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Clinical Perimetry 1

THE ROLE OF PERIMETRY IN ASSESSING THE OPHTHALMOLOGIC SAFETY OF DRUGS: THE PREGABALIN EXPERIENCE. MG Brigell, Pfizer Inc, Ann Arbor, MI USA

Purpose: With increased sensitivity of regulators to potential visual adverse effects of drugs, safety studies monitoring longitudinal visual field status have become increasingly common. Issues around study design, case definitions and interpretation of results will be discussed in this paper.

Methods: A review of the pregabalin phase 3 visual safety program will be presented. Patients were followed with Humphrey 120 point screening visual fields. Fields were followed in 3621 patients treated for epilepsy, pain or anxiety disorder in randomized clinical trials (RCTs) of up to 12 weeks in duration and in uncontrolled longterm open-label (OL) studies. Cases of potential progression were defined by either patient adverse events; examining ophthalmologist impression of field deterioration, or an increase of 10 or more points missed from baseline on any visit. This pool of cases was then reviewed by 3 visual field experts who validated a clinically significant change and, for open-label studies, assessed whether the change was clinically expected based on ophthalmologic history. **Results**: Baseline field abnormalities were present in 15.1% of patients. In RCTs the percent of cases of apparent visual field progression was equivalent between pregabalin treated patients and controls using the all case (12.4% vs 11.7%) and validated case (5.3% vs 4.8%) definitions. However, when stratified by dose, a higher rate of field progression cases was seen at an intermediate dose compared to placebo, but not at lower or higher doses. With long-term exposure in OL studies, the rate of field deterioration remained

<u>Conclusion:</u> Visual field results were as good as could be expected with a CNS active drug that causes some somnolence. Despite this, the FDA was not convinced of the visual safety of pregabalin and included a patient precaution regarding ophthalmologic safety in the product label. Lessons learned from this experience and a more optimal way to design studies to demonstrate the absence of a drug related visual field defect will be discussed.

VISUAL PERFORMANCE TEST: RESULTS IN HEMIOPIC DEFECTS AND IN FOLLOW-UP OF COMPENSATIONAL REHABILITATION TRAINING

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<u>Purpose</u>: To demonstrate a test for assessing the real handicap due to visual pathway lesions and for follow-up of rehabilitation training.

Methods: This test measures the binocular reaction time for black objects on a CRT screen in a symmetrical grid of 11 positions within the central 34° field, superimposed on a bright landscape. Saccades are recommended. Reaction times are saved for 2 consecutive series. An asymmetry index gives the mean of differences in reaction time within each pair of corresponding search targets in % of the time in the center. This exam was performed in 38 patients with absolute homonymous visual field defects, 29 of them complaining of restrictions in daily life. In 3, neglect was primarily treated by neuropsychologists. Visual fields were obtained with the Octube Easyfield screening program (Center for Neurological Therapy) or with the Octopus 1-2-3 program G1X (Outpatient Unit). Compensational visual rehabilitation training of search saccades was individually selected and administered.

<u>Results:</u> The reaction time was in most patients prolonged within the homonymous field defect, at least in parts of it. The response before the training within the "unaffected" hemifield, however, was in 24 of all 38 cases also abnormally delayed. Nineteen symptomatic patients received compensational visual rehabilitation training, improving asymmetry in $2/3^{rds}$ of cases, whereas $1/3^{rd}$ showed considerable fluctuations due to other neurological and neuropsychological deficits. The asymmetry index before the training was between 867 and 134 (mean 392), reduced by 21-89% (mean 61%) after the training. The prolonged reaction time in the "unaffected" hemifield, as present in all but one of these treated patients, was also highly reduced after the training, whereas all visual fields were unchanged.

Conclusions: This simple and quick visual performance test is a valuable quantitative diagnostic tool in addition to the more tiresome conventional static perimetry and to neuropsychological tests for divided and selective attention as well as for neglect syndrome. It allows quality assessment of compensational visual rehabilitation training.

PATHO-PHYSIOLOGY OF NASAL MYOPIC SUPER-TRACTION & POSSIBLE RELATED COMPLICATIONS

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UC San Francisco², San Francisco, USA, Department of Ophthalmology, UC Davis³, Sacramento, USA, School of Public Health⁴, UCB, Berkeley, USA, Department of Molecular and Cell Biology, UCB⁵, USA.

Purpose: Since the late 19th Century, aspects of patho-physiology of "nasal myopic super-traction of the retina and choroid onto the optic nerve head" have been known. These have been poorly elucidated. We consider here a number of issues pertaining to this and other common disc-related complications of high myopia.

Methods: In cooperation with the Armed Forces Institute of Pathology, Washington, DC, histological findings in "nasal myopic super-traction", were presented. We considered early German investigations of this disorder, e.g., Elschnig, 1901, and recent important data of Shimada, et al., 2006. We sought to understand both "myopic conus" and encroachment of retina and choroid onto the optic disc. We introduced OCT II records of this disorder, and perimetric data utilizing fundus-camera-perimetry. We attempted to relate patho-anatomical findings to separately-determined visual functions upon and adjacent to the disc in affected individuals.

<u>Results:</u> Separate or partially related mechanisms may cause nasal myopic supertraction, myopic conus, and peripapillary detachment in pathological myopia (PDPM). We differentiated between different degrees of hyperemia on the disc in individuals with nasal myopic super-traction, and considered neural pathways of nerve fiber bundles at the disc. We related our data to subject OCT II records. We discuss the fate of the residuum of the RPE in morning glory anomaly, and separately in OCT II studies, and address research of Shimada on PDPM and note its relationship to nasal myopic super-traction. <u>**Conclusions:**</u> Three disc-related anomalies associated with high and pathological myopia have been considered; nasal myopic super-traction has been emphasized. Available histology, similarities and differences were addressed. OCT records have been presented and compared. Distinct patterning was found. In the presence of nasal myopic super-traction, on-disc visual functions exhibited reduced sensitivity, and transient alterations in stimulus detection and photoreceptor alignments.

VISUAL FIELD ABNORMALITIES 10 YEARS AFTER OPTIC NEURITIS: EXPERIENCE IN THE OPTIC NEURITIS TREATMENT TRIAL (ONTT)

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<u>Purpose</u>: To evaluate visual field abnormalities 1- 5 and 10 years after the Optic Neuritis Treatment Trial (ONTT).

Methods: Three readers independently classified 1,684 visual fields 1, 5 and 10 years after acute optic neuritis. Two readers independently classified 2,148 visual fields 2, 3, and 4 years after optic neuritis. Readers used a classification system developed for the ONTT which consisted of 21 monocular classifications and 10 binocular classifications. Reader agreement determinations are still pending the third reader's evaluations. **Results:** Abnormal visual field and binocular classification frequencies remained consistent at 41% for years 1, 5, and 10. Abnormal visual field and binocular classification frequencies were similar at 46%, 39%, and 41% for years 2, 3, and 4, respectively. The most common monocular classifications were paracentral and partial arcuate defects for all years 1 - 5 and 10; the most common binocular classification for all years was binocular unrelated.

