

WEDNESDAY SEPTEMBER 28<sup>TH</sup> 2016

## PERIMETRY I

**ARE BIG STIMULI “EASIER” TO SEE? AN ANALYSIS OF RESPONSE TIMES FROM FREQUENCY-OF-SEEING DATA**Paul H. Artes<sup>1</sup>, Matthias Monhart<sup>2</sup>, Marco Miranda<sup>3</sup><sup>1</sup>Eye and Vision Research group, Plymouth University, UK; <sup>2</sup>Carl Zeiss AG, Feldbach ZH, CH; <sup>3</sup>NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust & UCL Institute of Ophthalmology, London, UK

**Purpose:** Patients have commented that visual field tests with larger stimuli are easier to perform. We investigated if response times (RTs) provide objective evidence for this - on the premise that more certain responses have shorter and/or less variable latencies.

**Methods:** We analysed data from frequency-of-seeing (FOS) experiments on 20 healthy controls and 7 patients with glaucoma. FOS data were obtained at 5 central and 5 peripheral locations, up to 85° from fixation. At each location, 10 stimuli were presented, in random order, at each of 8 intensities (800 stimuli per experiment). Stimulus sizes III (0.43°) and V (1.70°) were used during separate sessions. Experiments were performed on an Octopus 900 perimeter controlled through the Open Perimetry Interface. The variability of response latencies from individual observers was expressed as the interquartile range (IQR), after stratifying responses into “near-threshold” (within ±3 dB of FOS threshold) and “highly visible” (>10 dB brighter than FOS threshold) categories.

**Results:** For stimuli within 3 dB of threshold, RT distributions with size III and size V stimuli were nearly identical, both in average as well as variability (Table 1). For highly visible stimuli (>10 dB above threshold), responses to size V stimuli occurred ~50 ms faster, and with slightly less variable latencies, compared to those of size III.

*Table 1) Response times to size III and size V stimuli, stratified by proximity to individual point-wise thresholds. Near-threshold responses were those to stimuli within ±3 dB of the estimated 50% FOS threshold, and supra-threshold responses were those to stimuli at least 10 dB brighter than the estimated FOS threshold.*

|  | Size III       | Size V         |
|--|----------------|----------------|
| Stimuli near threshold (±3 dB)         |                |                |
| Overall median RT, IQR (ms)            | 495 (470, 530) | 500 (450, 530) |
| individual RT variability, median (ms) | 125            | 135            |
|  |                |                |
| Stimuli above (>10 dB) threshold       |                |                |
| Overall median RT, IQR (ms)            | 395 (350, 415) | 350 (310, 390) |
| individual RT variability, median (ms) | 95             | 75             |

**Conclusions:** We found no evidence for our hypothesis that responses times to near-threshold stimuli of size V were either faster or less variable than those of size III. This suggests that response times either do not reflect perceptual difficulty, or that there was no meaningful difference in perceptual difficulty between near-threshold stimuli of size III and V. We need better objective measures for “human factors” aspects in perimetry.

**EFFECT OF LOCALIZED DEFOCUS ON MEASUREMENTS OF SPATIAL SUMMATION OF PERIMETRIC STIMULI**Shindy Je, Julia M. Rose, James E. Morgan, Tony Redmond  
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**Purpose:** To investigate the effect of localised defocus on measurements of the area of complete spatial summation (Ricco’s area) in the peripheral visual field.

**Methods:** Achromatic visual field sensitivity was measured with circular incremental stimuli of different area (Goldmann I-V; 0.02°-1.7° diameter) at 3 inferotemporal visual field locations (12°, 21°, and 29° eccentricity) in 5 young healthy participants (age: 23, range 21 - 25 years). Spatial summation functions were determined at each visual field location under six optical conditions: baseline refractive error, and after the addition of full aperture trial lenses from +1D to +5D in 1D steps. Each threshold on each spatial summation curve represented an average of 3 measurements. Ricco’s area was estimated from spatial summation functions with two-phase regression analysis. Experiments were performed on an Octopus 900 perimeter (Haag Streit, Koeniz, Switzerland), with the Open Perimetry Interface. Peripheral refractive error was measured with retinoscopy at each test location. The effect of defocus on Ricco’s area was assessed with a repeated measures ANOVA.

**Results:** Median (IQR) baseline refractive error of the participants was +0.75D (+0.50D, +1.25D). There was a statistically significant increase in refractive error with eccentricity across all subjects prior to the addition of blurring lenses ( $p < 0.01$ ; average (sd): +0.53D (0.17) at 12°, +0.81D (0.17) at 21°, +1.14D (0.23) at 29°). Median (IQR) Ricco's area without blur lenses was -0.89 (-0.76, -0.97) at 12°, -0.84 (-0.74, -1.06) at 21°, and -0.53 (-0.40, -0.60) at 29°. The maximum total refractive error (baseline + induced blur) in the cohort was +6.14D. Threshold was elevated for all stimuli with defocus, and although there was a slight increase in the size of Ricco's area with defocus on average, this did not reach statistical significance ( $p = 0.55$ ).

**Conclusions:** There was a small, but statistically non-significant overall effect of localized defocus on the measurement of Ricco's area, over the approximately 6 dioptre range of refractive errors recorded in this study. In the context of normal variability in measurements of spatial summation, these findings suggest that small fluctuations in refractive error between tests are unlikely to pose a major limitation to the identification of disease- or therapy-related changes in spatial summation over time in clinical trials.

## MISMATCH (MM). A NEW DISHARMONY INDEX FOR DIAGNOSIS IN THE GLAUCOMATOUS VISUAL FIELD

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**Purpose:** To evaluate new perimetric indexes, based on harmony: diagnostic ability in comparison to conventional functional and morphologic ones in suspects and initial glaucoma patients.

**Materials and methods:** 105 healthy subjects and 113 early and suspect glaucomas (MD > -6dB) were examined twice with Oculus Smartfield perimeter (Spark strategy) and twice with Humphrey (24-2 SITA-Fast). Spark examines 66 points and SITA 52 points. Statistical data analysis performed only included the average of the two results obtained in both exams of the matching 52 points. We also carried out Cirrus OCT the same day. Upper anatomic regions values were compared with the specular lower, averaging their absolute differences ("HEMIZONE indexes"). Disharmony in the visual field is evaluated including vertical thresholds symmetry (VTS), homogeneity (thresholds standard deviation, TSD) and threshold rank (THR), using the patient himself as a reference. We also evaluate the disharmony in combination with the mean deviation (MD) in a single index (MISMATCH MM index).

**Results:** Exam duration was: 2:57 minutes (sd=0:02) in Spark and 2:47 minutes (sd=0:37) in SITA-Fast ( $p < 0.001$ ). Four exams average MD was  $-0.10\text{dB} \pm 1.15$  in healthy and  $-1.36\text{dB} \pm 2.16$  in suspect and initial glaucoma ( $p < 0.001$ ). When the average threshold was higher than 20dB test-retest fluctuations were  $1.10\text{dB} \pm 1.11$  in Spark and  $1.29\text{dB} \pm 1.51$  in SITA ( $p < 0.001$ ), and when lower than 20dB, they were  $2.57\text{dB} \pm 2.73$  in Spark and  $3.81\text{dB} + 4.32$  in SITA ( $p < 0.001$ ). Harmony based indexes had, at least, similar diagnostic ability compared to those obtained by normal reference values (MD and PSD). For 95% specificity, the higher sensitivities were: 30.1% for OCT vertical C/D ratio; 46% for Spark MM; 40.75% for SITA TSD and 49.1% for an all indexes combined analysis. Retinal macular thickness and ganglion cells layer did not show significant advantages respect to other indexes. Also the morphologic "HEMIZONE" indexes did not show better diagnostic ability.

**Conclusions:** Disharmony alone or combined with normative values based indexes is useful for diagnosis. Morphological examinations of macular thickness and ganglion cells layer thickness, in this area, do not seem to present the diagnostic advantages that have been previously described. Something similar occurs with the morphological comparisons between upper and lower regions.

## STRUCTURE I

### SIGNIFICANCE OF STRUCTURAL CHANGES IN PAPILLARY AND PERIPAPILLARY NERVE FIBER LAYER FOR GLAUCOMA

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**Purpose:** SD-OCT with the new "Glaucoma Module" offers new chances for early diagnosis of glaucoma. Thinning of the retinal nerve fiber layer is the generally accepted sign of glaucomatous damage. Hypodense regions in this tissue, like holes, have been described in glaucoma, as well as focal spongy swelling, followed by thinning later on. The frequency and appearance of structural changes has been analyzed.

**Materials and methods:** SD-OCT scans with the Glaucoma Module were analyzed retrospectively for the structure of the nerve fiber layer at and around the optic disc. Glaucoma or ocular hypertension was present in 177 of the 269 eyes of 138 patients. The remaining 92 eyes had no eye pathology (22 eyes) or suffered from other conditions of the retina, the optic disc or the visual pathway. Earlier tests for follow-up were available in 15 eyes.

**Results:** An irregular structure of the nerve fiber layer was frequently observed near vessels or underneath the ILM, especially with epiretinal membranes or vitreo-retinal traction. After exclusion of these conditions, focal holes or spongy structures were present in 48 eyes of 39 patients. The remaining 221 eyes of 142 patients did not show those abnormalities. In the 22 healthy eyes and 5 eyes with only PEX no structural changes have been found. Hypodense regions were seen in 1 of 32 eyes with ocular hypertension, 4 of 34 glaucoma suspects, 6 of 12 pre-perimetric and 23 of 88 perimetric glaucomas. Five of 14 eyes with ischemic optic neuropathy and 6 of 35 eyes with neurodegeneration were affected. From the remaining 21 eyes with different conditions, 3 had an abnormal structure.

**Conclusions:** Structural changes within the nerve fiber layer may precede thinning as the usual sign of glaucomatous damage. This feature can be observed in early and later stages of glaucoma, more frequently in meridians of the disc than in the 3 ring scans, predominantly in nerve fiber bundle shape. It is obviously an early sign of damage, explaining discrepancies between conventional structure analysis and function. However, it may also be present in other conditions, like ischemia, neuritis or in generalized neuropathies.

## TOPOGRAPHIC ESTIMATION OF HEMOGLOBIN IN THE OPTIC NERVE HEAD USING ONLY CONVENTIONAL PHOTOGRAPHIC IMAGES

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**Purpose:** To compare the diagnostic accuracy and reproducibility of the Laguna ONhE program with morphological and functional information.

**Materials and methods:** 47 healthy subjects and 64 glaucomas were examined twice with photographic images obtained with a fundus camera Horus DEC-200 (MiiS) and analyzed with Laguna ONhE (Insoft) software, twice with Cirrus OCT (Zeiss), once with Spectralis OCT (Heidelberg) and once with Octopus 300 TOP-32 (Haag-Streit).

Statistics used: Receiver operator characteristic (ROC) curve analysis, intraclass correlation coefficients (ICC) and respective confidence intervals (CI), and concordance index (kappa).

**Results:** Laguna ONhE glaucoma discriminant function (GDF) was among the indices of greatest area under the ROC curve (AUROC) (CI=0.88-0.96), similar to that obtained with Bruch's membrane opening-minimum rim width (BMO-MRW) of Spectralis (CI=0.89-0.97). Diagnostic concordance between the two was good (kappa =0.691) and similar to that observed, for example, between vertical cup/disk (C/D) ratio and retinal nerve fiber layer thickness (RNFT) of Cirrus (kappa=0.656). Based on hemoglobin information, Laguna ONhE estimation of rim and cup shape and size showed AUROC equivalent to those of Cirrus (Cirrus vertical C/D ratio CI=0.84-0.94, Estimated Laguna ONhE vertical C/D ratio CI=0.83-0.94). For a specificity of 95.7%, Laguna ONhE (estimated) and Cirrus vertical (measured) C/D ratio presented the same cut-off value (0.71). The reproducibility of Laguna ONhE indices measured with ICC was: GDF (CI=0.94-0.97), estimated Hb C/D area ratio (CI=0.95-0.98), estimated Hb C/D vertical ratio (CI=0.95-0.98). This proved similar to the Cirrus indices reproducibility: C/D area ratio (CI=0.91-0.96), C/D vertical ratio (CI=0.96-0.98). Cirrus RNFT reproducibility was slightly better (CI=0.98-0.99). Perimetric indices showed slightly lower diagnostic capacity, but this was not statistically significant: Mean defect AUROC (CI=0.81-0.92) and square root of loss variance AUROC (CI=0.78-0.90).

**Conclusions:** Laguna ONhE showed high diagnostic capacity and reproducibility, equivalent to other methods such as OCT. This procedure provides information different from functional or morphological data, related with optic nerve head perfusion. Morphological estimation using Laguna ONhE showed a similar range of diagnostic capacity in the sample analyzed.

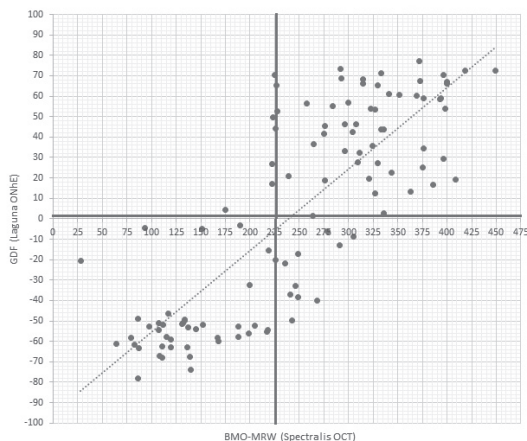
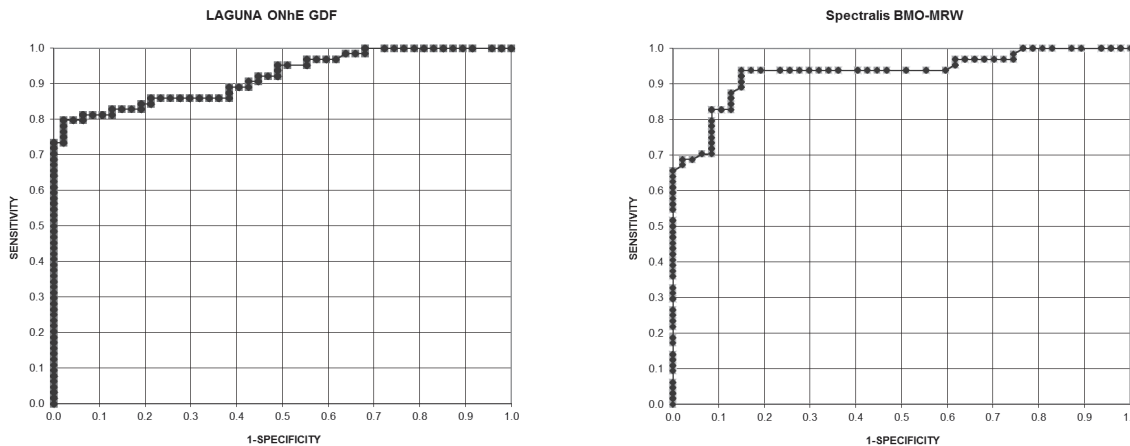


Figure: For a specificity of 95.7% the sensitivity of Laguna ONhE GDF was 79.7% (cut off= 2.4) and the sensitivity of Spectralis BMO-MRW was 68.8% (cut off= 225.6 microns).

ADDITIONAL FIGURES



**EXAMINING THE STRUCTURE-FUNCTION RELATIONSHIP IN GLAUCOMA WITH ACHROMATIC PERIMETRIC STIMULI EXHIBITING COMPLETE SPATIOTEMPORAL SUMMATION**

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**Purpose:** To investigate the relationship between retinal nerve fiber layer (RNFL) thickness and achromatic contrast thresholds collected using perimetric stimuli scaled to exhibit complete spatial, temporal or spatiotemporal summation.

**Materials and methods:** Fourteen patients with open-angle glaucoma (mean age: 68 years, mean MD: - 3.7 dB) and four healthy controls (mean age: 62.5 years, mean MD: 0.67 dB) were recruited for this study. Contrast thresholds were measured at four diagonal locations at 8.8° eccentricity for a GIII equivalent stimulus (0.43 deg.) of duration 200 ms (standard SAP stimulus; G), a GIII stimulus scaled to the critical duration (tc) for this stimulus in healthy observers (32 ms; T), and a stimulus scaled to the localized Ricco’s area (RA) in each subject and duration equal to tc for a RA equivalent stimulus in healthy observers (45 ms; ST). RNFL thickness measurements were collected using a Spectralis OCT (Heidelberg Engineering). Differences in both luminance ( $\Delta I$ , cd/m<sup>2</sup>) and contrast energy thresholds (expressed as contrast energy; cdm- 2.s.deg<sup>2</sup>) for each scaled stimulus were compared to thresholds for the G stimulus using a Wilcoxon rank sum test at all test locations. Passing Bablok regression was used to examine the relationship between contrast energy thresholds for the various functional measures collected and corresponding RNFL thickness.

**Results:** Contrast energy thresholds were significantly higher in the glaucoma group for all stimuli compared to healthy subjects (all  $P < 0.05$ ). There was no statistically significant difference in contrast energy thresholds in the glaucoma group for the T and ST stimuli compared with the G stimulus (all  $P > 0.05$ ). A significant increase in luminance contrast thresholds was, however, observed for all scaled stimuli compared to the G stimulus (all  $P < 0.001$ ). A statistically significant correlation was observed between contrast energy thresholds for all stimuli and corresponding RNFL thickness (all  $P < 0.05$ ). Permutation analysis revealed there to be no statistically significant difference ( $P > 0.05$ ) in the strength of this relationship for any stimulus examined.

**Conclusions:** Whilst a statistically significant relationship between measures of visual function and retinal structure are seen for all stimuli in this study, there was no difference in the strength of this association for the stimuli investigated. As spatiotemporal summation is known to change in glaucoma it is possible that this alteration is moderated at a more distal location in the visual pathway.

**ADJUSTING CIRCUMPAPILLARY RETINAL NERVE FIBER LAYER THICKNESS PROFILE MEASURED WITH OPTICAL COHERENCE TOMOGRAPHY USING THE RETINAL ARTERY POSITION IMPROVES THE STRUCTURE-FUNCTION RELATIONSHIP**

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**Purpose:** To investigate whether correcting the circumpapillary retinal nerve fiber layer (cpRNFL) thickness profile, using retinal artery position and papillomacular bundle tilt, can improve the structure-function relationship in glaucoma patients.

**Materials and methods:** Spectral-domain optical coherence tomography (SD-OCT) and visual field measurements were conducted in 142 eyes of 90 subjects with open angle glaucoma. The SD-OCT cpRNFL thickness profile was corrected for retinal artery position and/or papillomacular tilt in all twelve 308 sectors of the optic disc, and the structure–function relationship against corresponding 308 sectorial retinal sensitivity was investigated by using linear mixed model.

**Results:** Applying a correction to the cpRNFL thickness profile for retinal artery position resulted in a stronger structure–function relationship in all 12 sectors of the optic disc. Furthermore, applying a further adjustment for papillomacular tilt resulted in a further improvement in 9 of 12 sectors.

