performed the scans on all three OCT devices for a given patient. Macular thickness measurements of 9 standard subfields were obtained and analyzed. Agreement in macular thickness across two eyes was assessed via Bland-Altman (BA) plots. Intra-class reproducibility was evaluated by Intra-class Correlation Coefficient (ICC).

**Results:** Scans for Cirrus SD-OCT and Spectralis SD-OCT showed higher macular thickness values in all subfields compared to Stratus TD-OCT. Mean central 1mm foveal thickness in μm (± Standard Deviation) was 282.80 (±99.88), 320.62 (±106.91) and 336.44 (±111.44) for Stratus TM, Cirrus™ and Spectralis™ respectively. The BA plots gave a mean difference for the central subfield, in μm (% Confidence Interval (CI)) of 37.8 (129.3, -53.6) ± 26.8, -134) and 15.8 (47.5, -79%) for Stratus vs. Cirrus, Cirrus vs. Spectralis and Cirrus vs. Spectralis respectively. High intra-class reproducibility was seen among all three systems: StratusTM: ICC of 0.99 (95% CI; 0.97, 0.99); Cirrus™: ICC of 0.98 (95% CI; 0.96, 0.99); Spectralis™: ICC of 0.99 (95% CI; 0.99, 0.99).

**Conclusions:** All three OCT machines showed different macular thickness measurements. Low agreement in macular thickness measurements among machines makes it difficult to use them interchangeably in patients with DME. However, based on the high ICCs, we conclude that there is excellent reproducibility in thickness values and all three OCT machines are reliable in measuring macular thickness in patients with DME.

**CR:** A.A. Khwaaja, None; E.H. Naimi, None; R. Channa, None; M. Ibrahim, None; M. Shulman, None; Z. Rentiya, None; J. Talmud, None; D.V. Du, Heidelberg Inc., F; Q.D. Nguyen. Heidelberg Inc., F.

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**Sensitivity and Specificity of Time-Domain versus Spectral-Domain Optical Coherence Tomography in the Diagnosis of Diabetic Macular Edema**

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**Purpose:** To evaluate the sensitivity and specificity of measurements of central macular thickness (CMT) thickness in diabetic macular edema using Stratus time-domain and Cirrus spectral-domain optical coherence tomography (OCT; Carl Zeiss Meditec, Dublin, CA).

**Design:** Evaluation of diagnostic technology.

**Methods:** 36 eyes from 19 patients with clinically significant diabetic macular edema (DME) were included. All participants underwent Cirrus HD-OCT and Stratus OCT examinations on the same day with a maximum of 3 consecutive scans per patient on each machine. The sensitivity/specificity of retinal thickness measurements was calculated from published normative data. Agreement was calculated using Bland-Altman method. Interclass and interobserver repeatability were calculated for each device. The receiver operating characteristic curves (ROC) and areas under the ROC were plotted.

**Results:** The mean difference between the Cirrus HD-OCT and Stratus OCT in the central foveal zone was 49.9um. Bland-Altman analysis confirmed that the retinal thickness measurements had poor agreement. Intrasessional repeatability studies indicate the coefficient of variation being 0.9833 and 0.833 using Stratus and the Cirrus HD-OCT respectively. The areas under the ROC for retinal thickness measurements were 0.88 using Cirrus HD-OCT and 0.94 with Stratus.

**Conclusions:** In patients with DME, the Cirrus HD-OCT gives a higher reading than Stratus OCT with poor agreement between the devices in most regions within the nine subfield zones. The sensitivity and specificity of the Stratus OCT was comparable to the Cirrus.

**CR:** N. Patel, None; H.R. Chowdury, None; R. Leung, None; S. Sivaprasad, None.

Support: None
Comparison of Macula and RNFL Thickness Measurements Between Cirrus Model 400 and Cirrus Model 4000 HD-OCT Instruments

T. Callan, M. Durbin, A. Clinical Affairs, Research and Development, Carl Zeiss Meditec Inc, Dublin, CA.

Purpose: To compare macula and retinal nerve fiber layer (RNFL) thickness measurements from two models of the Cirrus HD-OCT. The original Cirrus HD-OCT (Model 4000) uses a line-scanning ophthalmoscope (LSO) to generate an image of the fundus for alignment and reference. The newer Model 400 does not use an LSO but utilizes the OCT scanning beam to generate the fundus image in addition to creating the B-scan OCT images.

Methods: The same Cirrus HD-OCT was used for all measurements. Changing the software allowed the study to be conducted utilizing the LSO (as a Model 4000) and without the LSO (as a Model 400). Sixteen volunteer subjects were scanned twice with the Macula 512 x 128 Cube scan (right eye) and twice with the Optic Nerve 200 x 200 Cube scan (left eye) on the same day.

Results: All measured differences were less than one micron. No statistically significant differences were found by paired t-test analysis (P < 0.05) for any of the compared macula or RNFL thickness measurements. The distribution of differences and the repeatability of each system were consistent with the previously reported repeatability of Cirrus. See Table 1 and Table 2.