Conclusion: Frequencies for the 1-5 and 10-year visual field classifications were similar, with paracentral and partial arcuate defects as the most common monocular classifications and binocular unrelated as the most common binocular classification.

USE OF THE SIZE I TEST OBJECT FOR SUBTLE OPTIC NEUROPATHIES AND MACULAR PATHOLOGY.

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Purpose: Although standard perimetry (white on white) with a size III test object usually detects relatively subtle abnormalities in optic nerve and retinal function, in some early cases or patients with residual dysfunction the standard perimetry may be entirely normal. The use of a size I test object may be able to detect pathology otherwise unseen. **Materials & Methods:** In a series of 16 patients seen over a 20 year period at the University of Virginia the size I test object was utilized with either a 10-2 program or a 24-2 program to detect or confirm otherwise unseen or poorly defined defects. **Results:** In the series of patients the 10-2 with a size I was able to better define early maculopathy secondary to Chloroquine in 1 patient, to detect minimal residual arcuate changes due to optic neuropathy secondary to demyelinating disease, compressive optic neuropathy in 8 patients, and subtle bitemporal defects due to residual damage secondary to pituitary tumors in 2 patients.

<u>Conclusions</u>: The use of the size I test object may be helpful in detecting subtle abnormalities when the clinical history and examination suggests residual problems either due to subtle macula or optic nerve dysfunction. When the field looks normal and yet there is other evidence (afferent pupillary defect, optic atrophy, etc.) suggestive of pathology a size I may be useful in defining residual damage.

EVALUATION OF RELATIVE AFFERENT PUPILLARY DEFECT IN PATIENTS WITH HOMONYMOUS VISUAL FIELD DEFECTS DUE TO CEREBROVASCULAR LESIONS IN THE POSTERIOR AND MIDDLE CEREBRAL ARTERY TERRITORIES

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Purpose: (i) To assess the presence and magnitude of relative afferent pupillary defect (RAPD) in patients with homonymous visual field defects (HVFDs), (ii) to characterize the location of the cerebral lesions associated with the pupillary findings, and (iii) to assess the agreement of RAPD quantified with graded neutral density filters and automated video pupillography.

<u>Methods</u>: RAPD was initially quantified clinically by two independent examiners with graded neutral density filters (swinging flashlight test), and secondly by means of an automated infrared videopupillographic device (SWIFT = automated SWInging Flashlight Test). Agreement was measured by Cohen's kappa. Cerebral regions potentially involved in the afferent pupillary pathway were extracted by superimposing the MRI scans on the MRIcro software. Twenty-four patients (7 females, 17 males, aged 21-74 years) with HVFDs due to unilateral vascular brain lesions (minimal visual acuity 16/20) participated in this study.

<u>Results:</u> RAPD was present in 11/24 patients (magnitude: median 0.3 log units, range 0.3–0.9 log units). Agreement (Cohen's kappa) between examiners was 0.75 (SE 0.13), but only 0.11 (SE 0.22) between the senior examiner (U.S.) and SWIFT after dichotomization at 0.3 log units. RAPD occurred contralaterally to the affected hemisphere in all cases. In patients *without* RAPD, lesions were typically restricted to the primary visual cortex close to the calcarine sulcus, whereas in patients *with* RAPD, the lesion overlap affected the course of the optic radiation in the temporal white matter.

<u>**Conclusions:**</u> Clear anatomical differences were revealed between patients *with* and *without* RAPD. Automatically and clinically assessed RAPD showed only fair agreement, probably due to the low magnitude of RAPD.

Clinical Perimetry 2

CORRELATION OF M-CHARTS[™] AND PHP[™] FINDINGS WITH SUBJECTIVE PERCEPTION OF METAMORPHOPSIA IN PATIENTS WITH MACULAR DISEASES

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Purpose: We developed M-CHARTSTM for the quantification of metamorphopsia and reported its usefulness for macular diseases. PHPTM was also developed for detecting the metamorphopsia of AMD. However, it is still not clear if the metamorphopsia score obtained by M-CHARTSTM and PHPTM findings can really reflect the patient's subjective perception of metamorphopsia in their daily life. In this study, we designed a new metamorphopsia questionnaire for evaluating the patient's subjective severity of metamorphopsia and compared it with the metamorphopsia score obtained by M-CHARTSTM and PHPTM findings.

Subjects and Methods: Our new metamorphopsia questionnaire contains 10 questions which focus on the symptoms of metamorphopsia in the quality of vision. Using this questionnaire, we evaluated the severity of the subjective perception of metamorphopsia in daily life. For the qualification of metamorphopsia, the minimum visual angle of the dotted line needed to detect metamorphopsia was measured by M-CHARTSTM. PHPTM is designed to detect metamorphopsia using the hyper acuity function. We compared these three methods in 38 eyes of 38 idiopathic epiretinal membrane (ERM), 20 eyes of 20 idiopathic macular hole (MH) and 18 eyes of 18 age related macular degeneration (AMD) patients.

Results: There was significant correlation between the severity of the metamorphopsia perception using our questionnaire and the metamorphopsia score using M-CHARTSTM. If the metamorphopsia scores were about the same in all 3 disease groups, severe subjective metamorphopsia perception using our questionnaire was observed in patients with MH and AMD than with ERM. The sensitivity for detecting metamorphopsia was 38 % by PHPTM, 78% by M-CHARTSTM in ERM, 69% by PHPTM and 76% by M-CHARTSTM in AMD.

<u>Conclusion</u>: Metamorphopsia score by M-CHARTSTM reflects the subjective perception of metamorphopsia in patients with macular diseases. M-CHARTSTM can detect slight metamorphopsia as compared with PHPTM.

AUTOMATED STATIC PERIMETRY IN EYES WITH CENTRAL SEROUS CHORIORETINOPATHY

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Purpose: To study the central visual field abnormality seen in eyes with central serous chorioretinopathy (CSC), which has rarely been evaluated quantitatively using automated static perimetry in a clinical study. The author claims that the severity of the disease should be assessed by the mean deviation (MD) of the central 10-degree automated static perimetry, which is independent of the visual acuity.

Methods: We reviewed the results of Humphrey perimetry, central 10-2 program taken for 121 eyes of 118 patients (22 female and 96 male) with CSC seen in our hospital between 1993 and 2003. A total of 132 episodes of serous retinal detachment (98 initial and 34 recurrent) was studied. In order to study the effects of active serous retinal detachment on the central visual field, eyes with obvious RPE atrophy evidenced by the angiographic window defects were excluded.

<u>Results</u>: Central visual field abnormality in eyes with CSC varied from no defects to severe and large central scotoma. Mean deviation (MD) ranged from -21.1 dB to 2.6 dB with the mean of -3.8 dB. Thirty seven of 132 perimetric results (28%) showed MD lower than -5 dB. The best corrected visual acuity ranged between 0.07 and 1.5 with the median of 0.7. The correlation between MD and logarithm of minimum angle of resolution (logMAR) was not significant (r = -0.116, P = .186) implying that the severity of central field defects could not be predicted from the visual acuity.