**Conclusions:** Correcting cpRNFL profile, using the retinal artery position significantly strengthened the structure-function relationship. In most optic disc sectors, using the papillomacular bundle tilt improved cpRNFL thickness measurements.

## **AUTOMATICALLY IDENTIFYING THE TEMPORAL RAPHE FROM OCT MACULAR CUBE DATA**

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**Purpose:** We have previously described a method for determining customised maps between structure and function for individual patients which requires knowledge of the position of the temporal raphe. Non custom, high resolution OCT scanning is typically used to visualise the temporal raphe. The aim of this study was to determine a method for automatically determining the temporal raphe from more commonly collected macula cube scans, and to validate against high resolution transverse section analysis scans.

**Materials and methods:** Horizontal and vertical macular cubes (B-scan separation between 96 and 122  $\mu\text{m}$ ) were acquired from 14 healthy participants (Spectralis OCT, Heidelberg Engineering). Higher density cubes with scan separation of 11  $\mu\text{m}$  were also acquired from the same eyes. These latter scans were assigned to 3 experienced graders for subjective location of the raphe, providing the “ground truth” by which to assess the accuracy of the automated methods operating on the lower density data. Several approaches for automatically identifying the raphe were compared, using either thickness or intensity data from the scans.

**Results:** The results show that vertically oriented scans, purposeful misalignment of the pupil to avoid reflective artefacts, and the use of intensity as opposed to thickness of the nerve fibre layer were all critical to minimise error in automatically finding the raphe. The best performing automated approach involved projection of a fan of lines from each of several locations across the foveal pit; in each fan the line of dimmest average intensity was identified. The centroid of the crossing points of these lines provided the raphe orientation with an average error of 1.5° (range = 0.5 - 4.4°) relative to the mean of the human graders. The difference of opinion between human graders averaged 1.6° (range = 0.1 - 3.3°).

**Conclusions:** It is possible to automatically determine the position of the temporal raphe from macular cube scans with a degree of accuracy comparable to the differences of opinion between clinical graders. Automatic identification of the temporal raphe could be incorporated into a clinical tool to create custom structure-function maps for individuals using an OCT protocol that is relatively standard and clinically practical.

## **CONVENTIONAL AND COMPUTATIONAL (PATTERN RECOGNITION) DERIVED LOSS OF RETINAL GANGLION CELLS DURING AGING**

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**Purpose:** Retinal ganglion cell loss occurs as a function of age. Various methods have been employed to determine the pattern of age-related retinal ganglion cell layer (RGCL) thinning to allow the discrimination of aging changes from disease-related loss. The purpose of this study was to investigate the normal retinal ganglion cell layer (RGCL) thickness using retinal partitioning provided by the Spectralis optical coherence tomographer (OCT) as a function of age and determine the rate of thinning within the macular region. Additionally, we compared conventional analysis using linear regression of individual locations with isotransitional zones identified with computational approach (pattern recognition).

**Materials and methods:** OCT data from one eye of subjects who attended the Centre for Eye Health were included in the study (n =201). Exclusion criteria were age (< 20 years); sign of ocular disease that may impact on the integrity of the RGCL, including glaucoma, ocular hypertension; high ametropia; and suspicion of glaucoma based on visual field or optic disc appearance/imaging results. The final cohort had an age range of 20-85 and were separated into 7 decade based subgroups (average n=28.7 per group). The Spectralis OCT posterior pole scan for each subject was extracted and the average RGCL thickness values obtained for each of the 64 grid locations within the measurement area (approximately 6.88x6.88mm). Linear regression analysis was also conducted at each test location. For pattern

recognition, the thickness of each grid was converted to a pixel value and analyzed using an unsupervised classification (ISODATA clustering; PCI, Canada) using the decade subgroups. Separability of the identified clusters was confirmed using transformed divergence (TD) value at a criterion of  $>1.9$ .

**Results:** Linear regression showed a significant ( $p<0.05$ ) age-dependent reduction in RGCL loss in 46 of the 64 grid locations. Most grid locations that did not show significant change either were located around major retinal vessels or corresponded to the foveal pit. Pattern recognition identified 8 distinct isotransitional zones based on the pattern of RGCL thickness reduction, generally arranged in a concentric pattern; dot plot analysis of the RGCL change revealed a biphasic reduction in thickness with the cross-over at approximately 60 years of age.

**Conclusion:** Analysis of the Spectralis OCT macular scan confirmed RGCL thinning occurs as a result of aging. Pattern recognition revealed isotransitional zones generally grouped in a concentric pattern, suggesting that age related RGCL thinning is dependent on retinal eccentricity. Further, pattern recognition confirmed a biphasic change consistent with reported functional loss in contrast sensitivity. The normative RGCL thickness range and pattern of loss form the foundation for future investigations in ocular disease.

## PERIMETRY II

### PATTERN RECOGNITION APPLIED TO STATIC PERIMETRY REVEALS UNIQUE CONTRAST SENSITIVITY ISOCONTOURS ACROSS THE VISUAL FIELD

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**Purpose:** Isocontours from kinetic perimetry indicate that the visual system displays similar sensitivities across the visual field (VF) yet static perimetric contrast sensitivity isocontours (CSIs) have remained cryptic. Consequently, traditional static VF assessment involves statistical tests using prefigured sensitivity values in predetermined locations rather than identifying regions of CSIs. We hypothesized that static VF CSIs can be revealed using computational techniques (pattern recognition) and the number of CSIs would vary depending upon: (a) Goldmann test size, (b) the shape of the CS function (Hill of Vision), and (c) test grid sampling density profile.

**Methods:** The Humphrey Field Analyser (HFA) was used in full-threshold mode and measured Goldmann I to V (GI-GV). Normal subjects of various ages underwent foveal + 30-2 (N=58) or 10-2 grid (N=45) testing. The data were converted to a 50 year-old equivalent, randomly assigned into groups to generate multiple group-averaged data sets per test size. These data were converted to pixel values and analysed using unsupervised classification (ISODATA clustering; PCI, Canada). Class separation (unique CS signatures), was confirmed using transformed divergence  $>1.9$ . Post-classification analysis included the extraction of dot plots of the various CSIs for the different test grids and test size.

**Results:** Static perimetry displayed similar patterns to those of kinetic perimetry: symmetrical central CSIs and CSIs extending further out for inferior-temporal eccentricities. For the 30-2 grid, the number of CSIs varied with test size [GI (6 signatures) → GIII (4 signatures) → GV (3 signatures)]. The number of test points included in each isocontour increased leading to wider isocontours with increasing test size and the foveal point incorporated with other central points for GV. When using the 10-2 grid, CSIs again varied with test size [e.g. GIII (5 signatures) → GV (1 signature)], but the discrimination was less obvious for GI and GIII (both yielding 5 signatures), likely due to both displaying similar CS shaped changes for central locations created by high density sampling. GV showed a flat CS profile in central vision reflected in a single isocontour signature incorporating all test locations within the 10-2 grid.

**Conclusions:** Pattern recognition revealed isocontours in static perimetry with similar characteristics to those of kinetic perimetry. The number of CSIs was dependent upon test size with the maximum number provided by test stimuli operating within complete spatial summation. The 30-2 test pattern has poor sampling density for central vision, highlighted by the fact that multiple CSIs are missed and identified by the 10-2 grid. Extraction of dot plots allows for CSI profiles to be provided, allowing test points belonging to the same signature group to be averaged and analysed collectively in patients with ocular disease.

### ANALYSES OF GAZE POINTS DURING SIMULATED DRIVING IN NORMAL AND GLAUCOMA SUBJECTS

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**Background:** The shift of gaze points while driving and its association with traffic accidents is a recent focus of studies. Most of the previous studies, however, examined only normal subjects with unimpaired vision and few studies examined subjects with visual field defects (VFD). We carried out a comparative study between individuals with normal vision and those with

glaucomatous VFD where gaze movements during simulated driving were analyzed and correlated with the status of VF.

**Subjects and methods:** The current study included 117 normal subjects with unimpaired vision aged  $50.2 \pm 15.6$  yrs., and 75 primary open angle glaucoma patients aged  $65.24 \pm 9.85$  yrs. whose mean of VF sensitivity values of the binocular integrated VF of Humphrey Perimeter 24-2 SITA-S test results (BIVF) was  $21.18 \pm 6.15$  dB (mean  $\pm$  SD). The driving simulations were performed using Honda Safety Nave Glaucoma Edition 2 (Sanuki-Kunimatsu S et al. *BMH Open* 2015Sep;57:457-462) equipped with an eye tracking system (Eye Mark Recorders-9, NAC Image Technology Inc., Tokyo, Japan). All gaze points during simulated driving were measured. The sampling rate was 30 frames per second. EMR-dFactory eye mark analysis software (NAC, Image Technology Inc.) was used to analyze gaze points. The ellipse containing 95% of the measured gaze points (Gaze point ellipse), the dispersion index of the gaze point (Susuki Y et al. *SICE Journal of Control, Measurement and System Integration* 2016) were determined for each scenario of simulated drivings.

**Result:** The area of gaze point ellipse was greater in normal subjects than in glaucoma subjects (Wilcoxon rank sum test  $P < 0.0001$ ) and it became smaller as the glaucoma stage advanced ( $p < 0.0001$ ). The dispersion index of the gaze point was larger in glaucoma subjects. (Wilcoxon rank sum test  $P < 0.0001$ ). The Area of gaze point ellipse of participants without accidents while driving was greater than ones with accidents (Wilcoxon rank sum test  $P < 0.0001$ ) and the dispersion index of the gaze point of participants without accidents while driving was smaller than that of those with accidents. (Wilcoxon rank sum test  $P < 0.0001$ )

**Conclusion:** Gaze point analysis during simulated driving may be useful in estimating the type of danger-specific possibility of traffic accidents in the real world and for safe driving, especially that of patients with VFD.

## PHYSIOLOGIC STATOKINETIC DISSOCIATION IS ELIMINATED BY EQUATING THE PSYCHOPHYSICAL PROCEDURES OF STATIC AND KINETIC PERIMETRY

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**Purpose:** Discordance between static contrast detection thresholds and kinetic perimetry isopters has been reported in both patients with disease, and in normal observers ("physiologic statokinetic dissociation (SKD)"). Our aim was to examine the extent of physiologic SKD obtained from conventional perimetry (Humphrey Visual Field Analyzer, HFA; and Goldmann manual perimetry) and a psychophysical test that equates the static and kinetic detection task using an objective two-interval forced choice procedure (2IFC). We test the hypothesis that SKD is due to methodological differences between the procedures, in particular that they assess different points on a frequency of seeing (FOS) curve.

**Materials and methods:** In Experiment 1, the HFA was used in static or kinetic mode to measure contrast detection thresholds and inward isopters for a Goldmann II target ( $n=8$ ). The Goldmann perimeter (size II, 24 dB; velocity  $\sim 3^\circ/s$ ) was used to measure inward and outward isopters. The HFA 30-2 and custom test patterns (extending the temporal field to  $51^\circ$ ) were used to obtain a spatial map of static thresholds, upon which isopters were superimposed. In Experiment 2, Method of Constant Stimuli was used with a 2IFC procedure to determine the FOS of a fixed contrast size II stimulus as a function of eccentricity ( $n=6$ ). Nine positions were tested ( $\pm 1.5^\circ$  offset steps), centred upon  $24^\circ$  nasal and  $37^\circ$  temporal locations. The stimuli were presented statically and with inward or outward movement (at  $4^\circ/s$ ) for 200 ms.

**Results:** Experiment 1 showed that kinetic inward and outward isopters formed, using a 24 dB test stimulus, an isocontrast region ( $\sim 12^\circ$  wide) within which the average static perimetry thresholds were approximately 24 dB. Experiment 2 showed no significant differences between the eccentricity thresholds of static, kinetic inward or kinetic outward presentations nasally ( $p=0.3998$ ) and temporally ( $p=0.8652$ ). Eccentricity thresholds were approximately equal to the midpoint of the isocontrast region (i.e. offset of  $0^\circ$ ) found in Experiment 1 for static, inward and outward procedures for nasal ( $0.41^\circ$ ,  $0.75^\circ$  and  $0.95^\circ$  respectively), and temporal meridians ( $-0.20^\circ$ ,  $0.20^\circ$  and  $0.11^\circ$  respectively). The slopes of the FOS curves were not significantly different across presentation types (nasal:  $p=0.9537$ , temporal:  $p=0.8652$ ), suggesting that spatial uncertainty is the same in the procedurally equated tasks.

**Conclusion:** Physiologic SKD was not apparent when static and kinetic stimulus detection tasks and their testing conditions were psychophysically equated. Criterion bias, as a result of methodological differences, particularly the subjective nature of conventional kinetic perimetry, largely accounts for the disparity found when comparing isopter position to static contrast thresholds.

## CAN FUNCTIONAL AND STRUCTURAL OUTCOMES PREDICT VISION-RELATED QUALITY OF LIFE IN AGE-RELATED MACULAR DEGENERATION?

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**Purpose:** To evaluate, in individuals with age-related macular degeneration (AMD), the relationship between functional and structural outcome measures and vision-related quality of life (VRQoL).

**Materials and methods:** The cohort comprised 45 participants with early to late AMD. The median age was 80 yrs

(IQR 75, 83.5 yrs). All participants were otherwise ophthalmologically normal, with the exception of mild lens opacities ( $\leq$ Grade 2, LOCS III), and had no cognitive impairment by the Mini-Mental State Exam. Participants underwent ETDRS distance visual acuity (VA); Mars Letter contrast sensitivity (CS); International Reading Speed Texts; MAIA microperimetry (40 location 7° stimulus pattern; size III stimulus; 1.27cdm<sup>-2</sup> background); volumetric imaging with the Cirrus SD-OCT (20°x 20° scan, 512 x 128 A-scans); and Impact of Vision Impairment (IVI) questionnaire which was delivered face-to-face. Differential light sensitivity was referenced to a normative database (n=70). Volumetric scans were segmented (9 boundaries, 8 retinal layers) using the Iowa Reference Algorithm (Retinal Image Analysis Lab, Iowa). Robust regression was used to model the relationship between the functional and structural measures and VRQoL.

**Results:** The means (SD) were: Binocular VA, 0.13 LogMAR (0.18); Mean Sensitivity 21.75dB (5.81); Total Deviation -6.67dB (5.81); Pattern Deviations -4.17dB (2.95); number of locations exhibiting a probability level  $\leq$ 5% by TD probability analysis, 20.3 locations (13.9) and by PD probability analysis 8.6 locations (8.0); reading speed, 154.8wpm (47.9); and mean CS, 1.37 log units (0.27). The mean (SD) total retinal thickness, retinal pigment epithelium and outer segment layers were 292.0 $\mu$ m (22.2), 114.4 $\mu$ m (0.8) and 29.0 $\mu$ m (5.3), respectively. The total receptor layer plus RPE had the strongest individual relationships with functional measures. Binocular VA, Mean Sensitivity, reading speed and total receptor layer were predictors of IVI (reading and accessing information subscale) score and accounted for 25.3% of the variance.

**Conclusions:** Binocular VA, Mean Sensitivity, reading speed and total receptor layer thickness were weakly associated with VRQoL score. Longitudinal evaluation should be undertaken to determine whether these measures can be used as indicators of progressive deterioration in VRQoL.

## PROGRESSION ANALYSIS I

### STRUCTURAL CHANGE CAN BE DETECTED IN ADVANCED GLAUCOMA EYES

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**Purpose:** To compare spectral domain optical coherence tomography (SD-OCT) standard structural measures and a new 3D volume optic nerve head (ONH) change detection method for detecting change over time in severely advanced glaucoma (OAG) patients.

**Materials and Methods:** Thirty-five eyes of 35 patients with very advanced glaucoma (defined as visual field mean deviation < -21dB) and 46 eyes of 30 healthy subjects to estimate aging changes were included. Circumpapillary retinal fiber layer thickness (cpRNFL), minimum rim width (MRW), and macular retinal ganglion cell - inner plexiform layer (GCIPL) thicknesses was measured using the San Diego Automated Layer Segmentation Algorithm (SALSA). Progression was defined as structural loss faster than age-related change (>95<sup>th</sup> percentile of healthy eyes). 3D volume ONH change was estimated using the Bayesian-kernel detection scheme (BKDS) which does not require extensive retinal layer segmentation. In addition, 50 eyes from stable glaucoma patients imaged once every 5 weeks were used to train the 3D volume BKDS method to set the threshold for change to reduce the likelihood that changes due to measurement variability were classified as progression due to glaucoma.

**Results:** Glaucoma patients and healthy subjects were followed for a mean of 3.5  $\pm$  0.9 years and 2.8  $\pm$  0.4 years, respectively. The number of progressing glaucoma eyes identified was highest for 3D volume BKDS 13 (37%), followed by GCIPL 11 (31%), cpRNFL 4 (11%), and MRW 2 (6%). In advanced OAG eyes, only the mean rate of GCIPL change reached statistical significance -0.18  $\mu$ m / year (P=0.02); the mean rates of 24-2 visual field MD, cpRNFL and MRW change were not statistically different from zero. In healthy eyes, the mean rates of cpRNFL, MRW and GCIPL change were significantly different from zero (all P < 0.001); the mean rate of visual field MD was not (p=0.65).

**Conclusion:** GCIPL and 3D volume BKDS show promise for identifying change in severely advanced glaucoma. These results suggest that structural change can be detected in very advanced disease. Longer follow-up is needed to determine whether changes identified are false-positives or true progression.

### PERCENTILE PLOT - A NEW GRAPHICAL ANALYSIS OF THE QUANTITATIVE ASPECTS OF PROGRESSION

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**Purpose:** Visual field progression appears in various patterns, which are only incompletely described by typifications like diffuse loss and localized loss. Most field series present a mixture of diffuse and localized progression. Many other field series have areas with improvement as well as areas with progression, representing so-called balanced trends. As the existing statistical methods of progression analysis focus either on diffuse (global indices) or localized progression



(pointwise pattern analysis), there is a need for a method that is sensible for partial changes in the field.

**Materials and methods:** A graphical method was developed, that shows visual field percentiles, based on the defect depth / total deviation values, which are plotted versus time. The diagram shows 11 such lines (percentile 0 to 100 with a spacing of 10). In addition, regression analysis is calculated for each percentile line and significance is shown in a color change of the line. The new method was tested on 50 visual field series with at least 5 fields.

**Results:** The Percentile Plot (PP) shows progression very clearly. It allows a distinction between diffuse and localized progression at a glance. Changes of small portions of the field are visible as well. The PP is able to identify on-going progression in advanced fields when the ceiling effect limits progression of MD and reverses the progression of PSD / LV. Compared to local analysis, the PP is more powerful as each line is based on 6-7 measurements. Compared to regional analysis, the PP is more powerful if several regions are partly affected by progression, but each single region does not exceed the limits of significant change. Estimations which are made from the graphical impression of the plot are affirmed by the significance color of the lines.