Conclusions: The new Cirrus HD-OCT Model 400 measures macula and RNFL thicknesses on average within 1 micron of the original Cirrus HD-OCT Model 4000.

Retina Nerve Fiber Layer (RNFL) Thickness Measurement Reproducibility Comparison Across Three Spectral Domain Optical Coherence Tomography (SD-OCT) Devices With Systematic Bias Correction


Purpose: To compare the RNFL measurement reproducibility across three SD-OCT devices using their native default scan protocol and analysis while correcting for systematic measurement bias.

Methods: Forty eyes of 20 healthy volunteers underwent peripapillary RNFL thickness measurements using three SD-OCT devices: Cirrus HD-OCT optic nerve head (ONH) cube 20x20 200 protocol (Carl Zeiss Meditec, Dublin, CA); RTVue ONH protocol (16 radial lines and 8 eccentric circles of various diameters, each centered on the ONH; Optovue, Fremont, CA); 3D OCT-1000 3D Scan 256x256 protocol (Topcon, Paramus, NJ) on the same day. All images were qualified for the manufacturer recommended image quality. RNFL measurement reproducibility was assessed by calculating bias and imprecision using a structural equation model. Estimated imprecision after correcting for bias represented measurement reproducibility that was directly comparable across the different devices.

Results: Global mean RNFL thickness measurement showed estimated imprecision (scale bias corrected) of 2.76 (Cirrus), 7.76 (RTVue), and 4.36 (3D OCT-1000). In other words, RTVue was 2.8x more imprecise and 3D OCT-1000 was 1.6x more imprecise than Cirrus in global RNFL measurement.

Conclusions: Cirrus RNFL measurement had the best measurement reproducibility among the three tested SD-OCT devices. Three dimensional cube scanning with post-data scanning may be interpreted as a factor reducing imprecision.

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Conclusions: Cirrus RNFL measurement had the best measurement reproducibility among the three tested SD-OCT devices. Three dimensional cube scanning with post-data scanning may be interpreted as a factor reducing imprecision.
4397 - A230
Evaluation of the Reproducibility and Agreement of Optical Coherence Tomography Images for Patients With Neovascular Age-Related Macular Degeneration

*Purpose:* Optical coherence tomography (OCT) is currently employed to evaluate neovascular age-related macular degeneration (NVAMD). We compare intra-operator reproducibility and agreement for two Spectral-domain (SD) and one Time-domain (TD) OCT devices in patients with NVAMD. Thickness measurements before and after correction of boundaries on Spectralis™ images were also compared.

**Methods:** 42 eyes with NVAMD were scanned using Spectralis™ and Cirrus™ SD-OCT, and Stratus™ TD-OCT. The same operator scanned each eye twice on the three devices. The intra-class correlation coefficient (ICC) was calculated for reproducibility; Bland-Altman (BA) plots helped determine agreement among machines. For Spectralis™ images, automated algorithms were manually corrected to follow the inner and outer boundaries. A paired t-test was used to compare the retinal thickness before and after correction. The percentage of images with a thickness difference of >4μm in the central 1mm diameter before and after correction was determined.

**Results:** ICCs were greater than 0.95 for all the three machines. Mean central 1mm foveal thickness in μm (±SD) was 239.53 ± 82.63, 350.53 ± 122.67, and 297.94 ± 149.35 for Stratus™, Spectralis™, and Cirrus™, respectively. BA plots gave a mean difference in μm (%) CI interval of 43.3 (±92.19, ±3.51, ±51.28, ±187.93, and ±94.38 ± 30.93, ±220.31) for Spectralis™ vs. Stratus™, Spectralis™ vs. Cirrus™, and Spectralis™ vs. Stratus™ and Cirrus™, respectively. Thickness measurements before and after correction of boundaries were significantly different for all except the outer temporal subfield (p=0.05). 27.5% of the images of Spectralis™ had a difference of >4μm in thickness in the central 1mm subfield after correction.

**Conclusions:** Statistically significant differences in thickness measurements before and after correction of boundaries on Spectralis™ images suggest that manual correction for accuracy is necessary. However, more than 70% of thickness differences were below 4μm, suggesting that changes may be within the clinically accepted variability of the device. ICC values indicate that readings are reliable when scanning a patient on the same machine, but large BA plot confidence intervals show that values from different machines do not agree well.

We conclude that the same device gives reliable readings for a patient with NVAMD, but different machines may give very different thickness measurements.

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4399 - A232
The Effect of Scanning Pitfalls on Boundary Detection Errors and Macular Thickness Measurements of the RTVue MMS Protocol
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*Purpose:* To investigate whether examination settings of the RTVue FD-OCT have any influence on the errors in retinal boundary detection and retinal thickness measurements.