Conclusion: Eyes with CSC show various degrees of central visual field loss. Poor correlation between MD and corrected visual acuity implies that many eyes with CSC showing near normal visual acuity may suffer from severe central visual field abnormality. Automated static perimetry measuring the central 10-degree visual field in an eye with CSC provides additional information for assessing visual disability that could not be predicted by visual acuity testing.

RAREBIT FOVEA TEST IN DIABETES

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Purpose: The aim of this pilot study was to evaluate the ability of the Rarebit Fovea Test (RFT) to detect subclinical retinal damage in patients with diabetes. **Methods:** Forty-two eyes from 42 diabetic subjects, aged 18-55 years (mean 40.5 \pm 9.6 years), and with a duration of diabetes from 1 to 29 years (mean 10.9 \pm 7.4 SD) were examined. The inclusion criteria were no known macular or vascular changes, a best corrected VA of logMAR 0.0 or better and refraction within \pm 6D. All patients underwent an extensive examination including refraction measurement, VA testing using the ETDRS chart, fundus photography, analyzed using a grading scale, OCT measurement of the macula retinal thickness and determination of lens transparency using Scheimpflug photography. The Rarebit fovea Test (RFT) probes the integrity of the retinal architecture within the central 4 degrees. The stimuli are very small bright dots and the results are expressed as hit rate, i.e. per cent seen targets with a normal range of 100-97%. **Results:** Abnormal hit rate (50-96%) was found in 14 of the 42 eyes. In these eyes no signs of lens opacity, retinal thicknesing or maculopathy were observed. One subject had a mild diabetic retinopathy. There were no significant correlations between RFT results and

age, VA, macular thickness or lens transparency.

Conclusion: The findings indicate that RFT may provide information about macular function in a subgroup of patients with diabetes, uncorrelated to findings from conventional tests and screening methods. The prognostic and potentially therapeutic implications are currently investigated.

LOW SPATIAL FREQUENCY CONTRAST SENSITIVITY DEFICITS IN MAGNOCELLULAR AND PARVOCELLULAR PATHWAYS IN GLAUCOMA AM McKendrick¹, G Sampson¹, DR Badcock². University of Melbourne, Australia¹.

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Purpose: Early glaucomatous damage may result in pruning or loss of larger ganglion cells [1]. This study uses a recently described technique to measure low spatial frequency sensitivity in parvocellular pathways. We aimed to determine whether greater sensitivity loss exists at lower than medium spatial frequencies in presumed magnocellular (M) and parvocellular (P) processing.

<u>Methods</u>: Thirteen individuals with early glaucoma (aged 52-84 years) and 14 agesimilar controls (53-77 years) participated. Contrast sensitivity was measured using gabor stimuli (Gaussian modulated sinusoids of 0.25, 0.5, 1 and 2 c/°, stdev of Gaussian 4°). These were presented using both a steady pedestal paradigm (40ms presentation of the gabor against a continuously presented luminance pedestal) and a pulsed pedestal paradigm (40ms presentation of the gabor and pedestal). The steady and pulsed pedestal gabors permit determination of spatial frequency dependent deficits of M and P pathways respectively [2]. Contrast sensitivity was measured foveally, and at two mid-peripheral locations (10°). For each subject, one mid-peripheral location was within a quadrant of normal visual field (Standard Automated Perimetry, Medmont M700) with the other location being presented in a quadrant of early field loss.

<u>Results</u>: Glaucoma group performance was not significantly different from controls for either pedestal procedure when tested foveally or mid-peripherally within an area of normal visual field. Within a quadrant of early visual field loss, the glaucoma group had significantly reduced sensitivity of both presumed M and P processing (steady: F(25,1) = 23.01, p<0.05; pulsed: F(25, 1) = 11.50, p<0.05). Effect sizes demonstrated that the sensitivity loss was of a similar magnitude for all tested spatial frequencies.

<u>Conclusions</u>: This study shows non-selective loss of sensitivity in both M and P pathways for stimuli of low-medium spatial frequency. Testing P function may be equally as effective as testing M function for the detection of early visual field loss in glaucoma.

[1] Glovinsky et al. IOVS. 1991: 32: 484-91

[2] Leonova et al. Vis. Res. 2003: 43: 2133-9

COMPARISON OF VISUAL FIELDS AND VISION LOSS ON EVERYDAY FUNCTION IN OLDER DIABETICS RA Schuchard' AR Bengtzen Atlanta VA Rehabilitation R&D Center of Excellence

Purpose: This pilot study investigated diabetic vision loss by: 1) comparing the results of central visual field loss from three perimetry instruments (SLO, HFA, and Matrix), and 2) investigating the associations between vision loss assessed by these perimetry instrument results and other visual function results to the overall score on the NEI-VFQ. **Methods:** Fifteen older diabetic subjects (at least 50 yo, 5 years since onset of diabetes) had binocular vision loss assessed by visual acuity, contrast sensitivity, and dynamic visual fields (DVFs). DVFs were found by randomly presenting targets while subjects scanned the visual field. The targets were left on until the subject indicated the direction of the target (relative to the center). SLO (hybrid perimetry), HFA (24-2), and Matrix (24-2) perimetry assessed central visual field monocularly. The NEI-VFQ 25 question self-report survey assessed activities of daily living.

<u>Results:</u> Testing results found visual acuity from -0.14 to 1.44 logMAR, contrast sensitivity from 0.10 to 1.75 logcontrast, and average DVF response time from 1.1 to 6.0 seconds. Comparison of HFA to SLO found sensitivity = 0.77 (\pm 0.40), specificity = 0.31 (\pm 0.34) and Matrix to SLO found sensitivity = 0.69 (\pm 0.38), specificity = 0.50 ((\pm 0.34). Note that both the HFA and Matrix had high rates of false positive errors (69% and 50%). Single variable regression analysis of the independent vision loss variables on NEI-VFQ overall score found significance for contrast sensitivity, visual acuity, and average DVF response times (in order; $p \le 0.05$).

<u>**Conclusions:**</u> High false positive rates from standard perimetry instruments may be significantly overestimating the amount of central visual field loss in older diabetics. Eye movements to compensate for central visual field loss may be important as DVF was significantly related to NEI-VFQ scores while standard central visual field results were not. Contrast vision loss may be more important in everyday function as contrast sensitivity was found to be most strongly associated with overall NEI-VFQ scores in older diabetics.

THE RELATIONSHIP BETWEEN LOWERING INTRAOCULAR PRESSURE AND PROGNOSTIC FACTORS FOR PROGRESSION OF VISUAL FIELD DAMAGE IN PATIENTS WITH NORMAL TENSION GLAUCOMA

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<u>Purpose</u>: To study the relationship between lowering intraocular pressure (IOP) and prognostic factors for progression of visual field damage in Japanese patients with normal-tension glaucoma (NTG).

<u>Subjects and Methods</u>: Ninety-two eyes of 92 NTG patients were enrolled in the study. All patients were followed up for more than 2 years with topical antiglaucoma medications. The mean IOP of follow-up was used for the assessment of IOP control. The probability of visual field stability was analyzed using the Kaplan-Meier life-table analysis.