**Conclusions:** PP is a very useful tool that closes the gap between global and local progression analysis. In some cases, progression is identified easier and earlier by PP. This new diagram also helps to a better understanding of the nature of progression (local/diffuse) in individual cases. PP gives no spatial information and should be used only in conjunction with topographical progression analysis.

## SIGNIFICANT GLAUCOMATOUS VISUAL FIELD PROGRESSION IN THE FIRST TWO YEARS: WHAT DOES IT MEAN?

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**Purpose:** It has been recommended that six visual field examinations be performed in the first two years after glaucoma diagnosis so that rapid visual field progression ( $\leq -2\text{dB}/\text{year}$ , using ordinary least squares regression over time of the summary index Mean Deviation, or MD) can be ruled out. Here I investigate how predictive a statistically significant regression slope is of truly rapid visual field progression. I also investigate how looking for progression after each new field - rather than simply at two years - alters diagnostic performance.

**Materials and methods:** I simulated visual field series ( $N=100,000$ ) spaced at four-monthly intervals for the first two years. MD values had a standard deviation of 1dB. The true underlying rates of progression were selected from a modified hyperbolic secant with parameters averaged from fits to large datasets from Canada, Sweden and the USA.

**Results:** The power to detect rapid progression at two years was greater than 0.8, consistent with previous work (Chauhan *et al.*, 2008. *Brit J Ophthalmol* 92:569). If progression is defined as a significantly negative slope either at or any time before two years, the calculated power was not altered greatly (increase of 0.02). The positive predictive value (PPV) for rapid progression was 0.47 after two years, indicating that a significant regression slope was more likely to result from less than rapid progression. The negative predictive value (NPV) was  $>0.99$ , indicating that a failure to find significant progression was highly suggestive that rapid progression was not present. When using the criterion that a significant regression also had to have a slope of  $\leq -2\text{dB}/\text{year}$ , the PPV for rapid progression reduced substantially to 0.18 but the NPV was essentially unchanged (NPV  $>0.99$ ).

**Conclusions:** Although performing multiple visual fields in the first two years provides appropriate power to detect rapid progression, a significant regression slope in the first two years is not highly predictive of rapid progression, particularly so if slopes  $\leq -2\text{dB}/\text{year}$  only are considered. Therefore, confirmatory signs of rapid disease progression should be sought before attempting drastic treatment changes.

## THE USEFUL DYNAMIC RANGE OF STANDARD AUTOMATED PERIMETRY FOR PROGRESSION IN GLAUCOMA: SIZE III VS. SIZE V

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**Background:** It has been shown that the effective dynamic range for standard automated perimetry with Goldmann III stimuli may be considerably smaller than previously thought (Wall *et al.*, 2010). Gardiner *et al.* (2016) have recently shown that "censoring" of size III threshold estimates  $< 20$  dB has little effect on the ability to detect glaucomatous progression.

**Purpose:** Since stimulus size V has lower test-retest variability than size III, our goal is to compare the effect on visual field progression of selectively removing parts of the dynamic range (i.e. censoring of threshold estimates) with these two stimulus sizes.

**Methods:** Pointwise Linear Regression (PLR, Wall *et al.*, 2010), and PoPLR (O'Leary *et al.*, 2015), were performed on the Iowa Variability in Perimetry (VIP) study data (120 glaucoma subjects and 60 normals tested every six months for 4 years). With PLR, data were censored at each dB level, and hit rates were derived for a series of slope and p-value criteria of: 1) all progressing test locations, 2) 3 or more progressing test locations, and 3) 4 or more contiguous progressing test locations. With PoPLR, a single p-value for significant change was derived from 5000 permutations.

**Results:** The results show that size V stimuli performed at least as well or slightly better than size III stimuli at measuring change over time (progression). With both PLR criteria and PoPLR, omitting threshold estimates below 20 to 25 dB

had little effect on the progression rates in glaucoma patients. The comparison of size III versus size V data across a combination of PLR slope and p-value criteria suggests an advantage of size V stimulus for more conservative p-value criteria (<0.01), while the least conservative p-values favor size III data over the range of 0 dB to 20 dB. This hit rate advantage of size III is rapidly offset by an increasing type I error (false-positives; measured through “improvements” of > PLR slope of 1 dB per year).

**Conclusion:** There is no clinically meaningful loss of sensitivity to visual field progression when threshold estimates < 20 dB are removed. This confirms that there is minimal benefit in extending visual field measurements once locations have been damaged beyond these values. Size V testing for longitudinal glaucoma progression analysis performs as well as, if not better than size III.

### CLUSTER TREND ANALYSIS FOR DETECTION OF VISUAL FIELD CHANGE

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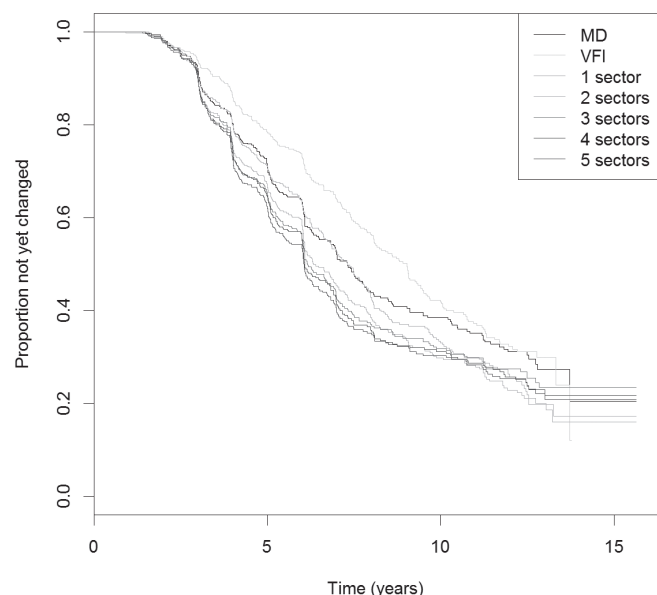
**Purpose:** Global perimetric indices may miss localized defects, but pointwise methods lack specificity and may be harder to interpret. Between these two extremes, the Octopus perimeter (Haag-Streit AG) provides cluster trend analysis as part of the EyeSuite software. The program averages deviations from age-corrected normal within 10 pre-defined clusters, and determines whether those cluster averages are significantly worsening. In this study, we assess this technique to detect change.

**Methods:** Visual fields (HFA; 24-2 SITA standard) were collected from a “test-retest” dataset consisted of 48 eyes of 28 participants, tested exactly 5 times within a few weeks; and a similar but separate “longitudinal” dataset consisted of 508 eyes of 315 participants, tested approximately every 6 months for a mean of 12.9 visits (range 4-23). Ten “Cluster Defect” (CD) values were extracted, defined as the mean Total Deviation within each cluster, together with Mean Deviation (MD) and Visual Field Index (VFI).

The five fields per eye in the test-retest cohort were assigned 6-monthly “test dates”. Rates of change of each CD, MD and VFI were calculated by linear regression. If they worsened over ‘time’, the p-value was recorded; otherwise, the series was assigned p=1.0. The 10 clusters’ p-values were sorted from smallest ( $P_1$ ) to largest ( $P_{10}$ ). This was repeated for all 120 possible re-orderings per eye, giving 5760 sets of 10 ordered p-values. Criteria for “change” were defined as “ $\geq N$  clusters with  $p < Crit_N$ ”, where  $Crit_N$  was defined as the 288<sup>th</sup> smallest value of  $P_N$ . This means that each criterion had 95% specificity in the test-retest cohort.  $Crit_{MD}$  and  $Crit_{VFI}$  were calculated similarly.

For each eye in the longitudinal cohort, the first time point was found at which each criteria for “change” was met. A Cox proportional hazards survival model was used (accounting for two eyes per individual) to determine whether one index detected change significantly sooner than another.

**Results:** Kaplan-Meier curves showing how soon each criterion detected change are shown below. Criteria with N between 2 and 7 outperformed MD with  $p < 0.001$ . Change was detected in 172 eyes both using cluster trend analysis with N=4 and using MD. Change was detected in a further 44 eyes with cluster trend only, and 11 eyes with MD only. VFI performed worse than MD with  $p = 0.002$ .



| Criterion | $Crit_N$ | Median years to detect change (95% confidence interval) |
|-----------|----------|---|
| MD        | 0.078    | 7.3 (6.8 – 7.9)   |
| VFI       | 0.085    | 9.0 (8.1 – 9.5)   |
| 1 sector  | 0.012    | 7.3 (6.8 – 7.9)   |
| 2 sectors | 0.055    | 6.3 (6.1 – 7.1)   |
| 3 sectors | 0.110    | 6.2 (6.0 – 6.9)   |
| 4 sectors | 0.174    | 6.1 (6.0 – 6.8)   |
| 5 sectors | 0.252    | 6.1 (5.7 – 6.5)   |
| 6 sectors | 0.337    | 6.1 (6.0 – 6.7)   |
| 7 sectors | 0.433    | 6.1 (6.0 – 7.0)   |
| 8 sectors | 0.553    | 6.6 (6.1 – 7.2)   |
| 9 sectors | 0.705    | 6.9 (6.4 – 8.0)   |

**Conclusions:** Cluster analysis seems to detect change sooner than MD and VFI, for the same specificity. Looking for 4 or 5 clusters changing may be a sensitive and specific criterion to use, detecting change over a year sooner than MD.

## POSTER SESSION A

### 1. FIXATIONAL EYE MOVEMENTS MEASURED BY EYE TRACKING SYSTEM EMR-9 IN THE STATIC VISUAL FIELD TESTING

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**Purpose:** In the threshold measurement of static visual field testing, various factors influence the results. Recently a new perimeter equipped with a fixation tracking system has been developed, which led to increasing demand for highly precise threshold measurement. However, the visual field testing needs the eye fixated at one point, while the involuntary fixational eye movement is a vital reaction. It is not clear how this fixational eye movement occurs during testing and influences the threshold. In this study, we investigated fixational eye movements during threshold measurement using the Eye Mark Recorder EMR-9 (NAC Image Technology, Inc., Tokyo, Japan) that is an eye tracking measurement and analysis system.

**Materials and methods:** We tested 10 eyes of 10 normal subjects between 24 and 33 years of age. The automated perimeter Octopus900 (Haag-Streit International, K oniz, Switzerland) combined with EMR-9 was used to measure fixational eye movements. We modified the eye frame of the EMR-9 to hold an eye camera so that we can use lenses adapted to subject's refraction. The Open Perimetry Initiative was used to examine the fixational movement at the time of target detection. We used the target that is 10 dB brighter than the normal values based on ages. The target stimulus duration was 200 ms. Eight testing points were arranged on the 45° meridian with the interval of 5°. Subjects were instructed to fixate on the central point in the same way as in the conventional testing and we measured fixational eye movement at each point at 400 ms before target presentation and at 600 ms after target presentation. The sampling rate of 240 Hz was used. Reproducibility was checked by measuring 4 times at each testing point. Fixational eye movement data were first smoothed by applying a five-point moving median filter, and then differentiated with a five-point low-passed differentiation filter to obtain eye velocity signals. A microsaccade was defined as a region in which eye velocity signals exceed a threshold of 250 unit/sec.

**Results:** The amplitude of fixational eye movement which occurred from the start to the end of testing was  $0.55 \pm 0.29^\circ$ . At the presentation and detection of the target, the frequency of microsaccade was significantly decreased compared with that before target presentation. At 600 ms after target presentation, the frequency significantly increased compared with that before target presentation and at the time of detection.

**Conclusions:** The amplitude of fixational eye movement was about  $0.5^\circ$  and the frequency of microsaccade was decreased synchronizing with target presentation timing. In the future, it might be possible to objectively evaluate the visual field using microsaccade measurement.

### 2. DEVELOPMENT OF A ROBOT ("LORIS") FOR VISUAL FIELD TESTING USING A HIGH DYNAMIC RANGE (HDR) CAMERA

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**Purpose:** Actual subjects are often used when developing or evaluating an algorithm for automated visual field (VF) testing. However, there are issues such as variations in response, fatigue, and ethical problems. We developed a robot ("Loris") that can perform VF testing automatically and evaluated its usefulness.

**Subjects and methods:** Loris consists of a wide-angle lens, a high dynamic range camera, a solenoid to push the response button, a control computer, and VF testing software. When Loris detected a test target inside the cupola of the perimeter, the response button would be automatically pushed at a threshold value set beforehand. In this study, the set response threshold values for Loris were 5.5, 10.5, 20.5, and 25.5 dB. Using these threshold values, 30-2 full threshold test of the Humphrey field analyzer was performed. Virtual patients with glaucomatous VF defects were also assessed using the full threshold and SITA-Standard strategies and the results were compared.

**Results:** Loris revealed a peripheral VF range of 30°, and an upper limit of 32 dB for the measurable luminance range. The mean sensitivity (MS) with the set threshold values for the 30-2 test were  $3.1 \pm 1.3$  (5.5) dB,  $9.8 \pm 1.0$  (10.5) dB,  $19.8 \pm 1.1$  (20.5) dB and  $24.1 \pm 1.3$  (25.5) dB. The MS values according to eccentricity were:

Within 0° - 10°:  $4.2 \pm 0.7$  (5.5) dB,  $10.3 \pm 0.7$  (10.5) dB,  $20.5 \pm 0.9$  (20.5) dB, and  $25.0 \pm 0.7$  (25.5) dB.

Within 10° - 20°:  $3.4 \pm 0.9$  (5.5) dB,  $10.1 \pm 0.8$  (10.5) dB,  $20.2 \pm 0.8$  (20.5) dB, and  $24.6 \pm 0.8$  (25.5) dB.

Within 20° - 30°:  $2.7 \pm 1.3$  (5.5) dB,  $9.4 \pm 1.1$  (10.5) dB,  $19.4 \pm 1.1$  (20.5) dB, and  $23.6 \pm 1.3$  (25.5) dB.

For the virtual patients with glaucomatous VF defects, the MS for the full threshold was lower than that for the SITA-Standard.

**Conclusion:** It is suggested that Loris could be a useful testing device for development and evaluation of perimeters.

### 3. VISUAL FIELD PARADIGMS FOR ASSESSING FUNCTIONAL FIELD LOSS

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**Purpose:** Visual field assessment is not only important to monitor disease progression, but also to reflect and predict functional difficulty in the real world, including consideration of criteria for visual impairment registration. The aim of this study is to develop an appropriate method of assessing field loss which reflects its functional consequences.

**Methods:** 50 participants with peripheral field impairment undertook three custom binocular visual field tests on the Octopus 900 that assessed the field out to 60 degrees from fixation: a threshold, 10dB supra-threshold, and a 10dB kinetic assessment. The average mean threshold, percentage of stimuli seen, and visual field area were used as the main outcome measures for analysis. Scores for different areas of the binocular field were compared to self-reported mobility function. Results were also compared to currently available methods of assessing functional visual field including integrated monocular threshold fields, and Esterman tests.

**Results:** Greater visual field loss was associated with greater self-reported mobility difficulty ( $R^2=0.49$ ;  $R^2=0.49$  and  $R^2=0.59$  for threshold, supra-threshold, and kinetic assessment respectively, all  $p<.001$ ). Perceived mobility function related similarly to Esterman scores ( $R^2=0.53$ ;  $p<.001$ ) and integrated monocular threshold scores ( $R^2=0.39$ ;  $p<.001$ ). Mean duration of the kinetic test was 1min 26sec ( $\pm 9$ sec), while for binocular threshold assessment was 7min 40sec ( $\pm 21$ sec), and for supra-threshold assessment was 3min 10sec ( $\pm 23$ sec). The Esterman test took on average 6min 20sec ( $\pm 19$ sec), and the mean duration of the monocular threshold assessments was 9min 23sec ( $\pm 24$  sec).

**Conclusion:** Binocular visual field tests can reflect self-reported mobility function. Analyses indicate a similar relationship between perceived mobility function and the visual field regardless of the method of assessment. However, a kinetic assessment of visual field area may be quicker and as effective at predicting mobility function as full threshold assessment. We will use the results of this study to inform our development of a visual field test that is optimised for assessing the functional visual field.

### 4. RELATIONSHIP BETWEEN RETINAL ARTERY TRAJECTORY AND OCULAR BIOMETRY IN JAPANESE ELEMENTARY AND JUNIOR HIGH SCHOOL STUDENTS

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**Purpose:** Trajectory of the supra- or infra- temporal retinal artery is associated with the position of nerve fiber layer defect in glaucomatous eyes. However, there is no report about the changes of retinal artery trajectory (RAT) along with growth. Therefore, the purpose of this study was to investigate the difference of RAT in eyes between elementary and junior high school students and its relationship to ocular biometry.

**Materials and methods:** Prospective cross-sectional observational study of 108 right eyes in healthy elementary school students, 54 male and 54 female (age 8 or 9 years) and 149 right eyes in healthy junior high school students, 73 male and 76 female (age 12 or 13 years). Axial length (AL), anterior chamber depth (ACD) and lens thickness (LT) were measured with OA-2000 (TOMEY, Japan). Color fundus photograph was taken by 3D OCT-1 Maestro (TOPCON, Japan). The RAT was plotted in the color fundus photographs and fitted to a second degree polynomial equation ( $ax^2/100+bx+c$ ) by ImageJ. The coefficient "a" represented the steepness of the trajectories. The formula for the anterior segment length (ASL) was  $ACD+LT/2$ . The formula for the posterior segment length (PSL) was  $AL-ACD-LT/2$ . The RAT and ocular biometry differences between elementary and junior high school students were investigated using Mann-Whitney U test. The association between RAT and ocular biometry was investigated using Spearman's correlation analysis.

**Results:** AL and RAT of junior high school students were significantly greater than that of elementary school students ( $p<0.01$ ). The RAT was significantly associated with AL and PSL in elementary school students ( $R=0.25, 0.30, p<0.05$ ). The RAT was significantly associated with AL, ASL and PSL in junior high school students ( $R=0.35, 0.18, 0.33, p<0.05$ ).

**Conclusions:** Junior high school students have longer AL and narrower RAT than elementary school students. A long AL and PSL are associated with narrow RAT in elementary and junior high school students.

### 5. THE RELATIONSHIP BETWEEN THE TARGET ENERGY AND REACTION TIME AT THE LOCATION OF KINETIC THRESHOLD

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**Design and methodology:** Kinetic visual field testing has the problem of underestimated visual field area, which is affected by the reaction time (RT). We investigated the relationship between the target energy and RT at the location of kinetic threshold using automated kinetic perimeter. Five normal eyes of 5 normal subjects were tested using an Octopus

900 perimeter with the target size and luminance of I/1/4e, I/4e, I/3e, I/2e and I/1e and with the target speed from 1 to 10°/sec (total 50 target conditions). The coordinate for average response points (local kinetic threshold; LKT) of 50 target conditions were determined on each meridian of 135° and 225°. Each target was arranged with 1° of the eccentricity farther outside from the coordinate for LKTs and target was presented 1° farther outside each time we obtained the response. The coordinate for the final response points were determined and set as the starting coordinate for RT-vector. RT-vector of all target conditions was presented perpendicularly to each meridian. We examined the difference of RT between the target energy and RT for each target speed.