**Methods:** 10 eyes of ten healthy subjects, 10 eyes with diabetic macular edema (DME) and 10 eyes with NVAMD were examined with RTVue FD-OCT device (Optovue Inc, Fremont, CA, USA). MMS protocol was used in two sessions to scan the macula. For the first session, the device was set 3.5 cm from the eye in order to obtain detectable signal with low signal-to-noise ratio. The scan was followed by a second imaging session 6 days later. A six-axis positioning stage was used to align the eye with the imaging system. Axial line scans were collected in both the superior and inferior retina at several locations proximal to the optic nerve head (1.3 to 3.0 mm). Baseline scanning laser ophthalmoscopy images were used as a basis to align scans performed during the follow-up session. The combined nerve fiber/retinal ganglion cell layer (RGCL) and retinal epithelial layers were segmented from axial B-scan images using custom Matlab routines. The difference in RGCL layer thickness and total retinal thickness between imaging sessions was calculated (mean ± SD) along with the 95% limits of agreement (LoA).

**Results:** RGCL and total retinal thickness differences in the superior retina were 1.188 ± 2.236 μm (LoA: -9.094 to 10.470 μm) and 0.963 ± 3.1793 μm (LoA: -7.588 to 9.514 μm) and for the inferior retina, 1.599 ± 2.114 μm (LoA: -9.484 to 9.624 μm) and -2.530 ± 2.036 μm (LoA: -12.694 to 7.794 μm).

**Conclusion:** Our results demonstrate that the between-session repeatability of RGCL and total retinal thickness measurements by in-vivo SD-OCT is excellent with limits of agreement that range between 1-3 pixels.

CR: D.C. Lozano, None; M.D. Twa, None.

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4400 - A233
Retinal Thickness for Patients With Neovascular Age-Related Macular Degeneration
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*Purpose:* To describe the rate and characteristics of errors in retinal thickness compare map of spectral domain optical coherence tomography (OCT) scans.

**Methods:** We retrospectively analyzed the compare map of OCT scans of patients with neovascular age-related macular degeneration with and without Significant Macular Edema (SME) who were imaged 2 or more times using Topcon 3D-OCT-100B.

**Results:** One hundred sixty-five patients with compare map were included. Ninety-three compare maps were derived from patients with the two scans obtained at the same day and 72 were not. Errors were detected in 121 (57%) of the 165 compare maps. Time interval between two scans comprising compare map did not influence the incidence of error. Errors were classified to fixation error (8%) from fixation loss during the each scanning, matching error (23%) from mismatching of the centers of the two scans, and segmentation error (26%). Fixation error was characterized by horizontal line on the compare map. Matching error was noted by two symmetric configurations on the map. Compare maps with segmentation error showed abrupt localized change of thickness.

**Conclusions:** Errors on compare map occur frequently with current segmentation and matching algorithms. They can be noticed with their characteristic configuration.

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4401 - A234
Spectral Domain OCT Segmentation Accuracy in Monkeys

Purpose: To evaluate segmentation accuracy and reproducibility using spectral-domain optical coherence tomography (OCT) in monkeys; correlate retinal thickness values with fluorescein angiography (FA) leakage scores in a laser model of choroidal neovascularization (CNV) and compare time domain (Stratus®) with spectral domain (Cirrus®) results.

Methods: Normal eyes from 4 cynomolgus monkeys and laserered eyes from 6 cynomolgus monkeys were studied. A Cirrus or Stratus OCT was used to acquire macular thickness cube scans or macular thickness map scans, respectively. The CNV laser model animals had FA performed on the same day as the OCT scans. Using the Cirrus software algorithm, segmentation lines were manually corrected in the set of CNV model monkeys.

Results: Average thickness and volume values vs FA Grade 4 leakage from CNV model animal resulted in R2 values of 0.54 and 0.52. This was a significant, though modest (5.4 μm) increase in thickness values post manual correction of segmentation errors, after which R2 was 0.66. Cirrus values (mean±SEM) for central subfield thickness (μm), average thickness (μm) in 20 normal animals (30 eyes) were 222.7±3.88, 10.6±0.17, 291.2±3.02 respectively. Stratus central subfield thickness (μm), volume (mm3), and average thickness (μm) in a gender matched group was 172.8±8.47, 7.2±0.17, 241.1±15.0 respectively. Age did not significantly affect thickness values (p=0.50). Signal strength average values were 9.83±0.09 for the Cirrus and 9.95±0.03 for the Stratus. Cirrus intra-session COV for the 12 CNV model eye ranges from 0.011 to 0.031; for 12 normal eyes 0.009 to 0.017; normal animals with the Stratus the 0.004 to 0.013.

Conclusions: Cirrus tended to underestimate CNV model thickness values. Manual segmentation of Cirrus scans resulted in a small increase in average thickness values and a mild improvement in correlation with FA grade. Stratus and Cirrus show comparable intra-session variability in normal eyes. Segmentation differences resulted in ~60μm average difference between Cirrus and Stratus values. Reproducible thickness values can be obtained in monkeys with both the Cirrus and Stratus instruments.

CR: K.B. McIntyre, None; C.A. Rasmussen, None; A.K. Goulding, None; V. Bantesee, None; J.N. Ver Hoeve, None; P.L. Kaufman, None; B.J. Christian, None; T.M. Nork, None.