<u>Results</u>: Eyes with mean IOP above than 13 mmHg showed statistically significant progression of visual field damage than those with mean IOP less than 13 mmHg (logrank test, p<0.05). Lowering IOP treatment could prevent the progression of visual field damage in patients without family history of cerebrovascular disease (p<0.02p) and cardiovascular disease (p<0.02), without personal past history of migraine (p<0.01), diabetes mellitus (p<0.01), cerebrovascular disease (p<0.02) and arrhythmia (p<0.02).

Conclusion: IOP lowering was strongly influenced to the existence of circulation disorders and satisfactory of treatment of IOP lowering would be expected to beneficial in patients with NTG who have the risk of disease progression.

Optic Nerve head and nerve fibre imaging

RELEVANCE VECTOR MACHINE FOR COMBINING HRT II AND SWAP RESULTS FOR DISCRIMINATING BETWEEN HEALTHY AND GLAUCOMA EYES

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Purpose: To determine the diagnostic accuracy for classifying healthy and glaucomatous eyes using relevance vector machine (RVM) learning classifiers trained on HRT II optic disc topography and SWAP visual sensitivity measurements, independently and combined.

Methods: 68 eves of 68 healthy controls and 144 eves of 144 glaucoma patients with glaucomatous appearing optic discs **and/or** repeatable abnormal standard automated perimetry (SAP) results were imaged using HRT II (Heidelberg Engineering, Dossenheim, Germany) and tested using full-threshold SWAP (Humphrey Field Analyzer II, Dublin, CA) within three months. RVMs were trained and tested on 80 HRTdetermined optic disc topography parameters and 52 SWAP threshold values from the 24-2 grid plus age, independently and in combination. Ten-fold cross-validation was used to train and test RVMs on unique subsets of the full 212-eye data set, and areas under the receiver operating characteristic curve (AUROC) for the classification of eves in the test set were generated for full dimension (FD) and optimized (OPT) (using backward elimination) input data sets. AUROC results from RVM trained on HRT and SWAP alone and in combination were compared. Results were also compared to currently available HRT linear discriminant function classifiers and SWAP global indices. **Results:** AUROCS for RVMs trained on HRT (0.88 FD, 0.89 OPT) were significantly larger than those trained on SWAP (0.72 FD, 0.75 OPT). They also were significantly larger than those for HRT classifiers (0.76 RB classifier, 0.81 FSM classifier) and SWAP global indices (MD=0.68, PSD=0.72) (all p<0.01). Combining HRT and SWAP (AUROC=0.90, FD and OPT) did not improve AUROCs compared to RVM trained on HRT alone (p>0.10), but did improve AUROCs compared to SWAP alone (p<.001). Conclusions: RVMs trained on HRT data have higher diagnostic accuracy than RVMs trained on SWAP data for detecting eyes with glaucoma. Combining these particular measures does not necessarily improve diagnostic accuracy.

EARLY GLAUCOMA DETECTION: A COMPARISON BETWEEN SCANNING LASER POLARIMETRY WITH A VARIABLE CORNEAL COMPENSATOR AND RAREBIT PERIMETRY

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<u>Purpose</u>: To compare the ability of scanning laser polarimetry (SLP) with a variable corneal polarization compensator (GDx-VCC) and Rarebit Perimetry (RBP) in the discrimination between healthy and early glaucomatous eyes.

Methods: Fifty patients with early glaucomatous visual field defects (mean MD -2.5 \pm 1.3 dB; mean PSD 3.2 \pm 1.2 dB), and 38 controls underwent RBP testing and GDx-VCC imaging. One eye per patient was considered. Differences between the groups were evaluated using the Mann-Whitney test. Sensitivity, specificity and area under the receiver operating characteristic curve (AROC) for discriminating healthy from glaucomatous eyes were evaluated for specific GDx-VCC and RBP parameters. Cut-off points, defined as the value dividing healthy from glaucomatous eyes with the highest probability, were determined. SAP test results were taken as the gold standard. The agreement between GDx-VCC and RBP results was assessed using the Cohen Kappa.

<u>Results</u>: Statistically significant differences were found between the groups for all GDx-VCC and RBP parameters. The AROC ranged respectively from 0.76 to 0.90 for the GDx-VCC parameters, and from 0.89 to 0.93 for the RBP parameters. The parameter giving the largest AROC with GDx-VCC was the Nerve Fiber Indicator (AROC 0.90; sensitivity 86%, specificity 89.5%; cut-off set at 25); with RBP, the parameter was Mean-Hit-Rate (AROC 0.93; sensitivity 90%, specificity 97.4%; cut-off set at 82%). The Cohen Kappa was 0.68.

Conclusions: Early detection of glaucoma should take into consideration initial signs of both structural and functional defects. Both GDx-VCC and RBP tests showed a good ability in discriminating between healthy and early glaucomatous eyes, suggesting that both can be of aid in the early diagnosis of glaucoma. The agreement between the two test results appeared to be moderate.

LONGITUDINAL EVALUATION OF EXPERIMENTAL RETINAL NERVE FIBER LAYER DEFECTS BY SLP, CSLO, AND OCT

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<u>Purpose</u>: To compare results from SLP, CSLO, and OCT before and after initiation of an experimental retinal nerve fiber layer defect (ERNFLD).

Methods: Four rhesus monkeys had retinal laser burns placed in an arc around the optic disc (~45° and 1.5 mm from the margin) to create an ERNFLD in one eye each. Baseline measurements of structure and function were obtained weekly for one month prior to, and 5 weeks after laser in both experimental and fellow control eyes. Functional evaluation included multifocal, full field and pattern-reversal electroretinography (ERG). Structural evaluation included stereophotography, SLP (GDx VCC), CSLO (HRT1), and OCT (Stratus). RNFL thickness estimates were exported for a 3.4 mm diameter, circumpapillary locus from the CSLO and OCT instruments to match the "medium" locus of the SLP instrument; comparisons were made between instruments and over time before and after laser.

<u>Results</u>: During pre-laser baseline, RNFL thickness estimates were more consistent between sessions, and between right and left eyes for SLP and OCT as compared with CSLO. The average RNFL thickness was 45.9 ± 8.3 , 95.4 ± 12.1 , and 147.2 ± 30.7 for SLP, OCT, and CSLO respectively. One week after laser, a statistically significant ERNFLD was present in 2/3 eyes by SLP and none by OCT or CSLO. Functional abnormalities were evident by multifocal ERG in 3/3 eyes (one experimental eye was omitted because of intraretinal hemorrhage). Between weeks 1 and 3, OCT estimates of RNFL increased, then declined in 3/3 eyes. CSLO never indicated any RNFL defect.

Conclusions: In this small group of macaques, OCT provided the most reproducible estimate of RNFL thickness, closely followed by SLP. The CSLO estimates were relatively unreliable and insensitive. SLP detected the ERNFLD prior to OCT and CSLO, at a time when functional loss was apparent. The pattern of results suggests that OCT detected axonal swelling during early stage damage, but that birefringent elements were already disrupted. The discrepancies between SLP and OCT estimates may be informative about the pathological status of RGC axons.