**Original data and results:** Significant negative correlation was observed between the target energy and RT for each target speed ( $r_s = -0.81 \sim -0.63$ ,  $p < 0.01$ , Spearman's rank correlation coefficient).

**Conclusion** (include a discussion about why this abstract is important): In automated kinetic perimetry, the target energy is one of the affecting factors for RT change. When we actually calculate the RT-corrected LKT, we should use the same target size and luminance that were used for the detection of the LKT for measuring RT.

## 6. AN INVESTIGATION OF THE ROBUSTNESS OF PREDICTION ACCURACY OF A DYNAMIC STRUCTURE-FUNCTION MODEL FOR GLAUCOMA PROGRESSION

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**Purpose:** We previously showed that there is no systematic difference in prediction error (PE) between the dynamic structure-function (DSF) model and ordinary least squares linear regression (OLSLR) over time (Hu et al, IOVS, 2014). In this study, we investigate the robustness of prediction accuracy of the DSF model in eyes with different combinations of trends for structural and functional measures over time.

**Materials and Methods:** 120 eyes of 120 patients with ocular hypertension or primary open-angle glaucoma were selected from the Diagnostic Innovations in Glaucoma Study or the African Descent and Glaucoma Evaluation Study. All patients had 11 visits over a period of 5 to 10 years, with rim area (RA) and mean sensitivity (MS) at each visit taken within 30 days. Visits were separated by at least 3 months. Using OLSLR to obtain the slope of RA and MS over time, patients were categorized in 4 groups: negative slopes for both RA and MS (RA-/MS-), positive slopes for both RA and MS (RA+/MS+), a positive slope for RA and a negative slope for MS (RA+/MS-), a negative slope for RA and a positive slope for MS (RA-/MS+). PE in estimating the 11th visit from the first 10 was obtained for OLSLR and the DSF model. The difference among the 4 groups in PE with DSF and OLSLR, respectively, and the difference of PE between these two methods were assessed by analysis of variance model.

**Results:** With the DSF, the mean PEs were 14.19, 10.83, 15.35, and 14.43 percent of mean normal, for RA-/MS-, RA+/MS+, RA+/MS-, and RA-/MS+, respectively. With OLSLR, the mean PEs were 14.03, 12.40, 14.95, and 13.07 percent of mean normal, respectively. The mean differences of PE between DSF and OLSLR in each group were -0.16, 1.58, -0.40, and -1.36 percent of mean normal. No significant difference in mean PE and mean difference of PE between two methods among groups was found. No systematic pattern in difference of PE at the 11<sup>th</sup> visit for the two methods along the magnitude change over time was identified.

**Conclusions:** The model performance in predicting the 11<sup>th</sup> visit for DSF was about the same as that for OLSLR. Prediction accuracy of the OLSLR and DSF models does not seem to differ for patients with agreement or disagreement in slope of RA and MS.

## 7. THE EFFECT OF CONCENTRIC CONSTRICTION OF THE VISUAL FIELD OF 10 AND 15 DEGREES ON AUTOMOBILE DRIVING

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**Purpose:** The condition of visual field (VF) constriction can be created artificially by having subjects with a normal VF wear pinhole glasses (PH). Even the PH of the same aperture creates a different level of VF constriction among individuals. Thus, there are few studies that have been conducted on strictly same visual angles. We devised PH with variable PH apertures to create specific visual angles. We evaluated the effect of concentric constriction of the VF on automobile driving, by comparing the number of accidents when subjects performed a glaucoma driving simulator (DS) with or without the PH.

**Materials and methods:** Eighty-eight subjects with a normal VF who performed the DS at Tajimi Iwase Eye Clinic were included. The PH with variable PH apertures were adjusted to mimic the conditions of concentric VF constrictions of 10

and 15 degrees, using a CLOCK CHART®. The subjects performed the DS (a total of eight scenes including six sudden appearances of vehicles), at first wearing PH (PH+) and then without the PH (PH-). Thirty-seven subjects were allocated to the 15 degree (PH15) group, and 51 subjects were allocated to the 10 degree (PH10) group. The number of accidents was compared between PH+ and PH- subjects in each group.

**Results:** In both the PH10 and PH15 groups, the number of accidents was significantly greater for the PH+ compared with the PH- group ( $p < 0.001$ ). In the comparisons between the PH15 and PH10 groups, the number of all types of accidents including the number of accidents due to sudden appearance of vehicles was higher in the PH10 group ( $p = 0.032$ ,  $p = 0.020$ ).

**Conclusions:** PH, which can create specific visual angles by adjusting the PH aperture, are useful in evaluating the effects of the conditions of peripheral VF on automobile driving.

## 8. AUTOMATED GLAUCOMA CLASSIFICATION IN VISUAL FIELDS

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**Purpose:** Automated perimetry is an efficient tool for the diagnosis of several eye diseases among which Glaucoma is often of great interest. Global indices such as mean sensitivity, mean defect, loss variance, etc. have particular importance for clinicians for Glaucoma diagnosis. However, such indices generally describe global aspects of the visual field and do not account for local and/or spatial information within visual field. Our goal is to explore the effect of local and spatial properties of visual fields in the identification of Glaucoma.

**Materials and Methods:** We are interested in expressing automatic Glaucoma identification from a machine learning point of view and define our problem as the classification of visual fields into two different classes being glaucomatous and nonglaucomatous. In order to both explore local aspects, or features, and their spatial extent within visual fields with respect to classification, we represent visual fields as voronoi diagrams and extract what is called Haar-like features from constructed diagrams. Then, we train a Boosted classifier that simultaneously produces strong classification performances but also results in the ranking of the features with respect to their contribution in identifying Glaucomatous visual fields.

**Results:** We applied the mentioned scheme to two different datasets and showed an improvement of Glaucoma diagnosis over the use of standard global indices. In particular, we obtained a 98.3% of ROC area performance which surpasses the performance of other classifiers with standard features. Besides, we produce importance maps reflecting the significance of different local regions of visual field in this classification task. Other classical classifiers such as Linear Discriminant Analysis and Quadratic Discriminant Analysis are also trained and tested with different features in order to assess the contribution of such local features in other setups.

**Conclusion:** This work studies the effect of using local information and spatial relationships inside the visual fields for automated Glaucoma diagnosis. Accordingly, it is shown that the local information is indeed useful and when combined with global indices, leads to improved assessment of Glaucoma. This approach could be also exploited in the identification of other defects or diseases that are harder to detect using standard visual field perimetry values or global indices.

THURSDAY SEPTEMBER 29<sup>TH</sup> 2016

## NEW INSTRUMENTS AND TECHNIQUES I

## PROPERTIES OF NORMATIVE DATA FOR THREE MULTIFOCAL PUPILLOGRAPHIC OBJECTIVE PERIMETRY (MFPOP) TESTS

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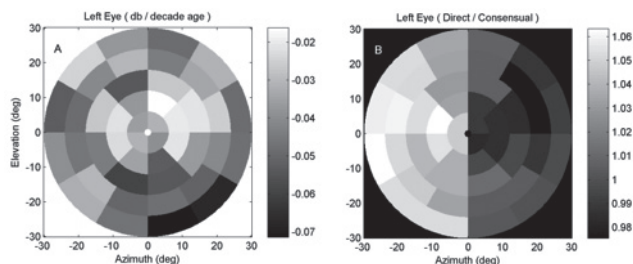
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**Purpose:** Multifocal pupillographic objective perimetry (mfPOP) assesses the visual fields of both eyes concurrently. This study produced normative data for 3 mfPOP methods: one macular and two wide-field tests for the FDA-cleared nuCoria Field Analyser (nCFA, Canberra, Australia).

**Materials and methods:** Responses of 168 normal control subjects aged 18 to 82 years were recorded using 3 variants of mfPOP. Tests were repeated about 2 weeks apart. Subjects were grouped into 5-year cohorts with a median of 12 subjects per cohort, half were males. Normal diagnosis was based upon: best corrected visual acuity, slit-lamp exam, Goldmann tonometry, and optic disc and posterior pole OCT scans. Diagnoses were confirmed by 2 ophthalmologists (RWE, OS) and a clinical optometrist (FS). All 3 mfPOP dichoptic test types presented 44 pseudorandomly-sequenced stimuli/eye at 11/s/eye. Recording duration was 6 min, divided into 9 segments of 40 s duration. The wide-field stimuli were either yellow on a yellow background (YY) or green on a red background (RG, e.g. Carle IOVS 54: 467-75) and extended  $\pm 30$  deg. The macular stimuli (MAC) were yellow on yellow and extended  $\pm 15$  deg. Estimated population values for baseline dB sensitivity/region and age effects were based on bootstrapped means.

**Results:** Age dependence of dB sensitivity per region was well fitted by linear regression. For YY, MAC, and RG the mean  $\pm$  SD slopes in dB/decade of age were respectively:  $-0.042 \pm 0.016$ ,  $-0.038 \pm 0.017$  and  $-0.052 \pm 0.015$ . The decline in sensitivity increased with eccentricity starting from about  $-0.02$  dB/decade centrally (Fig. A). Consistent with previous reports [Carle IOVS 52: 2365-71] the ratio of direct/consensual responses was close to 1.0 in the nasal field, but from the vertical meridian this increased to about 1.06 times on the far temporal side (Fig. B). Figures describe the YY test results. Results for RG and MAC are similar to this. Age dependence for response delay increased at:  $0.84 \pm 0.25$ ,  $0.73 \pm 0.23$ , and  $1.04 \pm 0.29$  ms/decade of age.

**Conclusions:** Use of standardised amplitudes [Carle IOVS 52: 604-10] reduces age dependence of nCFA sensitivity measures, the greatest reduction in sensitivity occurring peripherally. Delays increased with age, more so for the RG stimulus. nCFA responses do not appear to involve melanopsin-containing retinal ganglion cells [Carle IOVS 56: 6394-403].



## NEW PERIMETER WITH VIDEO IMAGING TECHNOLOGY – CLINICAL APPLICATIONS

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**Purpose:** Video imaging consists in recording the entire visual field process in synchrony with the video of the patient's head. Several clinical applications have been investigated to evaluate the clinical usefulness of this new technology.

**Methods:** The study included results from 48 visual field exams performed on a MonCvONE full field projection perimeter with synchronized video recording. The video from a large viewing field camera was recorded in synchrony with the position of the visual stimulus, with other test parameters such as luminance and size and with the patient's response obtained from the patient's press button or from the operator judgment. The study included patients who were unable to perform automated perimetry due to young age or handicap, patients with abnormal eye movements, head posture or ptosis and controls performed after automated perimetry.

**Results:** Video recording was extremely useful in the majority of clinical cases. 24 exams were performed on young children (age between 2 and 5 years) using attraction perimetry. The eye orientation responses could be interpreted and validated after the exam. In other cases, the video recording facilitated the interpretation and documentation of visual field

results with the inclusion of video snapshots in the examination report. Additional applications included the recording of cardinal eye gaze positions and of the fusion visual field.

**Conclusion:** Synchronized video imaging performed during visual field exams is a clinically useful tool for the examination of patients who cannot perform automated perimetry and for the documentation of artefacts and situations such as ptosis, abnormal eye movements, abnormal head posture and incorrect position of refraction.

## RESPONSE VARIABILITY FOR MULTI-DIMENSIONAL PERIMETRIC STIMULI IN GLAUCOMA

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**Purpose:** To investigate and compare the variability characteristics of four different stimulus forms for measuring changes in spatial summation clinically in patients with glaucoma.

**Materials and methods:** Psychometric functions were determined for each of four stimulus forms in 16 patients with glaucoma (median age 69.0 years, IQR: 66.7 - 74.0; mean MD -6.3 dB), and 8 age-similar healthy controls (median age 66.3 years, IQR: 62.9 - 71.7; mean MD +0.5 dB), using the method of constant stimuli. All stimuli were achromatic, circular increments, presented for 200ms at 4 visual field locations (9.9° from fixation along the 45°, 135°, 225°, and 315° meridians). Stimulus forms were: (i) a fixed contrast stimulus (0.5, suprathreshold at Ricco's area) varying in area; (ii) a fixed area stimulus (0.02 deg<sup>2</sup>), within Ricco's area, varying in contrast; (iii) a stimulus varying in area and contrast simultaneously, and (iv) a fixed area stimulus (0.15 deg<sup>2</sup>), equivalent to Goldmann III, varying in contrast (reference stimulus). Energy increments and visibility were equated across stimulus forms. Stimuli were presented on an OLED display (refresh rate: 60 Hz, background: 10 cd/m<sup>2</sup>). Threshold (50% seen) and response variability (slope), were derived from each function. The dependence of response variability on the level of visual field damage (expressed as threshold for the reference stimulus) was investigated with linear regression.

**Results:** Response variability increased with level of damage for all stimulus forms. The lowest dependence of response variability on level of damage was found for the stimulus with fixed contrast varying in area (i, above; regression line slope: 0.12,  $p=0.25$ ). The greater dependence of response variability on level of damage was statistically significant for all other stimuli (mean slope: 0.26, all  $p<0.01$ ).

**Conclusions:** By equating stimulus visibility and energy increments across the four stimulus forms, it can be observed that a stimulus of fixed contrast (suprathreshold at Ricco's area) varying in area offers low dependence of response variability on disease severity. Such a feature may offer advantages for more accurate identification of true changes in visual field damage, especially in moderate-advanced disease.

## VISUAL FIELD TESTING WITH NEW HEAD-MOUNTED PERIMETER "IMO"

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**Purpose:** We developed a new portable head-mounted perimeter named imo which provides visual field testing without a darkroom under flexible conditions. In addition to the monocular eye test, a test target can be presented randomly to either eye without occlusion (binocular random single eye test). We compared the visual field sensitivity obtained with the monocular and binocular random single eye tests.

**Methods:** In imo a test target is displayed using two sets of full HD transmissive liquid crystal displays and high intensity white LED backlights for each eye. The test target luminance is generated 0.1-10000 asb with the 31.4 asb background luminance using 10 bit resolutions. Test target sizes are Goldmann I to V, and any other optimal sizes and shapes are available. Both right and left pupils are illuminated by near infrared LED and the images obtained using SXVGA (1280 X 960 pixel) resolution CMOS sensor are usable for eye tracking system. Using imo, not only the traditional perimetry in which right and left eyes are tested separately, but also a new testing approach which we call binocular random single eye test is available. In the binocular random single eye test, the test target is presented randomly to either eye under non-occlusion condition without the subject being aware of which eye is tested. In this study, both monocular and binocular random single eye tests were performed on 40 eyes of 20 glaucoma subjects, and visual field sensitivity were compared with Humphrey Field Analyzer (HFA) results. The subjects were also asked whether they noticed which eye was tested during the test.

**Results:** The mean sensitivity (MS) with HFA were highly correlated with the MS obtained using imo monocular test (OD:  $r = 0.96$ , OS:  $r = 0.94$ ,  $p < 0.001$ ) and binocular random single eye test (OD:  $r = 0.97$ , OS:  $r = 0.98$ ,  $p < 0.001$ ). The MS of monocular and binocular random single eye tests were also highly correlated (OD:  $r = 0.96$ , OS:  $r = 0.95$ ,  $p < 0.001$ ). All



subjects could not recognize which eye was tested during the examination.

**Conclusions:** imo enabled us to measure the visual field with highly compatible sensitivity to standard automated perimeter. The binocular random single eye test provides non-occlusion test condition without the subject being aware of which eye is tested. This could contribute to the diagnosis of feigned blindness too.

## PROGRESSION ANALYSIS II

### COMPARISON OF GLAUCOMA PROGRESSION DETECTION USING 24-2 AND 10-2 VISUAL FIELDS

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**Purpose:** To compare 10-2 and 24-2 visual fields (VF) mean deviation (MD) for detection of glaucomatous progression.

**Materials and methods:** 24-2 and 10-2 VFs tests were acquired at 3 month intervals within a two year period for 162 eyes of 88 patients with a range of disease severity (mean±SD of baseline 24-2 VF MD:  $-4.50\pm 5.84$  dB and baseline RNFL thickness  $73.6\pm 14.9$   $\mu$ m). Only good quality 24-2 and 10-2 scans on the same visit were included in the analysis. Progression was defined as MD slopes significantly different from zero (one-sided  $p<0.05$ ). Agreement between 10-2 and 24-2 VFs was assessed and progression status at 6, 12, 18 months was compared to diagnosis after the full follow-up.

**Results:** Over 90% of eyes were classified as stable using 10-2 and 24-2 VF tests. A similar proportion of eyes progressed using each method; 11 eyes (6.8%) from 10 patients progressed using 24-2 MD regression, while 15 eyes (9.3%) from 14 patients progressed using 10-2 MD regression ( $p=0.23$ ). However, only 2 (8.3%) of the 24 progressing eyes were detected by both 10-2 and 24-2 testing. The severity of glaucoma (baseline 24-2 MD) was not a significant predictor of progression for either 10-2 or 24-2 MD regression and there was no significant difference between baseline MDs or baseline global retinal nerve fiber layer measurements in eyes progressing solely with 10-2 and 24-2 MD regression (means:  $-3.58$  dB vs  $-4.12$  dB,  $p=0.76$ ; and  $74.1$   $\mu$ m vs  $69.8$   $\mu$ m,  $p=0.47$ ). The specificity of 10-2 and 24-2 at 6, 12, and 18 month visits compared to full 24 month follow-up was good, > 90% after 6 months and in > 95% after 12 months and > 98% after 18 months. The sensitivity for 10-2 tests was approximately 54% for 10-2 testing at 6 and 12 months, rising to 86.7% (95% CI: 68.1-95.7) by 18 months. The sensitivity for 24-2 regression after 6 months was 25.0% (CI: 8.5-52.7), after 12 months (63.6% - CI: 39-83.3) and 100% by 18 months. The diagnostic accuracy (area under the receiver operating curve) of 10-2 and 24-2 MD regression was similar regardless of the length of follow-up (all  $p>0.1$ ).

**Conclusion:** Given that 10-2 and 24-2 visual field tests identify change in different patients, regardless of disease severity, it may be worth monitoring patients using 10-2 VFs alongside 24-2 testing. Longer follow-up is needed to determine whether this additional testing is cost-effective.

### THE USEFULNESS OF CORVISST TONOMETRY AND THE OCULAR RESPONSE ANALYZER TO ASSESS THE PROGRESSION OF GLAUCOMA

**Masato Matsuura**<sup>1</sup>, Kazunori Hirasawa<sup>1,2</sup>, Hiroshi Murata<sup>1</sup>, Shunsuke Nakakura<sup>3</sup>, Yoshiaki Kiuchi<sup>4</sup>, Ryo Asaoka<sup>1</sup>  
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**Purpose:** To investigate the association between Corneal Visualization Scheimpflug Technology (CST) and Ocular Response Analyzer (ORA) measurements and the progression of visual field (VF) damage in primary open angle glaucoma patients.