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4403 - A236
Effect of Age on Healthy Retinal Nerve Fiber Layer Thickness Measurements Using Spectral-Domain Optical Coherence Tomography (SD-OCT)
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Purpose: To investigate the effect of age on spectral-domain optical coherence tomography (SD-OCT) measurements of global and sectoral retinal nerve fiber layer (RNFL) thicknesses in healthy subjects.

Methods: Study design was retrospective, observational and cross-sectional. 102 healthy subjects (156 eyes) were scanned using a commercially available SD-OCT system (Spectralis, Heidelberg Engineering, Heidelberg, Germany). RNFL thickness parameter included global and quadrant measurements as well as measurements from 2 further subdivisions (the temporal and naso-aspects) of the superior and inferior quadrants. Patients were grouped according to age for analysis, and all RNFL parameters were analyzed using averages ± standard deviation.

Results: In the 10 to 35 years age group, mean ± SD = 26.0±2.60 μm, 60 to 70 years group mean ± SD = 25.9±2.60 μm, 70+ years group mean ± SD = 25.8±2.60 μm. All age groups were statistically similar (p=0.8). Slight changes in the scan lateral dimension would be most likely to affect the measured size of lateral retinal dimensions measured with optical coherence tomography (Johnson et al., ARVO, 2009). In younger myopic eyes with increased magnification, thicker regions surrounding the foveal pit might be included in a central 1’mm scan and thus may affect the reported central retinal thickness. We examined the effect of contact lens wear on measured retinal thickness over a range of myopic refractive errors in an effort to determine if the slight differences in retinal magnification that result from contact lens wear are associated with differences in reported central retinal thickness.

Conclusions: The results indicate that a significant number of young (10-20 years) soft contact lens wearers were refractive error subjects. The data for right eyes were reported here but similar results were observed in left eyes. Spherical equivalent refractive errors measured with an aberrometer ranged from -1.1 to -12.1 D (mean ± SD = 3.51±2.51). Axial lengths measured with a Zeiss IOL Master ranged from 23.63 to 25.56 mm (mean ± SD = 24.5±0.40). Retinal thickness in the macular region measured with and without contact lens correction, using an Optovue RTVue FD-OCT and the MM6 scan pattern that consists of twelve 6-mm rotational line scans through the fovea. Retinal thickness is reported for the central 1 mm, the paravesical ring from 1 to 3 mm diameter and the perifoveal ring from 3 to 6 mm diameter. Results: Mean central 1’mm foveal thickness was 245.8 ± 16.3mm without contacts and 241.1±15.0mm with contacts (p = 0.001 in a paired t-test). The mean paravesical thickness was 310.5 ± 12.2mm without contacts and 308.5 ± 12.8mm with contacts (p = 0.048, paired t-test). The mean parafoveal thickness was 268.8 ±13.2mm without contacts and 2679 ± 11.9mm with contacts (p = 0.05, paired t-test). The reduction in central 1’mm thickness with contact lens wear was more apparent with increasing myopia.

Conclusions: The reported central 1’mm retinal thickness was significantly reduced with contact lens wear. Contact lenses were worn, probably due to slight misalignment of the OCT scan. The reduction of this effect outside the central 1’mm is consistent with magnification. Slight changes in the scan lateral dimension would be most likely to affect where the thickness changes rapidly, such as near the foveal pit slope, rather than where the thickness changes gradually, such as in the parafovea or perifovea.

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4405 - 2384
Motion Artifact Correction in OCT Volume Scans Using Image Registration
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Purpose: Artifacts resulting from eye movement during 3D-OCT volume scanning degrade image quality and are a source of reproducibility error in quantitative measurements. We present a pure software based correction method that corrects motion in all three dimensions. It uses two consecutive 3D-OCT volume scans with orthogonal fast scan axis directions.
Methods: The two 3D-OCT data sets are registered in order to find the unknown eye motion. Registration is performed by optimizing a global objective function with two displacement fields and special regularization based on the time structure of the volume sampling process. To improve both speed and solution quality, a multi-resolution approach is used. After optimization, each volume is undistorted and a single merged volume is constructed as an adaptive weighted sum of both registration results.
Results: Data sets of the macula and optic disc from normal subjects and patients with retinal diseases were registered. The algorithm is able to correct for motion in all three dimensions. It can handle both slow drifting as well as saccadic movement. Quantitative assessment of registration performance using mutual information and visual inspection indicate very good registration results. The resulting volumes do not show visible motion artifacts. The algorithm produces stable results over a wide range of parameters. Images show single corresponding en face slices, from left to right: Fast horizontal, fast vertical input, registered and merged result.

Conclusions: The proposed method constitutes a robust, software based, motion artifact correction solution able to remove distortion introduced by movement in all three dimensions. These methods promise to enable the acquisition of large 3D-OCT data sets and improve measurement reproducibility without the need for active eye tracking.