AGE-RELATED LOSSES OF RETINAL GANGLION CELLS AND NERVE FIBER LAYER THICKNESS

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Purpose: To study age-related reductions in retinal nerve fiber layer thickness (RNFLT) with respect to two issues. 1) Aging effects on RNFLT are assumed to be the result of age-related losses in retinal ganglion cells (RGCs), but the rates are much different; age-related losses of RGCs are about 0.7%/year compared to 0.2%/year for RNFLT. 2) The loss of RNFLT is systematic throughout adulthood in humans, but for an experimental model it must be determined whether age-related reductions of RNFLT in monkeys are similar to humans.

Methods: In the first study, normative data for RNFLT and visual field sensitivities were obtained from the printouts of standard optical coherence tomography (OCT) and standard automated perimetry (SAP) for patients from ages of 25 to 95 years, in decade steps. These data were used in models to estimate the number of RGCs underlying each measure. In a second study, OCT data were collected from 40 macaque monkeys over an age range of 3 weeks to 10 years (a human-equivalent range of 0.06 to 40 years of age).

<u>Results:</u> The age-related losses of RGCs derived from normative perimetry data agreed closely with published histologic data, without an age-variable in the model. In contrast, the age-related losses of RGCs derived from normative RNFLT data required an age-variable of 0.01 μ /year increase in spacing between axons in the nerve fiber layer to account for the relatively slower rate of RNFL thinning than RGC loss. The RNFLT measurements on monkeys had considerable variability, but regression analysis of the data on a human age-equivalent scale showed that average RNFLT thinning occurred at the same rate (0.22 μ /year) as for human patients (r = -0.42).

Conclusions: The relationship between RNFLT and RGC axons varies with the number of neurons lost through normal aging, possibly because of a compensating increase in glial tissue in the nerve fiber layer. The histologic data that are needed for further studies of this relationship can be obtained from macaque monkeys because the OCT data demonstrate a similar normal aging effect on RNFLT as has been found for humans.

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DETECTING STRUCTURAL PROGRESSION IN LONGITUDINAL SERIES OF OPTIC DISC IMAGES

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Background: Statistic Image Mapping (SIM) is a proven method used in neuroimaging to identify areas of activity in images of the brain. The technique was adapted to detect progression in series of optic nerve head images (ONH) acquired from the Heidelberg Retina Tomograph (*Patterson et al IOVS 2005 46: 1659-67*).

Purpose: To develop new methods to lower and control the False Detection Rate (FDR). **Methods:** SIM is a quantitative technique which generates a 'change map' highlighting areas of active change. The technique produces a global p-value which measures change across the whole image. The global p-value is used to separate progressers from non-progressers. The cut-off for the global p-value may be modified according to the length of the patient series to account for the likelihood of detecting change by chance. When the technique was applied to normal age-matched controls the FDR was higher than expected. This study evaluates a new image alignment algorithm and techniques to lower the FDR including an omitting strategy and a confirmation strategy. The FDR was quantified from longitudinal patient series in 20 normal age-matched controls [range of follow-up 3.1 to 7.9 years]. The true-positive detection rate was quantified on 52 ocular hypertensive patients who progressed by visual field criteria during follow-up [range of follow-up 3.2 to 8.1 years].

<u>Results</u>: The new alignment algorithm lowered the FDR from 40% to 25%. The omitting and confirmation criteria lower the FDR to 15% and 10%, respectively. The existing cut-off criteria, omitting and confirmation criteria had true-positive rates of 88.5%, 80.8% and 73.1%, respectively.

<u>Conclusion</u>: The new image alignment algorithm lowered the FDR. Techniques have been developed to control the FDR in SIM. The technique will now be tested on new datasets to quantify SIM ability to separate progressers from non-progressers.

RELATIONSHIP OF BINOCULAR ASYMMETRY IN HRT NFL THICKNESS TO THE BINOCULAR ASYMMETRY OF HVF 24-2 AMONG CLINIC REFERRAL PATIENTS AND FDT SCREENING FAILURES IN BEXAR COUNTY, TEXAS

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Purpose: To compare the positive and negative predicative values obtained using the Heidelberg Retina Tomograph II (HRT II) for predicting the presence or absence of glaucomatous visual field loss, using the existing HRT II Moorfields (population-based) sectorial scoring algorithm versus values obtained using a new intrinsic intra-subject binocular asymmetry algorithm (Pearson Product Coefficient) now available in the HRT III. All HRTs had coefficients of variability bilaterally <50 microns and reliable concomitantly obtained bilateral Humphrey Visual Field Analyzer II SITA 24-2 results. Two comparable, predominantly Mexican-American clinical populations were assessed; one group being referred on the basis of FDT failure from open screenings in the community, and the other referred as glaucoma suspects to a subspecialty clinic by ophthalmologists and optometrists.

<u>Methods</u>: 44 clinic referral patients and 97 positive FDT screening failure subjects provided reliable bilateral HVF 24-2, and each visual field was classified in masked fashion as normal (level 0), early (level 1), moderate (level 2), or severe (level 3) glaucomatous loss according to Hodapp, Parrish, Anderson (HPA) scoring criteria. Paired visual fields were segregated into five categories; I: both eyes normal (i.e. R/L HPA levels 0/0), II: both eyes symmetrically abnormal (i.e. 1/1, 2/2, 3/3), and asymmetry categories III, IV, and V: asymmetric HVFs differing by 1 (i.e. R/L or L//R 0/1, 1/2, 2/3), 2 (i.e. 0/2, 1/3), or 3 (i.e. 0/3) HPA category levels, respectively. HRT II was performed on both eyes of all subjects, images from which were also reevaluated using the new HRT III asymmetry algorithm.

<u>Results</u>: The new intra-subject HRT III asymmetry algorithm gave much higher sensitivity, specificity, positive- and negative-predictive values than the HRT II population-based algorithm, in both referral populations. A strong linear correlation was found to exist between HRT and visual field asymmetry in both the clinical and screening referral populations, *with one very pronounced exception in both groups: the category V* (one eye normal and other eye severe VFL) *HVF pairs demonstrated normal bilateral symmetry of the nerve fiber layer*.

<u>Conclusion</u>: Remodelling of the peripapillary NFL appears to be associated with bilateral progressive visual field loss, but not with unilaterally severe glaucoma-type visual field loss.

MAPPING MEASUREMENTS OF THE RETINAL NERVE FIBRE LAYER TO THE VISUAL FIELD USING A NON-LINEAR BAYESIAN NEURAL NETWORK

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Background: Clinical measurements of structure and function in glaucoma are noisy but are central to patient management. Much could be gained clinically by 'blending' the information from these measurements especially in identifying disease progression.

Purpose: To develop a methodology for examining the precise spatial relationship between measurements of the retinal nerve fibre layer thickness (RNFLT) from GDx (VCC) scanning laser polarimetry (SLP) and visual field (VF) sensitivities from standard automated perimetry.