**Materials and method:** CST and ORA measurements were each carried out three times in 105 eyes of 69 patients with primary open-angle glaucoma. All patients had axial length (AL), central corneal thickness (CCT), intraocular pressure (IOP) with Goldmann applanation tonometry (GAT) and eight VFs with the Humphrey Field Analyzer measured. VF progression was summarized using a time trend analysis of mean total deviation (mTD) and the association between mTD progression rate and a number of ocular parameters (including CST and ORA measurements) was assessed using mixed linear regression analysis. The optimal model was selected based on the corrected Akaike Information Criteria (AICc) statistic.

**Results:** The optimal model of VF progression included ORA's corneal hysteresis (CH) parameter as well as a number of CST measurements. The equation for the optimal model was given by: mTD progression rate =  $1.2 - 0.070 * \text{mean GAT} + 0.090 * \text{CH} - 1.5 * \text{highest concavity deformation amplitude with CST} + 9.4 * \text{A1 deformation amplitude with CST} - 0.05 * \text{A2 length with CST}$  (AICc = 125.8).

**Conclusion:** CST measurements are helpful to model and understand VF progression in glaucoma patients. Further, CST parameters are significant in a model of VF progression that already includes ORA and IOP measurements. Eyes

with corneas that experience deep indentation at the maximum deformation, shallow indentation at the first applanation and wide indentation at the second applanation in the CST measurement are more likely to experience faster rates of VF progression.

## VISUAL FIELD ANALYSIS TOOLS FOR REAL WORLD CLINICS

Susan Bryan, David Crabb

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**Purpose:** To demonstrate a new approach for assessing visual field progression in clinics using two easily understood parameters: *Rate of Progression* (RP: mean deviation [MD] loss [dB] per year) and *Loss of Sight Years* (LSY). These parameters are presented in a novel visualisation (*Hedgehog Plot*) and we aim to illustrate how they can be used to help determine patients requiring prioritised clinical care.

**Materials and methods:** We used a subset of visual field series from 9884 patients in real clinics (Boodhna et al. *Eye* 2015). RP is calculated per eye using a two level hierarchical regression model (level 1: individual and level 2: eye). LSY is a novel parameter, linked to actuarial data, which estimates the number of years that a patient will have bilateral visual field loss worse than MD of -20dB in their predicted remaining lifetime. A reliability measure, Reliability of Rate (RR), is determined for each patient based on the variability in the MD recorded in both eyes while taking into account that the variability is expected to be higher for eyes with lower MD measurements (Crabb et al. *IOVS* 2012). Every eye is given a rank (percentile) within the sample based on RP and LSY allowing for 'at risk' patients to be easily identified.

**Results:** RP for every eye in a 'clinic' is shown in a *Hedgehog Plot* (Figure 1). Each line represents an eye with size indicating length of follow-up and location of the line is aligned to the patient's age (x-axis) and severity of initial loss (y-axis); steeply declining lines indicate rapidly changing eyes. Eyes are ranked against all other eyes by RP and can be corrected for RR as a measure of reliability. The application allows the user to easily 'drill down' to individual patients and four are shown in Figure 2. LSY is given as a whole number in years and patients with LSY >0 can also be highlighted. A purpose written interactive application demonstrating the techniques is available: <https://crabblab.shinyapps.io/hedgehog>

**Conclusions:** RP and LSY can be ranked for all patients in a clinic in order to help identify worse cases of visual field progression without using inferential statistics. *Hedgehog Plots* provide a tool for clinicians to visualize all of their glaucoma patients simultaneously and could be helpful in prioritising clinical care.

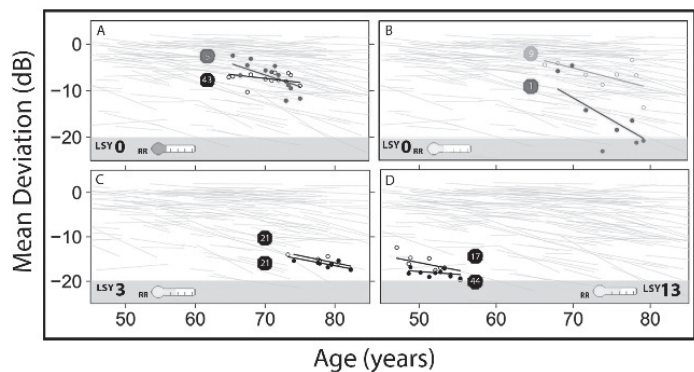
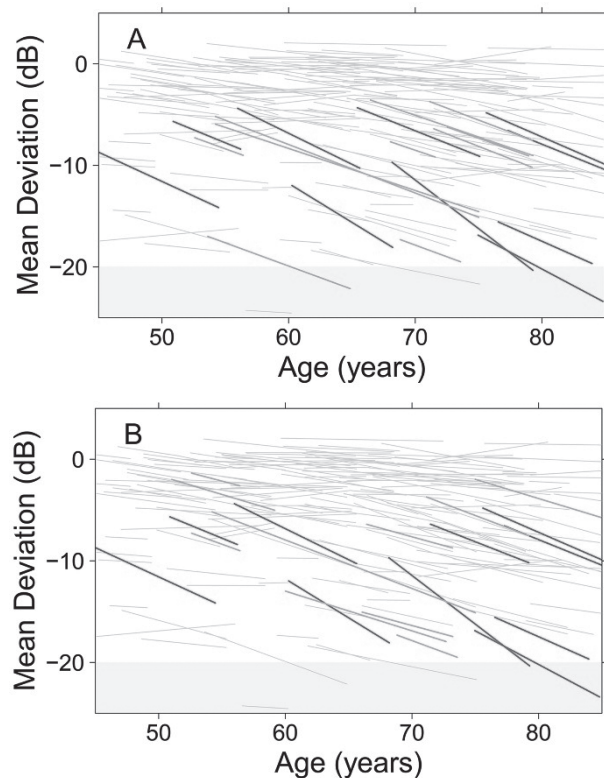


Figure 2: Panel A and B shows patients with rapidly progressing eyes. The solid symbols contain a single number depicting the rate of progression (RP) shown as a percentile rank. For example, patient B has eyes within the 1st and 9th percentile of most rapidly progressing eyes compared to all others. The application also allows the user/clinician to identify patients where loss of sight years (LSY) is >0 (panel C and D). Interestingly patient D has relatively slowly progressing eyes (17th and 44th respectively) but VFs are already quite damaged at diagnosis (worse than -12dB) and the patient is still relatively young; RR 'thermometer' indicates a good test taker too. So this patient might be highlighted to warrant more careful monitoring, or intensified treatment, to prevent loss of sight years.

Figure 1: Hedgehog plot showing rate of visual field progression status in a sample of 200 eyes from 100 patients. The software highlights the 10% eyes with the fast progression (worse RP) with the worse 5% coloured red. Plot B shows the effect of adjusting the results by patient reliability (RR), so the highlighted lines are the worse 10% given that the patients are likely reliable test-takers.

## THE SYDNEY OPHTHALMIC GLAUCOMA STUDY (SOGS)

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**Purpose:** Open angle glaucoma is one of the most prevalent causes of progressive vision loss with increasing incidence in ageing populations. Early diagnosis and regular review cycles are paramount in the prevention of permanent visual deficits. The Sydney Ophthalmic Glaucoma Study (SOGS) which was launched at the Centre for Eye Health (CFEH) to track clinical progression in patients at risk of developing glaucoma and refine models to predict disease in this cohort. Initial hurdles in the development of SOGS, preliminary data, and anticipated outcomes will be presented.

**Materials and methods:** Routine glaucoma assessment performed at CFEH consists of patient ocular, family ocular and medical history, visual acuity, slit lamp biomicroscopy, gonioscopy, intraocular pressure (IOP), central corneal thickness, stereoscopic dilated fundus and optic nerve head (ONH) examination, standard automated perimetry, and imaging including stereoscopic optic disc, red-free photography and ocular coherence tomography. Diagnosis was performed by two staff optometrists and a consulting ophthalmologist. Patients at risk of developing open angle glaucoma, who were over 18 years of age and had provided written informed consent, were eligible for SOGS. Exclusion criteria included but were not limited to a history of intraocular surgery, secondary causes of elevated IOP, inability to visualise the optic disc, poor image quality, and ocular comorbidities including macular degeneration, diabetic retinopathy and closed angle glaucoma.

**Results:** To date, 6,392 patients met the inclusion criteria. Exclusion criteria applied to 81% of the cohort and 159 individuals were lost to follow up leading to 1,030 patients enrolled in the study. The study end point, defined as a minimum of five reliable visual fields and three ONH photographs and images, has been reached by 15% of the patients for whom preliminary analysis is currently underway. Of those, structural changes of the ONH and/or visual field progression consistent with glaucoma were thus far recorded in 21 patients.

**Discussion:** High frequency of co-morbidities at the typical age of onset for glaucoma poses a significant challenge for study recruitment even at sites with high patient throughput. Among patients that met inclusion criteria and clinical progression did not correlate with automated guided analysis, which appeared more sensitive for functional (10 statistically significant cases) than structural (6 statistically significant cases) progression. Based on preliminary results, the incidence rate for glaucomatous progression among our glaucoma suspect cohort may be as high as 12% over five years. These findings are in line with previous reports and will provide the foundation to develop multivariate models to further investigate the association between glaucoma risk factors and progression of clinical disease.

## POSTER SESSION B

### 9. DEVELOPMENT OF A TRAINING SYSTEM FOR THE MEASUREMENT OF MANUAL KINETIC PERIMETRY USING THE GOLDMANN PERIMETER

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**Purpose:** To develop a training system for the measurement of manual kinetic perimetry using the Goldmann perimeter (GP), and to attempt to introduce the system in orthoptist education.

**Materials and methods:** This system was developed with Visual Basic.NET 2010 (Microsoft). The sensitivity distribution of the visual field was calculated automatically based on the target size and brightness, by capturing the results of the measurement of kinetic perimetry and manually plotting the points on the isopters in advance. In order to capture the track of the target, the sensor unit of a slim pen tablet (PTB-STRP1, PRINCETON) was placed behind the recording sheet, and a touch pen was installed on the tip of the pantograph. The computer sounded a beep when the location of the target reached the threshold of the visual field. The system that was developed in this study can also measure static perimetry. The trainee, who were orthoptic students, used this system to measure the manual kinetic perimetry using the GP. The trainer monitored the movement of the target by the trainee on the computer during training and advised the trainee on the method of manual kinetic perimetry using the results recorded in this system after measurement.

**Results:** By using this system, the trainees were able to measure manual kinetic perimetry without requiring test subjects. The trainee's measurement quality was improved as a result of the trainer's advice on using this system. The information

that was recorded in this system (e.g. selected targets, target tracks, target velocity, examination time) was utilized to review training process and stood both the trainer and trainee in good stead.

**Conclusions:** Experiencing various cases of perimetry is indispensable for improvement of the measurement of manual kinetic perimetry. The system developed in this study was capable of the training of manual kinetic perimetry using the GP and has proved to be useful for self-education in orthoptist education.

## 10. STATISTICS OF JOINT STRUCTURAL AND FUNCTIONAL CHANGES IN EYES WITH GLAUCOMA AFTER SHORT SERIES OF VISITS

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**Purpose:** An exploratory analysis was conducted to assess the descriptive and predictive capabilities of two simple models for joint structure and function progression in glaucoma.

**Methods:** Series of 7 visits for pairs of rim area (RA) and mean sensitivity (MS) were selected from 680 eyes of 395 patients with ocular hypertension or primary open-angle glaucoma and pairs of nerve fiber layer thickness (RNFLT) and MS from 79 eyes of 49 patients. Subjects were selected from the Diagnostic Innovations in Glaucoma Study or the African Descent and Glaucoma Evaluation Study (DIGS/ADAGES). Separation between RA or RNFLT and MS in each pair was less than a month and separation between visits was at least 6 months. For each sector defined in the Garway-Heath map (IOVS, 2002), slopes were estimated with ordinary least square (OLS) for pairs of RA and MS and for pairs of RNFLT and MS. Linear correlations were calculated between slopes for RA and MS and for RNFLT and MS. Prediction errors (PE) were obtained for the OLS and DSF models (Hu et al, IOVS, 2014) and compared against a model of no progression for which the average over visits 1 to 6 was used as the prediction for visit 7.

**Results:** Correlations between RA and MS were about 0.35 for IT and ST and < 0.26 for all other sectors. They were about 0.58 for IT and ST and < 0.34 for all other sectors for RNFLT and MS. Correlations between slopes for RA and MS were < 0.10 for all sectors. They were about 0.15 for IT and ST and between -0.12 and -0.03 for all other sectors for RNFLT and MS. None of the correlations were significantly different from zero ( $p > 0.01$ ) after Bonferroni correction. Median PE for RA and MS and RNFLT and MS for each model varied from 10 to 16% of mean normal for IT and ST, about 4% of mean normal smaller than for all other sectors. Median PE for DSF and OLS were never significantly smaller than that for the no progression model.

**Discussion:** The low correlations observed between rates of change may be due to large proportions of non-progressing patients; roughly 20% in, e.g., Bowd et al (IOVS, 2012). If correlations between slopes were 0.75 for the 20% of progressing patients, then correlations for all patients are expected to be about 0.15, as obtained for RNFLT and MS in IT and ST sectors. The challenge remains to devise strategies that increase correlation between rates of change and improve over predictions that assume no progression.

## 11. COMPARING MULTIFOCAL PUPILLOGRAPHIC OBJECTIVE PERIMETRY (MFPOP) AND MULTIFOCAL VISUAL EVOKED POTENTIALS (MFVEP) IN RETINAL DISEASES

Corinne F. Carle<sup>1</sup>, Ted Maddess<sup>1</sup>, Andrew C. James<sup>1</sup>, Rohan W. Essex<sup>2,3</sup>, Andrew Bell<sup>1</sup>, Faran Sabeti<sup>1,3</sup>

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**Purpose:** Multifocal pupillographic objective perimetry (mfPOP) shows regions of slight hyper-sensitivity away from retinal regions damaged by diabetes or AMD. This study examines if such results also appear in multifocal visual evoked potentials (mfVEPs) recorded on the same day in the same patients. The pupil control system receives input from the extra-striate cortex, so we examined evidence for such input.

**Materials and methods:** Study 1 included 23 subjects with early type 2 diabetes (T2D) and 23 age- and sex-matched control subjects. The patients had no signs of retinal vasculopathy. Study 2 had 20 patients with unilateral exudative AMD, and 20 age- and sex-matched control subjects. The AMD patients' fellow eyes, had either a normal fundus, or early AMD characterised by drusen & pigmentary changes. mfVEPs were recorded with and 64 EEG electrodes in a 10-20 array and the dichoptically presented stimuli had 84 test regions/eye. For analysis EEG electrodes were divided into to groups. The occipital (Occ) electrodes were Iz, Oz, POz, Pz, O1, PO1, PO3, P1, O2, PO2, PO4, P2; the other (Oth) set were PO7, P7, P5, P3, P4, P6, P8, PO8, P10. The mfPOP stimuli had 44 regions per eye. Both stimulus types were presented using a prototype of the nuCoria Field Analyser (Canberra, Australia).

**Results:** Population average responses of the diabetes patients, and the normal fellow eyes of AMD patients, showed multiple regions of significant hypersensitivity ( $p < 0.05$ ) on both mfPOP and mfVEPs. For mfVEPs the Oth electrodes showed more of these regions than Occ. More advanced AMD showed regions of suppression becoming centrally concentrated in the Wet AMD ideas.

**Conclusions:** mfVEP electrodes biased towards extra-striate cortical responses (Oth) appear to show similar hypersensitive visual field locations to mfPOP in early stage diabetic and AMD damage. Our previous study showed that wet AMD patients with such hyper-sensitive regions respond better to anti-VEGF treatment [Sabeti et al. IOVS 53: 253-260]. We have previously shown that the conjunction of hyper-sensitive and hyper-sensitive regions drives asymmetry between the eyes, which is highly diagnostic of early stage retinal disease [e.g. Sabeti et al. IOVS 56: 4504-13].

## 12. MONITORING QUALITY AND VIGILANCE DURING AUTOMATED STATIC PERIMETRY. A PROOF-OF-CONCEPT-STUDY USING VIDEO-PUPILLOGRAPHY, HEART RATE RECORDING, AND AN INCREASED NUMBER OF CATCH TRIALS

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**Purpose:** To monitor quality and vigilance by video-pupillography and heart rate recording during automated static perimetry.

**Materials and methods:** Method of constant stimuli was used to assess differential luminance sensitivity with the OCTOPUS 900 perimeter (Haag-Streit AG, Koeniz, Switzerland) using OPI (Open Perimetry Interface): Stimulus intensity was varied in nine steps between 0.04 and 160 cd/m<sup>2</sup> with a background luminance of 10 cd/m<sup>2</sup>. Altogether, 1,560 stimuli were presented in approximately 48 minutes. An increased rate of false-positive and false-negative catch trials was implemented (40% each). Pupil data were extracted from the built-in camera. Heart rate was recorded with the H7 heart rate monitor and chest strap (Polar Elektro GmbH, Buettelborn, Germany).

The quality of visual field testing was defined by the response behavior to catch trials. An "agreement index" was determined, relating periods with increased variabilities of (i) pupil diameter, (ii) heart rate, and (iii) reaction time to periods with increased number of false responses to catch trials. The agreement index was calculated as the ratio between *event overlap* and *total event occurrence* periods.

**Results:** Sufficient data were obtained from five subjects (3 male, 2 female; age range from 25 to 58 years). Agreement indices are:

Tab. 1: Agreement indices

|  | Subject 1 | Subject 2 | Subject 3 | Subject 4 | Subject 5 |
|--|-----------|-----------|-----------|-----------|-----------|
| Period with increased no. of false responses to catch trials | 17.6 min. | 2.9 min.  | 2.0 min.  | 27.7 min. | 0 min.    |
| Pupil diameter variability                                   | 0.35      | 0.33      | 0.10      | 0.70      | 0         |
| Heart rate variability                                       | 0         | 0         | 0         | 0.03      | 0         |
| Reaction time variability                                    | 0.32      | 0.41      | 0         | 0.08      | 0         |

Pupil diameter variability showed the highest agreement indices, whereas reaction time and heart rate variabilities showed low or no agreement.

**Conclusions:** In this study, pupil diameter variability was closer related to response behavior to catch trials than heart rate and reaction time variabilities. Pupil diameter variability can be considered as an indicator for decreasing quality of subjects' responses, thereby allowing a termination criterion of a perimetric session before its considerable contamination due to vigilance-related issues.

## 13. MONOCULAR SENSITIVITY MEASURED WITH BOTH EYES OPEN USING THE HEAD-MOUNTED PERIMETER IMO<sup>®</sup>

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**Purpose:** Monocular sensitivity is usually measured with occlusion (the non-tested eye is occluded) and yet, the influence of the occlusion on the measured sensitivity is not known in detail. The head-mounted perimeter imo<sup>®</sup> can measure the sensitivity of each eye with both eyes open (binocular condition) and without the examinee being aware of the tested eye. Using imo<sup>®</sup>, we investigated whether monocular sensitivities measured with occlusion and under binocular condition were different, and if the sensitivity difference was influenced by eccentricity.