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4407 - A240
Evaluation of the Retinal Pigmented Epithelium Layer in Human Albinism
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Purpose: Although various Optical Coherence Tomography (OCT) studies have examined the architecture of the albino retina, thus far, none of them have focused on the Retinal Pigmented Epithelium (RPE) layer. We describe the structure of the RPE layer in patients affected by albinism by means of high-resolution, spectral-domain OCT.

Methods: High-resolution spectral domain OCT (SOCT Copernicus, 3 μm, B scan acquisition time 23ms) was used to image retinae in 24 patients and 20 healthy volunteers, scanning each eye at least 3 times. Three of the albino eyes had to be excluded due to poor image quality. B scans were flattened along the OCT layer and a reflectance profile at the fovea was generated using ImageJ software, averaging 3 profiles from each eye. The graphs were then scored for the presence of peaks and troughs in the RPE region and amplitude measurements were estimated using Spike 2 software.

Results: Analysis of the RPE layer revealed 3 peaks in 72.7% of the albino eyes compared to 100% in the control group. A distinct deep trough (T1 peak) compared to controls (10.0%, SD3.94 of RPE peak).

Conclusions: Using high resolution spectral domain OCT, we have been able to determine subtle differences in the RPE layer of the albino retina compared to normal healthy retina for the first time. Being able to characterize these differences will lead to a greater understanding of the pathophysiology of visual defects associated with albinism and assist in the accurate diagnosis of albinism.

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4408 - A241
Various Phenotypes Ranging From OCA1 to Normal Pigmentation Caused by Compound Tyrosinase Gene Variant R402Q
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Introduction: Mutations in the tyrosinase (TYR) gene, cause oculoauriculovertebral dysplasia type I (OCA1), an autosomal recessive albinism (AROA). About 30 AROA mutations were reported as compound heterozygous (CH) for various “severe” TYR mutations, and the common polymorphism R402Q. Expression studies showed thermodabile tyrosinase activity due to the R402Q mutation. However, CH for various “severe” TYR mutations, and R402Q was reported in normally pigmented parents of albino’s with the severe phenotype of OCA1A.

Purpose: To determine whether R402Q is a pathogenic mutation or common polymorphism.

Methods: Phenotypic evaluation included description of hair, eye and skin color, presence of nevus, hypopigmentation and papillae, and visibility of choroidal vessels and hypoplasia of the macula. Blood DNA was PCR amplified followed by restriction digest or sequencing. However, families with a CH albino child are at risk for additional albinism phenotypes. We have screened Israeli Jewish albinos and first degree relatives for the R402Q variant and severe and variable TYR mutations, and identified 23 albinos and 50 self declared normally pigmented relatives who are CH for a severe TYR mutation, and R402Q. Three of these albino genes were previously determined as OCA1A by histological examination. The entire TYR gene was sequenced in the CH albinos, and no additional TYR mutations were identified. Two TYR mutations - MIW and E294K are always in cis (same allele) with R402Q. Next, we evaluated the phenotype of 20 of the CH albinos, 16 of the normally pigmented CH relatives and their family members. Moderate to mild phenotypes of OCA1B, OCA1A and OA, with marked interfamilial variability, were detected in the CH albinos. Some “albinotic” characteristics were observed in all tested “normal” siblings of CH albinos which share the same genotype. This usually includes hypopigmentation compared to other family members, and (or) in few cases very mild albinotic symptoms (e.g., eye examination). CH parents of OA1A albinos had normal vision and only few were hypopigmented.

Results: In most cases CH for severe TYR mutations and R402Q will have normal vision and no albinotic symptoms. However, families with a CH albino child are at risk for additional albinism (OCA or OA) or hypopigmented sibling with the same genotype. The familial clustering and inter and intrafamilial variability indicate the existence of a modifier of severity.

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4409 - 2394
The Role of Pigmentation in Foveal Pit Morphology: An SD-OCT Study
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Purpose: There have been a few reports showing race and gender related differences in macular thickness as measured with OCT. Recently, we developed an automated metric to assess foveal morphology (depth, diameter, slope) and found significant variation in these parameters between individuals with normal vision. It is also known that a disruption in melanin biosynthesis (as occurs in albinism) interferes with normal foveal development, and results in foveal hypoplasia. Here we sought to assess how race and pigmentation relate to macular thickness and foveal morphology.

Methods: One hundred sixty-two eyes of 81 healthy patients (45 female, 36 male) underwent retinal imaging with SD-OCT (Bioptron, Inc. & Carl Zeiss Meditec, Inc.). Skin pigmentation was assessed based on the von Luschan scale, with subjective grading performed by two independent observers. Ethnicity and eye and hair color were also recorded. Central subfield thickness and average retinal thickness was calculated from the Circus macular volume scans.

Results: Foveal morphology was measured using previously described Matlab software.

Conclusions: There were significant differences across race and gender in macular thickness and foveal morphology.
4409 - A242
New Insights Into the Spectrum of Foveal Development in Albinism
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Purpose: Albinism is characterized by foveal hypoplasia, although a spectrum of development occurs in those with better VA. We sought to further study foveal morphology in individuals with albinism.