Methods: Two cross-sectional datasets were used where both SLP scans and 24-2 VF tests were available: 1800 eyes (normal and glaucoma suspects) from the population-based Blue Mountains Eye Study were used along with 105 eyes (54 normal subjects and 51 glaucoma patients) reported by Schlottmann et al (2004 *IOVS* 45:1823-9). First, (logarithmic) linear 'correlation/regression' analysis similar to that of Gardiner et al (2005 *IOVS* 46:3712-7) was used to predict sensitivities at individual VF locations using 64 RNFLT retardation values. Next, VF and RNFLT were incorporated into a multi-layered Bayesian neural network (BNN) for the same prediction task. BNN makes no linearity assumption, iteratively minimises the error in the predicted VF pattern and considers VF and SLP measurements to interact as 'groups' rather than single independent measurements. The BNN analysis provides a map of VF points related to RNFLT using expected Jacobian derivative w.r.t RNFLT distribution.

<u>Results</u>: The BNN VF sensitivity predictions were on average at least twice as accurate as those predictions based on (logarithmic) linear regression. The improved prediction (4.3dB average BNN prediction error against 13.2dB in Glaucomatous subjects) verifies the non-linear change on glaucomatous VF caused by RNFLT thickness damage. Prediction confidence intervals widen in the VF periphery and with the reduction of VF sensitivity.

<u>Conclusions</u>: The methodology in this work provides significantly more accurate predictions of VF sensitivity using RNFLT measurements compared with predictions of linear regression. The topographical maps of how RNFLT are related to groups of locations in VF derived from this methodology could be useful in describing precise function-structure relationship.

DIFFERENCES BETWEEN SWAP AND WHITE-ON-WHITE VISUAL FIELDS:

EFFECTS OF VISUAL ADAPTATION WITHIN A HEALTHY POPULATION Alvin Eisner, Ph.D.^{1,2} Maureen D. Toomey, B.S.^{1,2} Lisa J. Incognito, M.A.^{1,2} Jean P. O'Malley, M.P.H.^{1,2} John R. Samples, M.D.²; Neurological Sciences Institute¹, Casey Eye Institute², Oregon Health & Science University, Portland, Oregon USA

Purpose: To test the hypothesis that differences between SWAP and white-on-white visualfield sensitivities are related to variation in the adaptation properties of SWS cone pathways. Methods: Twenty-six healthy amenorrheic (peri- or post-menopausal) middle-aged women not using hormone replacement were tested. Two types of visual fields were measured standard procedure Full Threshold 24-2 SWAP blue-on-yellow (B/Y) fields, and Full Threshold 24-2 SITA white-on-white (W/W) fields. The age-corrected sensitivity differences between the 2 visual fields were compared against foveal measures of visual sensitivity and adaptation obtained psychophysically using dim and bright yellow backgrounds. A11 measurements for each subject were made at a single session. Comparisons were made for the entire visual field and for separate portions of the field. Visual-field pupil-size was included in the analyses.

Results: The B/Y-W/W mean-deviation difference was successfully described (R = .80) by a multilinear model with 3 significant factors: (i) an adaptation factor and (ii) a baseline sensitivity factor, each derived from the foveal psychophysical data, and (iii) a pupil size factor, as recorded for SWAP. The total-deviation differences in the periphery (~22° from fixation) were described (R = .87) by a model with 4 significant factors, the fourth factor being an "eccentricity factor" describing the rate of change of the B/Y-W/W total-deviation difference measured as a function of increasing retinal eccentricity between about 9°-17° from fixation. More than 40% of the variance in the B/Y-W/W mean-deviation differences was accounted for either directly or indirectly (via pupil size effects) by variations in adaptation to the yellow background used for SWAP.

Conclusions: A portion of the extra variability in SWAP sensitivities may depend on differences in the degree of desensitization induced by the yellow background used for SWAP. For clinical practice, pupil status (dilated or undilated) should be altered only with caution from one SWAP testing session to another.

LONG-TERM FLUCTUATION, LEARNING EFFECT, SENSITIVITY AND SPECIFICITY OF STANDARD AUTOMATIC PERIMETRY, PULSAR PERIMETRY AND FREQUENCY-DOUBLING TECHNOLOGY

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Purpose: Analyze the stability and accuracy of three perimetric techniques.

Methods: 104 stable eyes (65 subjects) with ocular hypertension and early glaucoma (group G, mean MD 1.08dB, SD 2.0dB) were examined 5 times during 18 months using: A.- Standard Octopus 311 TOP Automatic Perimetry (SAP). B.- Pulsar Temporal Modulation perimetry (T30W) and C.- Frequency-Doubling Technology (FDT N30). All subjects had previous SAP experience. Examination of 90 eyes from 90 normal controls was compared with the first examination of group G.

<u>Results:</u> Learning effect was minimal in the 3 techniques, but higher in Pulsar (1.0 src, p<0.05) than in SAP and FDT (0.4 dB). Long-term fluctuation (LF), calculated as SD of threshold values, was significantly higher in FDT (3.1 dB, SD 1.4, p<0.0001) than in SAP (2.3 dB, SD 1.1) and in Pulsar (1.9 src, SD 0.7). In G, the number of cases with MD >3 units (dB or src) was 14.9% in SAP, 19.6% in Pulsar and 31.8% in FDT. The same percentages in controls were 11.1%, 7.9% and 17.8%. ROC analysis, for a specificity of 95.6%, showed MD and sLV-PSD sensitivity of: SAP 7.7% and 5.7%, Pulsar 14.4% and 22.1%, and FDT 10.6% and 11.6% respectively.

Conclusions: Although Pulsar presents slightly higher changes over time due to greater learning effect, its overall stability is greater than the other two systems. The opposite occurred with FDT: reduced learning effect coincided with maximum LF. ROC analysis including previous data suggests that Pulsar's greater stability with respect to FDT favours greater sensitivity, although it is possibly a more complex task for the patient which induces greater learning effect.

EVALUATION OF THE SCREENING PERFORMANCE OF THE OCULUS EASYFIELD AND FREQUENCY DOUBLING TECHNOLOGY (FDT) PERIMETERS

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<u>Purpose:</u> To evaluate the clinical performance (sensitivity, specificity, ease of use, test duration, etc.) of the Easyfield and FDT perimeters for detection of glaucomatous visual field loss.

Methods: Visual field testing of both instruments was performed in 68 normal control subjects (136 eyes) and 80 patients with glaucomatous visual field loss (158 eyes) at two clinical centers, according to the procedures recommended by the manufacturers. All participants underwent a thorough eye examination, HFA SITA Standard visual field evaluations to be included in the study. Glaucoma patients were required to have mild to moderate visual field loss (no worse than -12 dB MD for the HFA II procedure) and normal controls were required to have a normal eye exam and HFA visual fields. Sensitivity, specificity, test duration, and ease of use were evaluated for each instrument. **Results:** Both devices were easy to use. In contrast to the FDT device, the Easyfield required the use of a central lens correction, was more difficult to maintain eye alignment, required the use of an eve patch, and took about 25% longer for testing glaucoma patients and 50% longer for normal controls. Both procedures took less than 1.5 minutes per eye to complete. Specificity for the FDT device was between 92 and 99%, and sensitivity was between 75 and 94%, depending on which criteria were used. For the Easyfield, specificity was between 67 and 86% and sensitivity was between 63 and 88%.