**Materials and Methods:** Subjects were 16 normal volunteers (mean age, 28.6 ± 4.6 years). Monocular sensitivities were measured by imo<sup>®</sup> with occlusion and under binocular condition. Binocular condition was further divided into three test

conditions: with fusional fixation target, without fusional fixation target, and with the binocular random single eye test. In the binocular random single eye test, the target was randomly presented on the test points for each eye in a single test. The binocular condition with fusional fixation target used the fusion patterns as the fixation target and sensitivity was measured with the fusion condition confirmed. The fusion patterns used a 3° circle with a 135° line for the right eye and a 3° circle with a 45° line for the left eye. Sensitivities were determined using a 4-2 dB bracketing staircase measurement procedure. A total of 29 locations at the fovea and at 3° intervals on the 45°, 135°, 225°, and 315° meridians within the central 25° visual field (VF) were tested. Each condition was tested twice and the average of the two sensitivity measurements was used. Test conditions and locations were tested in a random order.

**Results:** The mean sensitivity with occlusion was  $29.6 \pm 1.7$  dB. The mean sensitivities for the binocular conditions with fusional fixation target, without fusional fixation target, and with the binocular random single eye test were  $30.4 \pm 1.7$  dB,  $30.3 \pm 1.6$  dB, and  $30.3 \pm 1.5$  dB, respectively. Monocular sensitivities under binocular conditions were significantly higher than that with occlusion ( $P < 0.01$ ). Moreover, the sensitivity difference between test conditions of binocularity and occlusion was significant beyond the central 5° VF ( $P < 0.01$ ) but not at the fovea ( $P = 0.60$ ) or within the central 5° ( $P = 0.22$ ). No significant sensitivity difference was observed among the three binocular conditions ( $P = 0.82$ ).

**Conclusion:** Monocular sensitivity is higher under binocular condition especially beyond the central 5° VF. This indicates that the presentation of a uniform background to both eyes activates the function of binocular interaction and thus affects the monocular sensitivity.

#### 14. VISUAL FIELD TESTING USING A PORTABLE TABLET DEVICE

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**Purpose:** To determine the accuracy and inter-session repeatability of a portable iPad tablet perimeter in defining the visual fields of patients with normal or visual field loss on the Humphrey Field Analyzer (HFA).

**Materials and methods:** A tangent perimeter (Melbourne Rapid Field, MRF) was designed on an iPad by incorporating features including altering fixation and fast thresholding using Bayes logic (TVST 2016). A cross-sectional study on 90 eyes from 90 participants was conducted: 12 had normal visual fields and 78 had glaucoma (41 Mild and 37 moderate-severe) with visual field loss. Exclusion criteria were patients with worse than 20/40 vision, recent intraocular surgery or previous unreliable visual field tests on HFA. The visual field outcomes of MRF were compared against those returned from the HFA 24-2 SITA standard. Participants were tested twice on the MRF to establish test-retest repeatability.

**Results:** Test durations were shorter on MRF than HFA (5.7 vs. 6.3 minutes). The MRF showed a high level of concordance in its outcomes with HFA (intraclass coefficient ICC=0.93 for MD and 0.86 for PD) although the MRF tended to give a less negative MD (1.4 dB) compared with the HFA. Regional analysis showed that the peripheral nasal region had the strongest correlation between MRF and HFA estimates (ICC 0.91-0.92), while the correlation was weaker in peripheral temporal regions (ICC 0.71). Test-retest reliability of MRF test was high (ICC=0.93 for MD and 0.89 for PD, 95% limits of agreement -4.5 to 4.3 dB).

**Conclusions:** The MRF provides outcomes that correlate strongly with HFA outcomes. MRF on iPad may prove useful in situations where the HFA test is unavailable or unsuitable, and has potential for patient self-monitoring at home.

#### 15. UTILITY OF STRUCTURAL AND FUNCTIONAL MEASUREMENTS IN DETECTING EARLY GLAUCOMA

Kazunori Hirasawa<sup>1</sup>, Natsumi Takahashi<sup>2</sup>, Kazuhiro Matsumura<sup>2</sup>, Masayuki Kasahara<sup>2</sup>, Nobuyuki Shoji<sup>1</sup>

<sup>1</sup>Department of Orthoptic and Visual Science, School of Allied Health Sciences, Kitasato University, Kanagawa, Japan; <sup>2</sup>Department of Ophthalmology, School of Medicine, Kitasato University, Kanagawa, Japan

**Purpose:** To assess the utility of structural measurements (spectral-domain optical coherence tomography [SD-OCT]) and functional measurements (Pulsar perimetry [Pulsar] and Flicker perimetry [Flicker]) in detecting early glaucoma.

**Methods:** This prospective observational case control study included 53 eyes of 53 patients with early primary open angle glaucoma and 42 eyes of 42 healthy participants. The patients with rim thinning or retinal nerve fiber layer defect, and with a mean deviation better than -3 dB on the Humphrey Field Analyzer were classified as early glaucoma patients. The Pulsar and Flicker perimetry examinations were performed with the OCTOPUS 600 and 311 perimeters, respectively, using the 32 Tendency Oriented Perimetry strategy. SD-OCT was performed with 3D-OCT 2000 using the 3D optic disc scan and 3D macular vertical scan mode. The best cut-off parameter for discriminating between healthy and glaucomatous eyes was determined using the highest area under the curve (AUC) calculated by receiver operating characteristic analysis. The sensitivity at 80% specificity was also calculated for each device.

**Results:** The best parameters for detecting glaucoma with Pulsar and Flicker perimetry and SD-OCT were mean sensitivity (sensitivity=90.6%, specificity=71.4%, and AUC=0.814); number of corrected probability with  $p < 5\%$  (sensitivity=67.9%,

specificity=85.7%, and AUC=0.778); and superior cpRNFL thickness (sensitivity=60.4%, specificity=97.6%, and AUC=0.830). There was no significant difference in AUC among the three devices. The sensitivities at 80% specificity for Pulsar perimetry, Flicker perimetry, and SD-OCT were 80.4%, 67.9%, and 75.5%, respectively.

**Conclusions:** Pulsar perimetry, Flicker perimetry, and SD-OCT did not show a significant difference in terms of their utility for detecting early glaucoma, suggesting that structural measurements are not necessarily superior to functional measurements. Both structural and functional measurements would be required to detect early glaucoma with precision.

## THE AULHORN LECTURE

### WHAT HAPPENS IN THE BACK OF THE EYE WHEN IOP DROPS?

**Stefano Gandolfi**

*Dept. of Ophthalmology, Parma University, Italy*

The biomechanics of the optic nerve head is becoming increasingly relevant in understanding the mechanism leading to the damage in chronic glaucoma. Therefore, new technologies are being developed to fully capture the changes in both structure and function occurring upon variations of trans-laminar pressures. This lecture will review the most recent developments on what actually happens in the back of the eye when IOP changes. A tentative road-map on possible future achievements (particularly focused on individualizing the treatment approach and pursuing the goal of a “personalized medicine in glaucoma”) will be thereafter discussed.

FRIDAY SEPTEMBER 30<sup>TH</sup> 2016

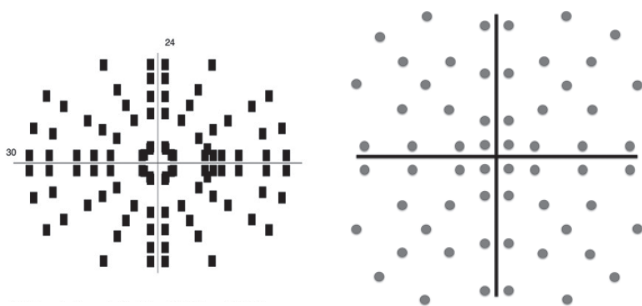
## NEW INSTRUMENTS AND TECHNIQUES II

## TABLET VISUAL FIELD SCREENING: COMPARISON OF TESTS AND EXAM CONDITIONS

Chris A. Johnson<sup>1</sup>, Swati Upadhyaya<sup>2</sup>, Suman Thapa<sup>3</sup>, Alan Robin<sup>4</sup>, Jenny Reiniger<sup>5</sup>, Johanne Forkel<sup>5</sup><sup>1</sup>Dept of Ophthalmology, University of Iowa, USA; <sup>2</sup>Aravind Eye Hospital India; <sup>3</sup>Tilganga Inst of Ophthalmology, Nepal;<sup>4</sup>Wilmer Eye Institute, Johns Hopkins University, Baltimore, USA; <sup>5</sup>School of Optometry, Aalen University, Germany

**Purpose:** Many investigators are now developing visual function test procedures for smart phones and tablets. Recently, several groups have developed visual field screening procedures. The purpose of the present investigation was to compare two tablet based visual field screening procedures, assess its performance in relation to the Humphrey Field Analyzer (HFA) 24-2 SITA Standard test, and evaluate its performance for different levels of refractive error and stimulus and background adaptation luminance.

**Methods:** The Visual Fields Easy procedure on the iPad presents 96 stimuli (24 per quadrant) throughout the central 30 degrees as shown in the display with black stimulus locations to the far left. The display to the near left with red stimulus



locations presents the arrangement of 60 stimuli (15 per quadrant) for the visual field screening procedure generated on a Dell tablet display. Each test procedure uses a background luminance of 31.5 apostilbs (10 cd/m<sup>2</sup>), a 788 apostilb (250 cd/m<sup>2</sup>) stimulus luminance (16 dB), a Goldmann size V stimulus, and a 200 millisecond presentation time. Testing time is approximately 3 minutes and 20 seconds per eye for the Visual Fields Easy iPad test and 2 minutes and 5 seconds for the Dell tablet visual field test. At a testing distance of 33 centimeters, both tests provided evaluation of the central 30 degree radius of the visual field. Both tablet procedures were calibrated with

a Photo Research Model 670-PR photometer/radiometer. Results for the two screening procedures were evaluated and compared to the HFA SITA Standard 24-2 visual field indices. Comparisons were obtained for 28 healthy normal eyes and 109 eyes with glaucomatous visual field loss. The effects of refractive error stimulus luminance and ambient background room illumination were assessed in 2 young (24,28 years old) and 2 older (63 and 65 years old) healthy normal participants.

**Results:** There was only a 2-4% variation in background illumination of the two screening tests throughout the battery life (100% to less than 3% charge) of the tablets, and variation in luminance across different portions of the display was less than 8%. For the size V target, each of the 4 participants detected all of the stimuli for the 60 stimulus test for refractive errors of up to 9 diopters. Using a soft contact lens, the young participants were able to see all stimuli at 15 and 20 diopters of refractive error, whereas the older participants missed approximately 5% of the targets at 15 and 20 diopters of refractive error. Variations in stimulus luminance of 6 dB did not affect test results for the 4 healthy normal participants, and changes in ambient room illumination of approximately 20 dB also did not influence results. For the comparison of tablet visual field screening tests, the Visual Fields Easy iPad test correlated with the HFA 24-2 SITA Standard Mean Deviation (MD,  $r=0.50$ ,  $p<0.0001$ ) and Pattern Standard Deviation (PSD,  $r=0.49$ ,  $p<0.0001$ ), as did the other tablet based visual field screening test (MD,  $r=0.33$ ,  $p<0.0001$ ; PSD,  $r=0.33$ ,  $p<0.008$ ). The location of missed stimuli for both tests demonstrated good correspondence. Results from a larger sample of participants will also be presented.

**Discussion:** The tablet based visual field screening tests provide accurate and reproducible testing conditions, are tolerant of moderate to large variations in refractive error, and are unaffected by moderate variations in stimulus luminance and ambient background room illumination. They correlate quite well with visual field indices obtained with the HFA SITA Standard procedure. Both tests have elevated false positive rates, so they are most appropriate for detection of moderate and advanced visual field loss. With the large dynamic range available on tablet displays, development of quantitative threshold procedures is possible.

## NOVEL PERIMETRY USING EYE TRACKING ON A TABLET COMPUTER - A FEASIBILITY STUDY

David Crabb, Wei Bi, Nicholas Smith

Optometry and Visual Science, School of Health Science, City University London, UK

**Purpose:** Visual field (VF) examination by standard automated perimetry (SAP) is an important but often challenging, or sometimes impractical, clinical assessment. We propose a new approach to central VF assessment using an inexpensive eye tracker and implement it on a tablet computer (*Eyecatcher*). We examine the usability of *Eyecatcher* and concordance with results from SAP in people with glaucoma and visually healthy peers.

**Methods:** *Eyecatcher* utilises software producing a sequence of stimuli (Goldmann Size III) of fixed contrast (approximately equivalent to 15dB on a Humphrey Field Analyser [HFA]) presented at different locations on a tablet computer with an



attached “clip-on” eye tracker (Tobii Pro-X2 30; Tobii, Danderyd, Sweden). The test task is to simply follow the sequence of stimuli without any button pressing (monocular without a chin rest). Start and end fixations are then processed in a novel fashion to determine stimuli that were seen and unseen to build a continuous map of sensitivity loss across a VF of approximately 20°. Average examination time for *Eyecatcher* is approximately 4 minutes. A group of glaucoma patients and age-related visually healthy people were tested on *Eyecatcher* and SAP (HFA SITA standard 24-2) in both eyes. The VF surface generated from *Eyecatcher* was thresholded to produce suprathreshold defects at SAP locations; these defects were then compared to SAP defects defined as sensitivity below 25dB. Percentage of concordant ‘defect’ and ‘no defect’ locations per eye was used as an outcome measure for agreement between the VFs. In addition participants were asked to rate preferences for each examination on a series of questions on a 5-point Likert scale.

**Results:** Twenty-two eyes from 12 patients (median [interquartile range; IQR] age 70 [67 to 76] years) and 12 eyes from 6 visually healthy people (76 [73 to 79] years) were examined. Eyes with glaucoma had a range of VF loss; median HFA MD was -12 [-17 to -6]dB. Median suprathreshold defect concordance between *Eyecatcher* and SAP was 83 (62 to 90) % and 96 (92 to 97) % in patients and visually healthy people respectively. Participants preferred *Eyecatcher* to SAP (median 4/5 vs 3/5;  $p < 0.01$  Wilcoxon test).

**Conclusions:** Visual fields measured by *Eyecatcher* show good concordance with those measured by SAP. *Eyecatcher*, requiring simple user interaction, was a preferred examination in this group of people. Perimetry using an inexpensive eye tracker on a tablet computer is feasible.

## THE FACTORS OF VISUAL FIELD SENSITIVITY FLUCTUATION ON HIGH RESOLUTION PERIMETRY WITH 0.5-DEGREE INTERVAL

Takuya Numata<sup>1</sup>, Chota Matsumoto<sup>1</sup>, Sachiko Okuyama<sup>1</sup>, Fumi Tanabe<sup>1</sup>, Shigeki Hashimoto<sup>1</sup>, Tomoyasu Kayazawa<sup>1</sup>, Ted Maddess<sup>2</sup>, Yoshikazu Shimomura<sup>1</sup>

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**Purpose:** Fluctuation of the visual field (VF) is known to be low when the sensitivity is high, and high when sensitivity is low. Some possible factors influencing the fluctuation of measured VF sensitivity are physiological characteristics based upon the frequency-of-seeing and the presence of scotoma edges. We performed an observational clinical study using high resolution perimetry with 0.5 degree intervals to investigate factors determining VF sensitivity fluctuation.

**Methods:** Sixteen eyes of 16 patients with glaucoma (mean  $\pm$  SD age: 63.1  $\pm$  5.9) were studied. An Octopus 900 Custom test program was used with target size III and a background luminance of 31.4 asb. Sensitivity was measured on the upper temporal meridian at 45 degrees from the fixation to an eccentricity of 30 degrees with an interval of 0.5 degrees. The sensitivity was evaluated 3 times at each point and the mean sensitivity and standard deviation (SD) were calculated. The SD quantified the local sensitivity fluctuation. In order to evaluate a threshold shifts across scotomas etc., we also computed the Spatial SD along each sample line using a moving window 3 points wide. We investigated the correlation between the local mean sensitivities and their corresponding sensitivity fluctuations. We also did a multivariate regression analysis to look for the independent factors that best determined the sensitivity fluctuation.

**Results:** In the range of where the mean sensitivity is normal, the sensitivity fluctuation was small. Where the mean sensitivity was low, the sensitivity fluctuation was large. In univariate analysis the sensitivity fluctuation was correlated with the mean sensitivity ( $p < 0.0001$ ;  $r = 0.342$ ) and Spatial SD ( $p < 0.0001$ ;  $r = 0.452$ ). Multivariate regression analysis showed sensitivity fluctuation was mainly determined by mean sensitivity ( $p < 0.01$ ; t-value 5.05) and Spatial SD ( $p < 0.01$ ; t-value 12.48).

**Conclusion:** The sensitivity fluctuations found in automated perimetry appear to be substantially determined by spatial variability driven by factors such as scotoma edges.

## PERFORMANCE EVALUATION OF A NOVEL COMPUTER-BASED SELF-ADMINISTERED VISUAL FIELD SCREENING TEST FOR GLAUCOMA

Emmanouil Tsamis, Cecilia Fenerty, Robert Harper, Tariq Aslam, David Henson  
University of Manchester, UK

**Purpose:** Due to glaucoma’s asymptomatic nature at early stages early detection only occurs through screening, normally carried out by optometrists. Those not seeking optometric care are more likely to present late and are at greater risk of future visual impairment. New approaches to glaucoma screening are needed; one such approach is the development and distribution of a self-administered visual field (VF) test that can run on a wide range of personal computers. Early work led to the development of such a test whose diagnostic performance is evaluated in this presentation.

**Materials and Methods:** The new test uses a multiple stimulus supra-threshold algorithm to test a 20 location subset of the 24-2 pattern. One eye of 140 normal patients (no VF loss) were tested 4 times; once without a simulated defect and with 3 different simulated glaucoma defects randomly selected from a pool of 30 defects (10 from stages 1-3 of the Glaucoma Staging System 2). Location and depth of the defects were derived from stable diagnosed glaucoma cases

tested with a 24-2 SITA threshold algorithm on a Humphrey perimeter. In simulation cases the intensity of the presented stimuli were attenuated by the defect values of the randomly selected case with appropriately added variability. All patients performed the test with a supra-threshold increment of 10dB. During analysis estimates of sensitivity, specificity and positive and negative predictive value were calculated at different cut-off criteria. Patients followed the written instructions on the screen including a demonstration trial. A researcher remained in the room during the tests to give further support if needed.

**Results:** All patients completed the self-administered tests with little, if any, help from the researcher. The sensitivity and specificity of the new test on detecting glaucomatous Stage 1 defects were 93.5 and 97.1% respectively with 1 missed location as cut-off criteria. For stages 2 and 3 the sensitivities were 94.8 and 100% with specificities of 97.1%. Median testing time was ~155 seconds per test (i.e. ~2.5 minutes - IQR 41.5 seconds).

**Conclusions:** The newly developed self-administered screening test was well received by patients and was shown to have high discriminatory power and is thus suitable for distribution to high-risk patients for self-testing.