Methods: SD-OCT was used to obtain cross-sectional and volumetric images of the macula. An adaptive optics fundus camera was used to image the cone photoreceptor mosaic.

Results: Individuals with albinism had OAI (n=2) or OCA1B (n=4). Subject age was 10 to 32 years and BCVA was 20/20 to 20/70. We found a continuum of foveal development, from nearly planar thickness to a shallow foveal depression and some excavation of inner retinal layers, correlating with BCVA. Normal central outer and inner segment thickness was not seen in those without a visible pit, whereas individuals with a rudimentary pit had normal outer and inner segment thickness. Cone packing varied from normal to absent of central cone packing despite degree of foveal development and was not uniformly related to outer segment thickness. The preferred retinal locus for fixation was temporal to the identified the foveal pit (or mounding in cases of an undeveloped pit) in 4 subjects.

Conclusions: The spectrum of foveal morphology seen in albinism involves not only the development of a foveal pit but also inner and outer segment thicknessing and cone packing, perhaps determined by the gene mutation and inherent pigmentation.

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4411 - A244
Evaluation of Nerve Fiber Layer and Ganglion Cells Layer Thickness in Parkinson’s Disease
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Purpose: To evaluate differences in Retinal Nerve Fiber Layer (RNFL) thickness and RNFL+ Ganglion Cells Layer (GCL) in patients affected by Parkinson’s Disease (PD), compared to age and sex-matched healthy subjects.

Methods: Patients and controls underwent neurological examination, Mini Mental State Examination (MMSE), clock drawing test (CDT) and comprehensive ophthalmic evaluation. Spectral-Domain Optical Coherence Tomography (SD-OCT) examination was performed with Spectralis (Heidelberg Engineering) and RTVue-100 (Optovue Inc). RNFL thickness map was obtained with Spectralis volume protocol with 19 lines on 30° field centered on fovea. On each B-scan the outer RNFL limit was manually set. RNFL+GCL thickness map was obtained with RTVue-100 MM6 protocol. Maps were divided in 9 zones (central, superior internal, temporal internal, inferior internal, nasal internal, superior external, temporal external, inferior external, nasal external) and each map value in every field was evaluated. Exclusion criteria were the presence of any possible cause of RNFL and GCL thickness alteration.

Results: We analyzed 22 PD patients (22 eyes) and 28 healthy subjects (28 eyes) with both RTVue-100 and Spectralis OCT. No significant difference in RNFL+GCL thickness measurements in PD patients was demonstrated in any field (ANOVA; p value between 0.2733 and 0.8634), compared to healthy subjects. RNFL thickness measurements in PD patients are reduced in central and temporal internal fields only (ANOVA; p value respectively 0.0009 and 0.0022), compared to healthy subjects.

Conclusions: The difference between Spectralis and RTVue-100 in the central and temporal internal fields seems suggest that the alteration in these sectors are related only to retinal fiber layer, without involvement of ganglion cells. More studies are necessary to understand the significance of these results.

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4412 - A245
Retinal Vessel Imaging and Alzheimer’s Disease Risk

Purpose: Retinal imaging has revealed significantly narrow retinal venules in patients with early Alzheimer’s Disease (AD). The purpose of this study was to determine if this narrowing is detectable in individuals without dementia but who possess a genetic risk factor, apolipoprotein epsilon 4 (apoE4), for Alzheimer’s disease.

Methods: For this prospective, cross-sectional study, a pool of healthy participants was recruited from another study and had undergone a complete neuropsychological assessment. All had well-controlled blood pressure and HbA1c of 6.1 or less; none smoked or had dementia, diabetes, glaucoma, retinal defects, ocular inflammation, diplopia, or history of intraocular surgery other than uncomplicated cataract surgery. An examiner blind to the apoE4 status of the participants conducted a clinical exam including dilution with 0.5% tropicamide, A-scan, and acquisition of two 45-degree digital fundus photographs from each eye. A reader blind to apoE4 status determined central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE) from fundus photographs using a semi-automated, published protocol (IVAN, University of Wisconsin, Madison). Relatively high AD risk was defined by the presence of the apoE4 allele.

Results: 8 of 26 participants were positive for apoE4. Neither CRAE nor CRVE was significantly associated with apoE4. Post-hoc analysis showed CRAE was positively associated with performance on two tests of executive function, the Stroop test (p = 0.0022) and category fluency (p = 0.0025).

Conclusions: Retinal venular caliber was not associated with AD risk or cognition in healthy individuals. Retinal arteriolar caliber was associated with two measures of executive function, which is more typically affected early in vascular cognitive impairment. The ophthalmic artery originates near those supplying regions of the brain that mediate executive function. To our knowledge, this is the first study showing an association between generalized retinal vessel narrowing and cognitive function in healthy individuals. Further research is needed to determine whether generalized retinal arteriolar narrowing may be an early marker for risk of vascular dementia.