Discussion: Both devices provided reasonably good sensitivity and specificity characteristics, and could be used efficiently. The FDT procedure required less testing time and was somewhat easier to use. However, both instruments appear to be useful procedures for glaucoma visual field screening. The reproducibility characteristics of the two devices will also be presented.

A COMPARISON OF STANDARD AUTOMATED PERIMETRY, FDT N-30 AND FDT 24-2 TESTS OF VISUAL FUNCTION IN THE DIAGNOSTIC INNOVATIONS IN GLAUCOMA STUDY

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Purpose: To compare the diagnostic accuracy of standard automated perimetry, frequency-doubling technology perimetry (FDT) N-30 and FDT 24-2 tests of visual function.

Methods: One eye of each of one-hundred-and-fourteen glaucoma patients and 44 healthy controls was included. Optic disc stereophotographs (and not visual fields) were used to classify the eyes. Healthy controls also had intraocular pressure < 22 mmHg with no history of elevated intraocular pressure and a normal ocular examination. All participants had standard automated perimetry (SAP) with the 24-2 pattern and SITA strategy, FDT N-30 and FDT 24-2 tests performed within three months. The stereophotographs were taken within 6 months of the functional tests. Areas under the receiver operating characteristic (AUROC) curves were generated and used to determine sensitivity levels at a set specificity level (80%) calculated for the following parameters: Mean Deviation (MD), Pattern Standard Deviation (PSD), the number of Total Deviation (TD) and Pattern Deviation (PD) points triggered at less than 5% and 1%. **Results:** The best parameter for each test was MD for SAP (AUROC=0.678), PSD for FDT N-30 (AUROC=0.801) and the number of TD <5% points for FDT 24-2 (AUROC=0.824). For the best parameter of each test, significant differences were observed between the AUROC for SAP and FDT N-30 (p=0.01) SAP and FDT 24-2 (p<0.001). No significant difference was observed between the AUROCs for the best parameter of FDT N-30 and FDT 24-2 (p=0.60). At a set specificity of 80%, the sensitivity associated with the best parameter for each test was 49% (SAP), 65% (FDT N-30) and 67% (FDT 24-2).

Conclusion: Overall, both FDT tests had higher diagnostic accuracy and were more sensitive than SAP. The FDT 24-2 performs as well as the FDT N-30 in terms of diagnostic accuracy and sensitivity at a set level of specificity. The FDT 24-2 is, however, better suited for following patients over time.

RETEST VARIABILITY OF CONVENTIONAL AUTOMATED PERIMETRY OF SIZE V COMPARED TO SIZE III STIMULI IN GLAUCOMA PATIENTS M.Wall¹,², C.F. Brito³, K.R. Woodward², C.K. Doyle². Ophthalmology, University of Iowa, Iowa City, IA¹, Veterans Administration Hospital, Iowa City, IA²; Psychology, Eastern Illinois University, Charleston, IL³

Purpose. To compare the retest variability of Humphrey perimetry in glaucoma patients using size V and size III stimuli.

Methods. We tested one eye of 120 glaucoma patients with the Humphrey full threshold algorithm using size V stimuli and with SITA standard using size III stimuli. The patients were retested within 1-4 weeks. Test locations where 0 dB threshold was obtained on either the first test or the retest were excluded from analyses. We compared the mean scores, and point-wise sensitivities between the sizes and their retest variability within sizes. Two-factor, repeated ANOVAs were performed with the dependent variables as sensitivity (dB) and retest variability (dB differences) at each location.

Results. The sensitivities were on average 3.30 dB higher for size V and were different for the two tests (p < 0.001). The mean difference on retest across test locations was 2.55 dB \pm .04 for size III and 1.65 dB \pm 0.02 for size V. The difference in variability between size III and size V was small for about the first log unit of decrease. It then increased markedly with decreasing sensitivity (interaction was significant: p<.001), with size III having higher variability (Figure).

Conclusion. The retest variability in glaucoma patients is similar for the two tests for about the first log unit of sensitivity. Variability then rises substantially for size III stimuli compared to size V.



New Perimetric Techniques

A NEW APPROACH TO AUTOMATED KINETIC PERIMETRY

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<u>Purpose</u>: To develop a new automated kinetic algorithm (Program K) for detecting and evaluating abnormal isopter patterns using the Octopus101.

<u>Subjects and Methods:</u> Our new kinetic algorithm judged the abnormality of isopter patterns by the external angles of the response points. First (stage1), the test target was moved from periphery to the fixation point on the fixed meridian. The external angles of the response points were analyzed and additional tests were added automatically to the abnormal isopter area (stage 2). These sequences were repeated for detecting the abnormal isopter patterns. In this study, we simulated this algorithm on 100 glaucomatous visual fields obtained by Goldman perimeter and evaluated the suitable test parameters for this algorithm. Thirty four eyes of 34 normal subjects were tested for evaluating the inter-individual variation of automated kinetic perimetry under the test conditions of target sizes V/4e, I/4e, I/3e, I/2e, I/1e and target speeds 2, 4, 6 degree / sec. Eight eyes of 8 normal subjects were tested 5 times with the same test conditions for evaluating intra-individual variation. Using this algorithm, 18 eyes of 18 glaucoma patients were tested and compared with the Goldman kinetic perimetry

<u>Results:</u> The normal range of the external angle was from 150 to 240 degree in glaucoma patients. The external angles were not affected by subject age, target sizes or target speeds. Intra-individual variation was smaller than inter–individual variation in kinetic perimetry. Intra and inter-individual variation of the external angle were smaller on the peripheral isopters. In glaucoma patients, 13 eyes had good correspondence and 5 eyes had acceptable correspondence compared with the Goldmann perimetry.

<u>Conclusion</u>: Program K is a useful method for detecting and evaluating the automated kinetic visual fields.

MULTISAMPLING SUPRATHESHOLD PERIMETRY FOR MONITORING GLAUCOMA: AN EVALUATION OF TEST-RETEST VARIABILITY

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<u>Purpose:</u> To evaluate and describe the test-retest variability of Multisampling Suprathreshold perimetry in glaucoma patients in comparison with SITA Standard perimetry in a population of glaucoma patients.

<u>Methods</u>: 41 glaucoma patients, with a range of glaucoma defects, were recruited to the study. All subjects underwent test-retest examinations with the Humphrey Visual Field Analyzer (HFA) (SITA Standard 24-2) and the Henson Pro bowl perimeter (Multisampling 24-2 strategy) in one eye only. The retest examinations were conducted within 3 weeks of the initial examination (minimum interval 5 hours). The number of defective test location (Pattern Defect Probability<5% in threshold perimetry and <3/5 seen in multisampling) were compared for test-retest variability within and between strategies. In addition, spatial agreement and repeatability between the two strategies was evaluated.