## COMPARISON OF THE MACULAR MAPPING TEST (MMT) WITH NEAR VISUAL ACUITY, M-CHARTS AND THE AMSLER-GRID IN MACULAR DISEASES

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**Purpose:** To compare the performance of several function tests in macular pathologies, i.e., drusen, edema due to vascular occlusion, and, vitreo-retinal traction.

**Materials and Methods:** Of 55 consecutive subjects scheduled for refraction by SM between 2/12/2016 to 4/13/2016 over 60 years of age, 49 participate (98 eyes) met the entry criteria: no retinal surgery, no diabetic retinopathy nor optic neuropathy including glaucoma.

The Macular Mapping Test was conducted at two different contrast levels (100% + 10% Michelson contrast). The results were expressed as the General Field Score-Ratio (GFS-Ratio =  $MMT_{10\%}\text{-Score} / MMT_{100\%}\text{-Score}$ ). The following tests were performed: Best corrected visual acuity for near (VA-near), M-Charts, Amsler-Grid, Cirrus Zeiss-Meditec OCT macular test (pathological in 23 eyes), slit lamp examination in mydriasis including quantification of the lens opacity, non-contact tonometry or Pascal DCT. For this evaluation, the cut off value to detect pathology was set to  $MMT_{100\%} < 33$  (23 eyes),  $MMT_{10\%} < 17$  (24),  $GFS\text{-Ratio} < 0.5$  (25), near visual acuity  $< 0.8$  (21), M-Chart = „pathological“ (18), Amsler grid = „pathological“ (15). MZ evaluated the OCTs – relevant changes were considered as the „Golden Standard“.

### Results:

| Test        | Sensitivity | Specificity | Diagnostic power |
|-------------|-------------|-------------|------------------|
| MMT100%     | 48% (11/23) | 84% (12/75) | 66%              |
| MMT10%      | 65% (15/23) | 88% (9/75)  | 77%              |
| MMT GFS     | 65% (15/23) | 87% (10/75) | 76%              |
| VA-near     | 61% (14/23) | 91% (7/75)  | 76%              |
| M-Chart     | 57% (13/23) | 93% (5/75)  | 75%              |
| Amsler Grid | 52% (12/23) | 96% (3/75)  | 74%              |

**Conclusion:** In an academic setting, all tests had a similar diagnostic power (average of sensitivity and specificity) to detect relevant macular OCT pathologies. Further analysis, i.e., ROC-Curves and discriminant analysis will be presented. The tests performance in the follow-up of diseases is a different yet important subject.

## POSTER SESSION C

### 16. COMPARISON OF THE NEW COMPASS PERIMETER WITH HUMPHREY FIELD ANALYZER USING THE GLAUCOMA STAGING SYSTEM 2 (GSS 2)

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**Purpose:** To compare the results obtained using the Glaucoma Staging System 2 (GSS 2) in a cohort of subjects tested both with a new perimeter, the COMPASS, and the Humphrey Field Analyzer (HFA). The GSS 2 uses the Mean Deviation (MD) and Pattern Standard Deviation (PSD) values to stage glaucomatous visual field defects in 7 classes (stage 0, borderline and stages 1 to 5) and three types (generalized, localized, and mixed).

**Materials and methods:** One hundred and twenty patients affected with open-angle glaucoma with significant structural damage and 198 normal subjects underwent visual field testing using the program 24-2 of both HFA and COMPASS automated perimeters. The GSS 2 was employed to stage visual field defects. Sensitivity and specificity of HFA and

COMPASS GSS 2 classification was assessed, considering stages 0 and “border” as “normal”, and stages 1 through 5 as “glaucoma”. The agreement in defining visual field defect type was also studied.

**Results:** MD mean values were not significantly different between COMPASS and HFA, both for glaucomatous and normal subjects (T-Test,  $p > 0.05$ ), with an overall mean MD of  $-2.5 \text{ dB} \pm 5.5$  for COMPASS and  $-2.8 \text{ dB} \pm 5.4$  for HFA. PSD values were significantly different between COMPASS and HFA in the Normal group only ( $p < 0.01$ ), with an overall mean PSD of  $3.6 \pm 2.9$  for COMPASS and  $3.1 \pm 3.1$  for HFA. We computed GSS 2 output classes for all patients and compared the results, using HFA as reference. Stage severity was the same in 244 cases (76.7%), whereas fifty seven cases (18%) had a difference of 1 stage, and 16 (5%) of 2 stages with no apparent systematic over- or underestimation of COMPASS. Sensitivity of GSS 2 classification for COMPASS and HFA was 78.3% and 73.3%, respectively, while specificity was 89.4% for COMPASS and 89.9% for HFA. The agreement on the defect type classification between COMPASS and HFA on 90 patients who had a defined defect was 65.6%.

**Conclusions:** The agreement between the two automated perimeters was very good, as 77% of cases fell on the same GSS 2 stage. Discordances were in most cases partial. The use of GSS 2 can be useful for a standardized and objective comparison of data arising from these two instruments.

## 17. COMPARISON OF RADIAL PERIPAPILLARY CAPILLARIES BETWEEN TWO OCT-A SCANNING AREAS

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**Purpose:** Optical coherence tomography angiography (OCT-A) made it possible to visualize the microvasculature around the optic nerve head. In this study, we compared the density of radial peripapillary capillaries (RPC) with two scanning areas ( $3 \times 3 \text{ mm}$  or  $4.5 \times 4.5 \text{ mm}$ ) for the correlation with visual field sensitivity in participants with or without glaucoma.

**Methods:** Participants had OCT-A measurements with RTVue®XR™ Avanti™ (OptoVue) to measure the RPC density, and the two scans ( $3 \times 3 \text{ mm}$  and  $4.5 \times 4.5 \text{ mm}$ ) were performed at the same visit. According to Garway-Heath classification, peripapillary area was divided into 6 sectors; nasal, inferior nasal (IN), inferior temporal (IT), superior nasal (SN), superior temporal (ST), and temporal. Participants with reliable results of standard automated perimetry (Humphrey SITA™ Standard 24-2, Carl Zeiss Meditec) within 3 month of OCT measurements were included. Participants with other retinal, optic nerve and visual tract disorders, or intraocular surgeries were excluded. Spearman’s rank correlation coefficients were determined for the relationship between the two scan areas. Generalized linear mixed models were used to evaluate effects of individual characteristics for visual field sensitivity. Akaike’s Information Criterion (AIC) was used to evaluate statistical validity.

**Results:** Ninety-nine eyes of 71 individuals (glaucoma;  $n=75$ , preperimetric glaucoma;  $n=12$ , normal;  $n=12$ , male: female = 40:31) were analyzed. The RPC density was significantly correlated between the two scan size ( $\rho = 0.923, 0.854, 0.890, 0.891, 0.878, 0.883, 0.916$ , in total area, nasal, IN, IT, ST, SN, and temporal sectors, respectively;  $p < 0.001$  for all). Good visual field sensitivity and good image quality effected positively on RPC density, while glaucoma and aging effected negatively, in both of the two scan size ( $p < 0.05$ ). Large optic disc showed significantly negative effect on RPC density only for the  $3 \times 3 \text{ mm}$  scan ( $p < 0.05$ ). To predict visual field sensitivity, RPC density of  $4.5 \times 4.5 \text{ mm}$  scan showed better (lower) AIC than that of  $3 \times 3 \text{ mm}$  scan in total and all 6 sectors.

**Conclusion:** RPC density of  $4.5 \times 4.5 \text{ mm}$  scans maybe a good indicator of visual field sensitivity compared to  $3 \times 3 \text{ mm}$  scans. Image quality and optic disc size should be considered in OCT-A analysis.

## 18. THE OCT STAGING SYSTEM: A NEW METHOD FOR A STANDARDIZED CLASSIFICATION OF THE GLAUCOMATOUS RETINAL NERVE FIBER LAYER LOSS ASSESSED WITH OCT

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**Purpose:** To introduce a new standardized and easy-to-use method (the “OCT Staging System”) for classifying glaucomatous retinal nerve fiber layer (RNFL) damage assessed with Optical Coherence Tomography (sd-OCT).

**Material and methods:** The OCT Staging System was created based on 382 tests performed with the Nidek RS 3000 sd-OCT (Disc Map Protocol) in 98 healthy controls and 284 patients affected by either ocular hypertension or chronic open-angle glaucoma (OAG). This system uses the superior and inferior quadrant RNFL thickness values, corrected for age, plotted on an x-y diagram. The normative data provided by the sd-OCT Nidek RS-3000 were used to plot both the curvilinear lines that divide the normal results from borderline stage, and the borderline results from statistically abnormal data, respectively. In order to classify RNFL defects into different stages, an arbitrary subdivision was utilized. Sensitivity and specificity of the OCT Staging System were assessed in a different cohort including 64 patients with early OAG, and 62 normal subjects.

**Results:** The OCT Staging System classifies RNFL defects into 6 stages of increasing severity and 3 groups according

to defect localization (superior, inferior or diffuse defect). A non-linear equation and two regression lines describe the lines which separate the different sectors of the diagram. These mathematical formulas have been used to create a software, which provides a quick classification of the RNFL damage. Sensitivity and specificity of the OCT Staging System in discriminating between healthy and glaucomatous eyes were 95.2%, and 85.7%, respectively, considering borderline results as abnormal.

**Conclusions:** the OCT Staging System appears to provide a standardized and objective classification of glaucomatous RNFL damage. It can be used in day-to-day clinical setting for an easy and fast interpretation of RNFL measurements obtained with OCT.

## 19. EVALUATION OF THE AMBIENT INTERACTIVE ZEST (AIZE) OF A HEAD MOUNTED PERIMETER “IMO” IN NORMAL SUBJECTS

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**Purpose:** We developed a new threshold visual field strategy AIZE which was modified ZEST (Zippy Estimated by Sequential Testing) for “imo” visual field testing. This study is an evaluation of AIZE in normal subjects.

**Methods:** A hundred and sixty eight eyes of 168 normal subjects were tested by AIZE of imo. Test locations were same as Humphrey 30-2 and 10-2 test locations. Actual test times and mean thresholds were compared in age. Aging slopes for mean threshold of all test locations and each threshold for point-wise location were calculated.

**Results:** Mean age was 45.9±14.5, mean thresholds and test times were 28.0±1.9 dB and 281±40sec (30-2), 31.9±1.7dB and 198±47sec (10-2). Mean threshold tended to larger in younger subjects. Test time did not differ depending on ages. Aging slope for 30-2 locations was -0.052 dB/year, and for 10-2 locations was -0.047dB/year. In 30-2 test locations, aging slopes for both eccentricity 0-15 degree and 15-30 degree were -0.050 dB/year.

**Conclusion:** AIZE test can be shorter a duration of test time. Age dependent decrease of threshold does not much differ between center and peripheral regions.

## 20. INVESTIGATING THE USEFULNESS OF CLUSTER TREND ANALYSIS

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**Purpose:** To investigate the usefulness of Cluster Trend Analysis (CTA) in the comparison against mean total deviation (mTD: mean of 52 TD values) trend analysis.

**Method:** 491 eyes of 317 patients with primary open angle glaucoma patients with 10 reliable (fixation loss <20% and false positive <15%) visual field (VF) with the Humphrey Field Analyzer, spanning on 5.5±1.2 years were studied. Using various series of VFs (1st to 5th, to 1st to 9th), progressive eyes were identified as mTD progression rate <-0.5 dB/year with the p value <0.05. Using the Octopus EyeSuite’s 10 clusters, the progression rates of the average TD values (cluster defect progression rates) were calculated at each cluster, and the progressive clusters were identified using the definition of progression rate <-0.5 dB/year with the p value <0.05. The results of mTD and cluster trend analyses were compared.

**Result:** mTD values of 1st and 10th VFs were -6.7±6.2 and -7.9±6.8 [-27.4 to 2.7] dB, respectively. Between 86 (17.5%, VF1-10) and 40 (8.1%, VF1-5) eyes were progressive with mTD trend analysis. Between 239 (48.7%, VF1-10) and 131 (16.7%, VF1-5) eyes were progressive at least in one cluster, and only between 1 (0.2%, VF1-10) and 5 (1.0%, VF1-5) eyes were progressive only with mTD trend analysis (progressive with mTD trend analysis but not with Cluster Trend Analysis (or CTA)) which means CTA reliably detects the majority of progressive eyes detected by mTD trend analysis. The results of cluster trend analysis and mTD trend analysis were significantly correlated in any comparisons (p<0.05, chi-square test), but between approximately 30 to 60% of the progressive sectors were not detected with the mTD trend analysis.

**Conclusion:** It is clinically useful to use Octopus EyeSuite’s 10 clusters when analysing the progression of glaucoma.

## 21. PRECISION OF COMPASS PERIMETER: SHORT TERM REPEATABILITY

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**Purpose:** The purpose of this work is to assess the repeatability of visual field testing with COMPASS fundus perimeter both for Glaucomatous and Normal subjects.

**Materials and methods:** A subset of 89 normal subjects and 19 subjects with glaucoma were tested twice with the COMPASS perimeter for precision analysis.

**Results:** Mean age was lower for the Normal group (Mean±SD, 49.6±13.1), mostly due to the fact that younger ages were underrepresented in the Glaucoma group (Mean±SD, 72.2±8.2).

As expected, average retinal sensitivities for Normal subjects (Mean±SD, 29.3±3.0) were higher than those of pathological subjects (Mean±SD, 24.8±6.9); conversely standard deviations were lower in normal subjects.

To analyze the possible dependency of the test reproducibility on the mean sensitivity we used a Blandt-Altman plot. No obvious changes in reproducibility dependent on the sensitivity could be detected.

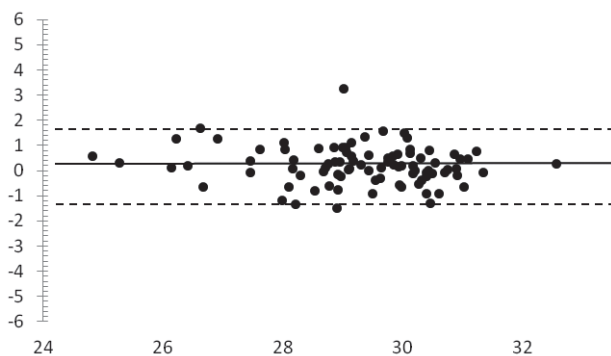


Figure 1 - Bland-Altman plots for mean differences (2° - 1° measurement), normal group  
The horizontal solid line represents the mean difference (0.21 dB), the dotted lines the 95% limits of agreement between measurements (-1.3 / +1.7 dB).

A Comparison with HFA data is provided below, based on literature. Since Humphrey 10-2 grid was used in the reference literature, only COMPASS data from the central 10° have been considered.

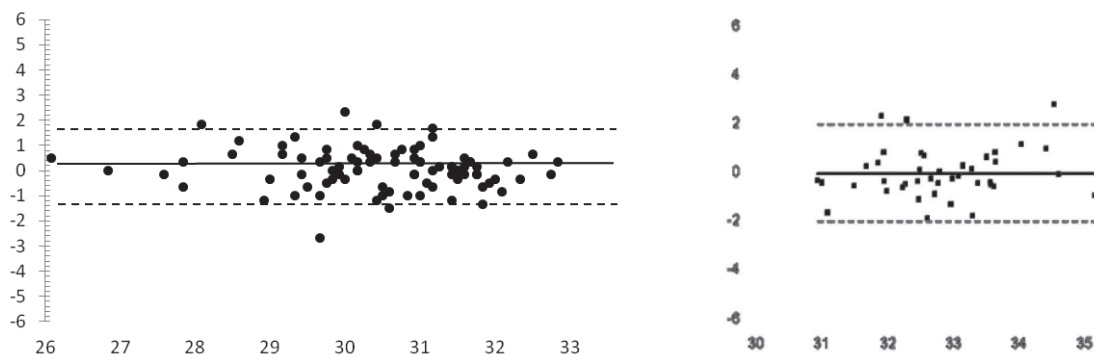


Figure 2 - Bland-Altman plots for mean differences, normal group (COMPASS left, HFA right). The horizontal solid line in figure represents the mean difference (COMPASS = 0.1 dB, HFA = 0.09 dB), the dotted lines the 95% limits of agreement (COMPASS = -1.5 / +1.6 dB; HFA ~ ±2 dB).

The COMPASS 95% limits of agreement are approximately 20% narrower than HFA's, suggesting a reduced variability. The repeatability SD for the average sensitivity is 0.76 dB for the Normal group and 0.67 dB for the Glaucoma group. Pointwise repeatability was also calculated, with a 95th Percentile Individual Stimulus Repeatability SD of 3.81 dB (Maximum 4.85 dB) for Normal subjects and 5.40 dB (Maximum 5.75 dB) in Glaucomatous subjects.

**Conclusions:** This study provides data on the repeatability of COMPASS measurements. Test-retest differences of the average sensitivity are comparable to those obtained with Humphrey. Nevertheless, a test-retest study on the two instruments is required to precisely quantify the differences in terms of both global and pointwise repeatability.

## PERIMETRY III

### TESTING OF THE FULL VISUAL FIELD IN EARLY GLAUCOMA: THE IOWA OPEN PERIMETRY INITIATIVE

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**Purpose:** To create an open source family of visual field tests with the Open Perimetry Interface (OPI) that incorporate recent advances in perimetry research, and to determine if static automated perimetry of the far periphery is useful in early glaucoma.

**Materials and Methods:** Using the OPI on the Octopus 900 platform we have created a series of automated static perimetry tests that evaluate both the central and far peripheral visual field using stimulus sizes III, V and VI. Probability maps were developed from data of 60 healthy adults (age range, 18-70, approximately 10 per decade). We also tested 25 glaucoma patients with early visual field damage (MD better than -4 dB) twice within a month. We standardized their results to age 50 and have compared their pointwise results with controls. Lastly, we have qualitatively correlated the visual function results with OCT of the retinal nerve fiber layer.

**Results:** Using stimulus size V for central and peripheral testing, we found the magnitude of visual loss in the glaucoma subjects with mild visual loss increased with eccentricity. This was most marked for the far nasal periphery reaching a magnitude of > 8 dB along the far nasal horizontal test locations – comparing individual slopes using ANOVA on Ranks ( $p < 0.001$ ). Qualitative structure function correlations of the central vs. far peripheral visual field using the OCT clock hour plots were best with the peripheral size V test for 8 glaucoma subjects; central visual field tests (sizes III and V) correlated best for 9 glaucoma subjects. Correlation between structure and function were best if results of central and peripheral visual field testing were combined.

**Conclusions:** While all subjects show a decrease in sensitivity with increasing visual field eccentricity, our new finding is that overall, glaucoma subjects demonstrate a significantly greater decrease in sensitivity with eccentricity along the nasal horizontal in the far nasal visual field ( $51^\circ$ ). Testing of the far periphery is likely to show defects in the periphery of some glaucoma patients when there is little damage in the central visual field. Using static automated perimetry of the far periphery provides a more comprehensive picture of structure/function relationships and may have clinical importance. Our study was substantially facilitated by use of the OPI.