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4413 - A246
Voxel-Based Analysis of the Optic Radiation Using Diffusion Tensor Imaging in Glaucoma Patients
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**Purpose:** To establish a registration based framework for the determination of local changes of the optic radiation (OR) due to glaucoma using Diffusion Tensor Imaging (DTI).

**Methods:** DTI-brain scans of 23 subjects using a 3 Tesla-MRI scanner were performed. The subjects are categorized into two age matched groups: 10 normal controls (mean age of 56.9±11.9 years) and 13 primary open angle glaucoma patients (mean age of 63±12.5 years). First, the OR is automatically identified using the authors’ previously published algorithm. Then, the axial slice that includes the largest part of the lateral geniculate nucleus (LGN) is selected for further analysis. The segmented OR is then manually corrected by two DTI experts. Second, all the segmented ORs are registered to a reference OR, the largest size OR (right of the figure), using a shape based non-rigid registration approach. The transformation fields of the registration are applied to the fractional anisotropy (FA) images to map them into the unified registration space. Then, the distributions of FA at each voxel in the unified space are statistically analyzed using Mann-Whitney U-test with regard to both groups. Finally, the significant voxels are determined (p-value < 0.05).

**Results:** The significant regions are determined by applying the proposed analysis to the normal and glaucoma groups. A concentration of significant voxels is observed on the core of the OR-bundle especially on the right bundle as shown by red voxels in figure (left).

**Conclusions:** The proposed analysis provides a framework to capture the significant local changes of the OR due to glaucoma. It can be extended to all tenor-derived parameters. Moreover, shape based registration is suitable for glaucoma as it avoids the dependence on tenor-derived parameters which are subject to changes in the presence of glaucoma.

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4414 - A247
Vitreous Volume of the Mouse Measured by Quantitative High-resolution MRI
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**Purpose:** The mice eye has been used for many important pathophysiological studies of visually-significant diseases. Experimental paradigms frequently involve the injection of diagnostic and/or therapeutic agents into the vitreous cavity, and the analysis of data is dependent on the volume of the vitreous cavity. We assessed the variation in the vitreous cavity in 2-month old mice using high-resolution MRI.

**Methods:** The vitreous volume of five 2-month old male C57BL6/mice was measured by high resolution MRI at 11.7T. Multi-slice spin-echo imaging covering the entire left eye were acquired at 100 × 100 × 100 μm resolution (TR 1 sec, TE 35 ms, average 4). Vitreous was manually identified on each image as the region exhibiting higher intensity than lens, iris, and retina (Fig 1A&B). To minimize the partial volume effect on vitreous volume measurement, the voxel volume at the edge of vitreous cavity was weighted by a factor of 0.5.

**Results:** The average vitreous volume of the mouse eye has a 19% variation (Fig 1C, mean = 4.4 ± 0.7 μl). Furthermore, the difference in vitreous cavity size is not correlated to the weight of the mouse (R² = 0.17).

**Conclusions:** The vitreous volume of the mouse eye can vary significantly in mice of the same age, and it is not related to weight of the mouse. Therefore, accurate conclusions concerning the dose effect of an intravitreal injection in the murine vitreous cavity may be biased by the variation in size of the vitreous cavity.

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4415 - A248
Anatomical and Functional MRI of the Human Retinas
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**Purpose:** Although MRI has comparatively lower spatial resolution compared to optical imaging techniques, it offers depth-resolved, and often quantitative, physiological parameters. In anesthetized rodents, anatomical, blood flow and blood oxygenation level dependent (BOLD) MRI has been used to image the thin retinas. Similar applications in the human retinas remain challenging because high spatial resolution on human MRI may be limiting and eye movement in awake subjects could be problematic. This study reports our initial experiences in anatomical MRI and BOLD MRI of O2 challenge of the human retinas.

**Methods:** MRI was performed on a 3T MRI scanner using a custom-made eye coil. Anatomical MRI detected 3 (bright-dark-bright) layers. The laminar thicknesses from the vitreous-retina boundary were respectively: 217±29, 227±11 and 232±8μm (mean±SD, N=8 measurements, P<0.05). The laminar thicknesses from the vitreous-retina boundary were respectively: 217±29, 227±11 and 232±8μm (mean±SD, N=8 measurements, P<0.05). The total retinal thickness including the choroid was 592±31μm, which was within thicknesses reported in the literatures but with a higher degree of shape similarity of the OR. Therefore, it is selected for further analysis. The segmented OR is manually corrected by two DTI experts. Second, all the segmented ORs are registered to a reference OR, the largest size OR (right of the figure), using a shape based non-rigid registration approach. Third, the transformation fields of the registration are applied to the fractional anisotropy (FA) images to map them into the unified registration space. Then, the distributions of FA at each voxel in the unified space are statistically analyzed using Mann-Whitney U-test with regard to both groups. Finally, the significant voxels are determined (p-value < 0.05).

**Results:** The average vitreous volume of the mouse eye has a 19% variation (Fig 1C, mean = 4.4 ± 0.7 μl). Furthermore, the difference in vitreous cavity size is not correlated to the weight of the mouse (R² = 0.17).

**Conclusions:** The vitreous volume of the mouse eye can vary significantly in mice of the same age, and it is not related to weight of the mouse. Therefore, accurate conclusions concerning the dose effect of an intravitreal injection in the murine vitreous cavity may be biased by the variation in size of the vitreous cavity.

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4416 - A249
Evolution of Lamellar Macular Hole Using SD-OCT
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**Purpose:** The evolution of lamellar macular holes using SD-OCT is of clinical interest. Inclusion criteria were a foveal defect on SD-OCT (Spectralis HRA + OCT, Heidelberg Engineering, Heidelberg, Germany) with residual foveal tissue above the retinal pigment epithelium and corresponding hyperautofluorescence on fundus autofluorescence imaging. Visual acuity and OCT findings were collected and compared at baseline and after 6 months of follow up. Main outcome measures were visual acuity changes (ETDRS charts) and progression of the lamellar macular defect. The latter was evaluated by measuring the distance between the inner/outer segment (IS/OE) interface and the internal limiting membrane in the fovea (software calipers).

**Results:** Seventeen eyes of 17 consecutive patients (8 males 9 females ), mean age 71 years ( range 53 – 86 ), mean refraction -0,5 sph ( range +2,5/-5,0 sph ) were included. SD-OCT data is dependent on the volume of the vitreous cavity, and the analysis of data is dependent on the volume of the vitreous cavity. We assessed the variation in the vitreous cavity in 2-month old mice using high-resolution MRI.

**Methods:** Patients diagnosed as having a lamellar macular hole have been followed prospectively since January 2009. Inclusion criteria were a foveal defect on SD-OCT ( Spectralis HRA + OCT, Heidelberg Engineering, Heidelberg, Germany) with residual foveal tissue above the retinal pigment epithelium and corresponding hyperautofluorescence on fundus autofluorescence imaging. Visual acuity and OCT findings were collected and compared at baseline and after 6 months of follow up. Main outcome measures were visual acuity changes (ETDRS charts) and progression of the lamellar macular defect. The latter was evaluated by measuring the distance between the inner/outer segment (IS/OE) interface and the internal limiting membrane in the fovea (software calipers).

**Results:** Seventeen eyes of 17 consecutive patients (8 males 9 females), mean age 71 years (range 53-86), mean refraction -0.5 sph (range +2.5/-5.0 sph) were included in the analysis. Mean BCVA at baseline (62 letters ETDRS) and after 6 months (60 letters ETDRS) was stable (signed rank test, p value 0.109). Mean foveal thickness at baseline (119 microns) and after 6 months (112 microns) was stable (signed rank test, p value 0.935). The patient with the thinnest residual foveal tissue developed a full thickness macular hole loosing also a line on the ETDRS chart. Seventeen eyes (100%) had an ERM and 8/47% a posterior vitreous detachment at baseline. A weak correlation between visual acuity and thickness of residual foveal tissue at baseline (p=0.2 correlation coefficient 0.44) and after 6 months follow up (p=0.37 correlation coefficient 0.24) was finally detected.

**Conclusions:** Lamellar macular holes at 6 months seem to be stable with no progression. Full thickness macular hole may develop in eyes with a very thin layer of residual tissue during follow up.

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Support: None.
Regional Age-Related Changes on Retinal Nerve Fiber Layer Thickness as Measured by Spectral Domain Optical Coherence Tomography


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Purpose: To evaluate the relationship between age and peripapillary retinal nerve fiber layer (RNFL) thickness in normal subjects, as determined by spectral domain optical coherence tomography (SD-OCT).

Methods: We prospectively enrolled 144 normal subjects (144 eyes), ranging from 16 to 84 years of age. After a complete ophthalmological examination, all patients underwent RNFL thickness measurement using SD-OCT (Spectral OCT/SLO, OPKO-OTI, Miami, FL). Two scans were performed per eye, each with 3 images analyzed (automatic tracking of the optic disc; diameter of 3.4 mm; resolution of 6 μm). The correlation between age and RNFL parameters (global and sectoral) was analyzed using linear regression analysis. The slope for each parameter was also calculated.

Results: The average RNFL thickness decreased significantly with increasing age, with a slope of -0.14 μm/year (r²=0.04, p<0.01). Six of the 30-degree sectors (12 clock hours) were significantly and inversely correlated with age, with slopes ranging from -0.10 to -0.23 μm/year (r²≥0.02, p≤0.04). While most (5/6) were localized in the inferior and temporal sectors, none of the nasal sectors correlated significantly with age (p≥0.06).

Conclusion: Our data suggest that both global and regional RNFL thickness, as assessed by SD-OCT, decrease with age. This reduction seems to be more pronounced in the infero-temporal sectors, resembling that found in glaucomatous eyes. It suggests a possible age-related pattern of regional susceptibility that should be considered when assessing eyes over time.

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