## PROPERTIES OF MICROPERIMETRIC DEFECTS AT THE MONOCULAR PREFERRED RETINAL LOCUS IN AMD DERIVED USING A NEW SPATIAL INTERPOLATION TECHNIQUE

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**Purpose:** Patients with age-related macular degeneration (AMD) fixate with disparate retinal locations, making comparison of microperimetric data to conventional, fixed-location normative data inaccurate. We recently demonstrated a spatial interpolation method that enables normative data comparison and calculation of conventional perimetric indices in microperimetry (Denniss & Astle, ARVO 2016). Here we report properties of microperimetric defects revealed by this technique in patients with AMD, in the region of their monocular preferred retinal locus (PRL).

**Materials and Methods:** Data from 95 eyes of 95 patients with AMD were included. Patients (median age 78 years, range 57-97) were tested using the 4-2 Expert strategy of the MAIA-2 (CenterVue, Padova, Italy) with the test grid (37 locations,  $5^\circ$  radius) centred on the monocular PRL as determined by the instrument. For each patient, age-corrected sensitivity at each location was compared to the corresponding point (resolution  $0.1^\circ$ ) on the previously described normative surface, and indices equivalent to those of the Humphrey Field Analyzer (Carl Zeiss Meditec, Jena, Germany), Total Deviation (TD), Pattern Deviation (PD), Mean Deviation (MD) and Pattern Standard Deviation (PSD), were computed. We also considered the spatial arrangement of total and pattern defects in relation to the PRL.

**Results:** Monocular PRL location (and therefore test grid centre) varied by  $\pm 7^\circ$  horizontally and  $\pm 5^\circ$  vertically. Median MD was -11.5dB (Interquartile range (IQR) -17.2 to -6.2dB). Median PSD was 6.5dB (IQR 4.0 to 8.6dB). Across all patients median 35 (IQR 27-37) locations fell below the TD 5% probability level, and median 22 (IQR 18-26) locations fell below the PD 5% probability level. At locations within  $1^\circ$  of the PRL median TD was -12.5dB (IQR -18.4 to -6.4dB) and median PD was -6.3dB (IQR -9.7 to -3.6dB) which was outside normative limits in 82% of patients. Alternative areas with normal sensitivity were present within the tested region in 46% of patients. Probability plots showed that 77% of patients fixated just foveal to a region of PD within normal limits; 63% of these regions were not apparent on TD probability plots.

**Conclusions:** Comparison to normative data and calculation of conventional perimetric indices is enabled by our spatial interpolation technique despite varied, non-foveal fixation. Patients with AMD demonstrated significant loss around their chosen monocular PRLs, though a common pattern of fixation just foveal to a region of normal PD was apparent, suggesting that a compromise between sensitivity and eccentricity guides PRL selection.

## THE INFLUENCE OF PERIMETRIC STIMULUS SIZE ON DEFECT DETECTABILITY IN EARLY GLAUCOMA

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**Purpose:** To investigate the influence of large perimetric stimulus size on defect detectability in patients with early glaucoma.

**Methods:** 118 healthy participants (H: 71 female, 47 male; 41 to 79 years) and 96 patients with early glaucoma (EG: 43

female, 53 male; 43 to 82 years; average mean deviation (MD):  $-1.37 \pm 1.40$  dB) were recruited from 3 sites. Subjects were included into the EG group if they had a clinical diagnosis of glaucoma, OCT findings characteristic of glaucoma, and a visual field (VF) MD of  $-4.0$  dB or better (SITA-Std, 24-2). For 1 eye of each subject, 3 VF tests were obtained using the Full Threshold 24-2 (FT) for Goldmann stimulus size III, V and VI; the VF tests were repeated within 90 days. Visit 2 data was used throughout. Data from healthy group were used to produce reference limits for normality for each stimulus size.

**Results:** Mean sensitivity (MS) increased with stimulus size (III:  $28.90 \pm 1.43$ ; V:  $34.21 \pm 1.15$ ; VI:  $35.26 \pm 1.26$ ) and decreased with age. The variance for the healthy group was lowest for stimulus size V, generating the smallest confidence intervals. Stimulus size V flagged the highest number of abnormal locations on total deviation (TD) analysis (III: 976/4992; V: 1066; VI: 914), although there was no significant difference between V and III. There was a significant difference between V and VI ( $p < 0.002$ ). Results were similar for pattern deviation (PD). ROC analysis of TD and PD demonstrated a significant difference between Size V and VI ( $p < 0.02$ ;  $p < 0.05$ ), but no differences between size III and V.

**Conclusions:** Goldmann stimulus size V and III were comparable in identifying defects in early glaucoma. Size V generated tighter reference intervals for normality and lower test-retest variability. There was no advantage in using a size VI.

## MULTIVARIABLE LOGISTIC REGRESSION OF ASYMMETRY INDICES FOR DETECTING EARLY POAG

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**Purpose:** To describe and measure the performance of a multivariable discriminant analysis incorporating global indices based upon, Sup/Inf hemifield asymmetry, R/L asymmetry and clustering of hemifield asymmetric locations, for detecting POAG and to determine the best combination of asymmetry indices for future inclusion in perimetric analytical software.

**Materials and Methods:** 412 eyes from 206 control patients (GSS2 stage 0) and 340 eyes from 170 patients with a clinical diagnosis of POAG and GSS2 stage  $< 2$ , were selected from a visual field database of patients attending MREH. Age adjusted defect asymmetries (outside 95% CI of the control population) were calculated for each of the 22 vertically mirrored test point pairs used in the Humphrey Zeiss GHT using a bootstrapping procedure with 2000 samples. The mean deviation of the hemifield differences (HMD), the standard deviation of the differences (HSD) and the number of pairs that fall outside the 95% CI (HNP) were calculated for the 22 pairs. R/L asymmetry used the same test locations giving a total of 44 mirrored test point pairs. The 95% CIs were calculated using a bootstrapping procedure of 2000 samples. The mean deviation of the R/L differences (R/L MD), the standard deviation (R/L SD) and the number of pairs that fall outside the 95% CI (R/L NP) were calculated for the whole field (44 pairs) and for the superior and inferior fields (22 pairs). In addition the number of sup/inf hemifield clusters (N Clusters) and number of hemifield asymmetric pairs within clusters (N Clustered) were calculated based on numbers of significantly asymmetric pairs. A multivariable logistic regression analysis was used (forward stepwise likelihood ratio) to determine the best combination of the 14 asymmetry indices. Areas under the receiver operating characteristic curve (AUROC) were derived for all single indices, GHT and the regression model.

**Results:** For single indices the best AUROCs were R/L NP=0.89 (95% CI 0.87-0.92) and R/L SD AUROC= 0.88 (95% CI 0.85-0.90). The multivariate logistic regression analysis model identified 6 significant asymmetry indices; HNP, R/L SD, R/L SD Inferior, R/L NP, R/L NP Inferior and R/L SD Superior as being independently related to a diagnosis of early glaucomatous field loss ( $p < 0.05$ ) with an AUROC of 0.94 (95% CI 0.92–0.95) a value that is significantly higher than all single asymmetry analyses. The model correctly classified 80% of POAG cases and 89% of controls.

**Conclusions:** A multivariable model based on 6 asymmetry indices performed best for discriminating between eyes clinically diagnosed with early POAG and those with a normal diagnosis and no visual field loss. This model was superior to all single asymmetry analyses.

## INVITED SPEAKER

### A POLYMERIC NEUROINTERFACE RESTORES LIGHT SENSITIVITY IN DEGENERATE RETINAS: POTENTIAL APPLICATION AS ARTIFICIAL RETINA

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Progressive degeneration of photoreceptors is one of the major causes of adult blindness in “industrialized” countries; as an example, Retinitis pigmentosa defines a set of monogenic hereditary retinal diseases, with a prevalence of 1:4000 worldwide, caused by single mutations in over 100 genes. In the past 20 years, several approaches have been attempted to treat Retinitis pigmentosa. However, there is currently no effective cure for the majority of genetic retinal diseases affecting photoreceptors. Sight restoration represents one of the new frontiers for prosthetic devices enabling the electrical stimulation of neurons. In particular, diseases that affect the retina pigmented epithelium and/or photoreceptors, but preserve the inner retinal layers are preferential targets for implantation of visual prostheses. In our work, we exploited the

use of conjugated polymers to generate an organic photovoltaic retinal prosthesis. Our research indicates that organic materials, in particular photovoltaic semiconducting polymers, are suitable for the generation of a fully organic retinal prosthesis, to restore light sensitivity in blindness caused by photoreceptor degeneration.

We found that primary neurons, grown onto a semiconductor polymer layer (P3HT), are depolarized and fire action potentials by appropriate light stimuli with a spatial resolution in the order of the neuronal cell body. Moreover, light stimulation of degenerate retinas placed on the organic polymer in sub-retinal configuration (i.e., external layers in contact with the polymer) showed that a light stimulus 16-fold lower than the safe limit for pulsed illumination elicited intense spiking activity in retinal ganglion cells (RGCs) to levels indistinguishable from those recorded in control retinas. A dose-response analysis of the RGC firing rate versus light intensity revealed a linear response in a range corresponding to daylight irradiance range, indicating that the interface could mimic functional photoreceptors.

We then started an in vivo study by implanting a prosthesis made by P3HT/PEDOT on a silk fibroin substrate in the eye of rats bearing photoreceptor degeneration due to mutation in the *merlk* gene (Royal College of Surgeons rats), a recognized animal model of human Retinitis pigmentosa. Rats were subjected to behavioral, electrophysiological, 2-DG positron-emission tomography (PET) and ocular coherence tomography (OCT) monitoring up to six months after the surgical implant. The data showed that: (i) the implant was very well tolerated and the inflammation markers progressively normalized after the surgery; (ii) the retina remained well attached over the entire implant surface and the polymeric layer was retained over time; (iii) in all tests of light sensitivity such as pupil constriction, flash-evoked visual potentials (fVEP), metabolic activation of V1 and light-dark behavior, implanted blind rats had responses similar to those of non-dystrophic controls; (iv) visual acuity determined by administering patterned stimuli and recording VEP amplitude in V1 (pVEP) revealed a recovery of the visual acuity to the levels of non-dystrophic controls. These results broaden the possibility of developing a new generation of fully organic prosthetic devices for sub-retinal implants.

## PERIMETRY IV

### VALIDATING VARIATIONAL BAYES LINEAR REGRESSION MODEL WITH MULTICENTRAL DATA

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**Purpose:** We reported a variational Bayes linear regression (VBLR) model for predicting future visual fields (VFs). (Murata et al., IOVS, 2014) The purpose of this study is to validate the model with multicentral data again.

**Method:** 7070 eyes of 3957 patients at the University of Tokyo Hospital were used as training data using VBLR, and the data from the Japanese Archive of Multicentral Database in Glaucoma (Fujino et al. IOVS, 2016) excluding the patients included in the training data was used as the test data for validation. The test data was consisted of 271 eyes of 177 patients with primary open angle glaucoma with at least 11 reliable VFs, defined as fixation loss <20% and false positive <15%. The performance of VBLR was compared against ordinary least-squares linear regression (OLSLR) by predicting VFs in the test dataset. The total deviation (TD) values of test patients' 11th VFs were predicted using TD values from their second to 10th VFs (VF2-10), and then the root mean squared error (RMSE) associated with each approach was calculated. The same process was repeated to predict 11<sup>th</sup> VFs using VF2-9, VF2-8, and so on till VF2-4. Similarly, mean of 52 TD values (mTD) of test patients' 11th VFs was predicted using VBLR and OLSLR, and the absolute prediction errors were compared.

**Result:** The RMSEs resulting from VBLR averaged between  $3.8 \pm 1.8$  (SD) and  $5.0 \pm 2.7$  dB for the prediction based on VF2-10 and VF2-4, respectively. The RMSE resulting from OLSLR was between  $3.9 \pm 1.7$  (VF2-10) and  $19.5 \pm 12.9$  (VF2-4) dB. The absolute prediction error (SD) for mTD using VBLR was between  $1.3 \pm 1.3$  (VF2-10) and  $2.1 \pm 2.2$  (VF2-4) dB, while the prediction error resulting from OLSLR was between  $1.2 \pm 1.1$  (VF2-10) and  $5.4 \pm 9.0$  (VF2-4) dB.

**Conclusion:** VBLR can predict future VFs more accurately than OLSLR, as confirmed with the multicentral data.

### INCORPORATING PROBABILISTIC GRAPHICAL MODELS INTO PERIMETRIC TEST PROCEDURES

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**Purpose:** There is spatial information in the visual field (VF) that is not currently used in a sophisticated manner in perimetric algorithms. We hypothesised that a perimetric algorithm (BARF: Bayesian Adaptive Random Field) that maintains a graphical model of the VF, allowing for a more holistic updating of VF sensitivities over the course of testing, would improve accuracy and precision of VF estimates.

**Materials and methods:** BARF is a maximum pseudolikelihood Bayesian procedure. A separate probability mass function (PMF) is maintained for each location in the VF. Each PMF begins as a uniform function and is updated with a likelihood



function during testing. The VF is represented as a graphical model by connecting first-degree neighbouring locations with edges (while respecting the horizontal midline nasal to the blind spot). A static PMF is created for each edge, which describes the probability of each possible pair of sensitivity values. A pseudolikelihood function can then be calculated for each location by combining the location and edge PMFs across locations that share an edge. A look-ahead procedure is used to maximise the expected change in the sum of the means of the pseudolikelihood functions. Test termination requires at least 2 presentations per location and  $n$  consecutive trials over which  $\leq d$  dB of change occurs in the sum of the mean of the pseudolikelihood functions. Final VF estimates are derived using iterated conditional modes sampling. BARF was tested using computer simulations of reliable (3% FP) and unreliable observers (15% FP) with a training dataset of 60 glaucomatous and 60 normal VFs (HFA 24-2 FT) and a test dataset of 40 normal (HFA 24-2 SITA) and 139 glaucomatous VFs (HFA 24-2 FT). ZEST was simulated as baseline algorithms. Output measures included: number of presentations and VF sensitivity estimates. Errors were calculated by subtracting the estimated VF from the input VF.

**Results:** We attempted to optimise BARF using termination criteria of  $n=1:10$  and  $d=(0.3, 0.5, 0.6, 0.7, 1, 2)$  with edge functions: (1) derived empirically from the training VF set, and (2) uniform functions. For all conditions listed and numerous others, BARF did not improve accuracy or precision for similar test times.

**Conclusions:** We have developed a novel perimetric algorithm that updates visual sensitivities across the VF during testing. However, given the variability inherent in perimetric responses and the desire for short test times, applying probabilistic graphical models to perimetric algorithms does not appear to yield benefit.

## SEQUENCE EFFECTS DURING FREQUENCY-OF-SEEING EXPERIMENTS IN PERIMETRY

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**Purpose:** Sequence effects, where the response to a stimulus is influenced by prior responses, have been reported for many psychophysical tasks. We investigated such effects in data from frequency-of-seeing (FOS) experiments.

**Methods:** Analysis was conducted on FOS data collected on 110 subjects with a range of visual field sensitivities (0 to 37 dB), at Moorfields Eye Hospital (London, UK) and Dalhousie University (Halifax, Canada). The method of constant stimuli was used to present Goldmann size III stimuli (diameter, 0.43 degrees) for 200 ms. One eye per subject was tested, and between 80 and 400 stimuli were presented at between 2 to 10 locations. Responses preceded by a seen presentation were separated from those which followed unseen ones, and separate FOS curves were derived. The Psignifit toolbox (v.3.0, Fründ *et al.* JOV 2011) was used to estimate the sensitivity value at 50% seeing (threshold), and variability (difference between 25% and 75% seen). Pairwise differences in threshold and variability were then evaluated.

**Results:** Threshold and variability differences were calculated from 315 pairs of FOS curves. A small decrease in median threshold (-0.45 dB;  $p<0.001$ ) occurred after an unseen presentation. Median FOS variability was 2% higher on this set of data ( $p<0.001$ ).

**Conclusions:** The findings suggest that sensitivity may reduce after unseen presentations. Taking sequence effects into account in the design of threshold algorithms may be of benefit to some participants performing clinical visual field assessment.

## DE VRIES-ROSE AND WEBER LAW IN GLAUCOMA

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**Purpose:** In the human visual system, contrast sensitivity (CS) increases proportional to the square root of the background luminance at low luminances (de Vries-Rose law) and is independent of the background luminance at high luminances (Weber law). The aim of this study was to determine if these psychophysical laws also rule in the intact areas of the visual field of patients with glaucoma.

**Materials and Methods:** Case-control study with 15 glaucoma patients and 45 controls. Cases were selected to have moderate or advanced visual field loss in combination with a normal visual acuity. Controls had to have a negative ophthalmic history (except for glasses and uneventful cataract extraction), no family history of glaucoma, an intraocular pressure of 21 mmHg or less, an age between 40 and 70, and a normal visual acuity. Experiments were performed monocularly; the dominant eye was selected if both eyes were eligible. Perimetry was performed using a high-luminance monitor (EIZO radiorforce G21; maximum luminance approximately 460 cd/m<sup>2</sup>) driven by the Psychophysics Toolbox (PTB-3; Brainard, 1997; Pelli, 1997) with Octave (version 3.2.4; [www.gnu.org/software/octave/](http://www.gnu.org/software/octave/)) for Linux (Ubuntu 10.10). A reduced testing grid was used, consisting of the fovea and 6 peripheral test locations. Stimulus was a Goldmann size III increment with a duration of 200 ms. A 4-2 dB staircase procedure was used to determine the threshold Weber contrast; CS is the inverse of this threshold. Output of a single visual field test was the median logCS of a subset of test locations that were, for that specific patient, normal on standard automated perimetry (unmarked or marked as  $P<5\%$  in the total deviation probability plot). Mean background luminance was 0.013, 0.13, 1.3, 13, and 130 cd/m<sup>2</sup>, obtained by using neutral density filters.

**Results:** In controls, logCS saturated around 130 cd/m<sup>2</sup> at 0.9 (range 0.7-1.1) and was proportional to the square root of the background luminance between 0.013 and 1.3 cd/m<sup>2</sup>. In glaucoma patients, the maximum stimulus contrast (corresponding to logCS = -0.4) was not seen at 0.013 cd/m<sup>2</sup> and logCS was approximately 0.4 lower than in the controls for the other background luminances.

**Conclusions:** De Vries-Rose and Weber law rule in the intact areas of the visual field of patients with glaucoma. The logCS versus log background luminance curve of glaucoma patients is shifted downwards when compared to controls. In the de Vries-Rose part of the curve, the logCS of glaucoma patients equals a value that is reached by controls already at a six- to sevenfold lower background luminance.

## IPS LECTURE

### THE VISUAL FIELD-MORE THAN JUST PERIMETRY

**Ulrich Schiefer**

*University of Applied Sciences Aalen, Germany, Eberhard Karls University, Tübingen, Germany*

This 2016 IPS lecture will address the following topics:

- What do we know about the peripheral visual field?
- Visual field: Is it all about contrast sensitivity?
- What about individualized progression analysis of visual field defects?
- When is it time to say good-bye in a perimetric session?
- Outlook: What are my personal interests over the next years?