<u>Results:</u> Both strategies showed good intra-strategy agreement of defect size from visit 1 to visit 2 ($R^2=0.78$, SD of the differences 7.56 Multisampling; $R^2=0.85$, SD of the differences 5.09 SITA). Inter-strategy correlation of defect size gave $R^2=0.76$ and a SD of the differences =7.53. The average number of overlapping defect points between visits was 13.5 for Multisampling and 14.07 for SITA (average defect size measured with Multisampling was 17.6 and 19.9 with SITA). The intra-strategy correlation of overlapping defective points was good (Multisampling: $R^2=0.93$, SD of differences 3.99 and SITA: $R^2=0.94$, SD of differences 3.18). The average percentage of overlapping defect points in Multisampling was 63.4% of the total possible defect area, whilst in SITA 24-2 it was 59.5 % of the total possible defect area. The number of overlapping points inter-strategy gave a good correlation of $R^2=0.92$, SD of differences 3.67.

<u>Conclusions</u>: Test-retest variability in Multisampling is comparable to that of SITA Standard 24-2 in stable glaucoma patients. The spatial repeatability of each program is comparable although the Multisampling strategy shows better repeatability with smaller defects.

MULTIFOCAL DICHOPTIC PUPILLOGRAPHY IN GLAUCOMA

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Purpose: This study was a preliminary investigation of a means of concurrently assessing the visual fields of both eyes by recording the responses of both pupils to dichoptic 24 region multifocal stimuli, to investigate the sensitivity and specificity of this as a method for objective perimetry.

Method: Dichoptic stimulation was provided by means of a pair of stereoscopically arranged LCD displays. Each display presented a circular dart-board-like array of 24 stimulus regions extending to 30° eccentricity. Each region in each eye received stimulus presentations at a mean rate of 1/s. The test recording duration was 4 minutes, divided into 8 segments. Four stimulus presentation conditions were tested: either a single or a 2x2 array of patches, being either steady for 133ms or flickered half-on half-off at 15 Hz for 266ms. The 20 normal subjects were given a thorough eye exam including 24-2 HFA fields and fundus photography assessed by a single skilled observer. The 26 patients had stable HFA fields.

<u>Results:</u> Both pupils were recorded with 24 regions mapped in each eye, giving a total of 96 measures from each 4 minute record, each with a rigorous estimate of standard error. The median peak response expressed as z-scores for the 4 conditions were 4.1, 3.3, 3.2 and 2.3. The best diagnostic performance was obtained by taking the mean of the 10 worst deviations from the normal profile across the visual field regions, providing a joint sensitivity and specificity of 85% for the flickered single patch condition. The analysis method meant that about 10% of each record could be lost due to blinks etc. without affecting accuracy.

Conclusions: The method provided diagnostic accuracy that was comparable to leading perimeters even though the raw test time was 2 min per eye. Measuring the visual fields of the two eyes simultaneously has advantages for comparing the two eyes. Larger scale trials will be needed to confirm these results.

SUB-LAYER SEGMENTATION ANALYSIS OF THE MACULAR OCT SCAN SIGNIFICANTLY DETECTS DAMAGE IN UNILATERAL OPTIC NEUROPATHY

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Introduction: Structural optic nerve damage causing axon loss may be difficult to detect with coexisting optic nerve edema, or other causes of a thickened retinal nerve fiber layer. Sub-layer segmentation of the macula scan using optical coherence tomography (OCT) may help to better define ganglion cell loss.

<u>Methods</u>: Nine patients with chronic unilateral optic neuropathy were tested by Stratus OCT3 (circular and macular fast scans) and analyzed by the both Stratus algorithm and by a novel segmentation image analysis technique to determine sub-layers of the retina. Boundaries were automatically determined in individual scans and in composite scans (averaging of 6 scans into one image) using a graph-based cost function approach that utilized edge/regional image information and a priori-determined constraints. Regional sub-layer analysis was also performed in four patients with altitudinal visual field loss.

<u>Results</u>: Significant differences between the affected and unaffected eyes were found with the inner sub-layer OCT macular analysis (p=0.013) but not with total retinal thickness (p=0.111). Significant altitudinal differences in inner retinal sub-layer thickness (p=0.046) were found in eyes with corresponding field loss. The two most significantly affected sub-layer corresponded to the expected location of the retinal ganglion cells and the most superficial nerve fiber layer. There was a significant linear correlation between the Stratus derived retinal layers (retinal nerve fiber layer in the circular scans and total retinal thickness) and our new segmenting algorithm.

<u>Conclusions</u>: The structural information in the sub-layer of the macular OCT scan corresponding to the location of retinal ganglion cells and also the nerve fiber layer appears to have important potential for assessing optic nerve damage and could be particularly useful when the retinal nerve fiber layer thickness in the circular scan does not correspond to the number of axons, as in case of optic disc edema.



CHARACTERISTICS OF THE NORMAL VALUES FOR FLICKER PERIMETRY WITH THE OCTOPUS 300 PERIMETERS

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Purpose: We have been studying flicker perimetry with the Octopus 1-2-3 perimeter and its remote software package since 1991. As flicker Perimetry now being commercially available as an optional program to the Octopus 300 series perimeters (Haag-Streit AG), through assessing and characterizing the values obtained from a normal population, we tried to develop a normative database for the test results of flicker perimetry with the Octopus 301 perimeter.

Methods: Critical flicker fusion frequencies (CFF) were measured at 39 test points in the central 30° visual field using 4-2Hz staircase procedure with the Octopus 301. The subjects were recruited at Kinki University, Keio University, Tohoku University and Sapporo Medical College in Japan. One hundred and thirty eyes of 130 normal subjects were included in this study. The age-corrected CFF values which were estimated by simple linear regression at each test points were interpolated, extrapolated and smoothed with the smallest residual variances.

<u>Results</u>: The hill of CFF had a gentle ridge at the eccentricity of approximately 10° . Mean values of the CFF over 39 test points decreased by approximately 1.3Hz per age decade. The regression slope of the CFF versus age did not significantly change with eccentricity. The regression of short term fluctuation of the single measured CFF values against age appeared to be insignificant. Interindividual variability of the CFF values increased with eccentricity with a standard deviation approximately from 4Hz (central) to 8Hz (peripheral).

Conclusions: To reliably estimate the clinical test results of flicker perimetry with the Octopus 300 series perimeters, we have developed a useful age-dependent normative database in the central 30° visual field.

A PERIMETRIC RE-TEST ALGORITHM THAT IS SIGNIFICANTLY MORE ACCURATE THAN CURRENT PROCEDURES

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<u>Purpose</u>: To develop a fast and accurate perimetric test procedure that makes use of threshold information derived from previous tests.

Methods: Computer simulation using 4 levels of patient error (none, false-positive, falsenegative, and unreliable) was used to analyse several retest algorithms. Baseline systems included simply running two existing threshold algorithms that do not make use of previous information, Full Threshold (FT) and ZEST (Z); allowing ZEST to continue from the previous test without re-initialising the input pdf (Z-CONT); and running ZEST with a Gaussian pdf about the previous measured threshold (Z-GAUSS). Our new algorithm (REMU) is based on our previously published EMU algorithm [1] which combines supra-threshold and ZEST threshold procedures to trade off test time and test accuracy. Specifically, a supra-threshold test is made for each location based on the previous threshold at that location with a general-height correction. If two or two of three supra-threshold presentations are seen, then the threshold reported is same as previous, otherwise a ZEST is performed using a Gaussian pdf centred 2 dB below the failed suprathreshold value. The pdf has an initial standard deviation of 3 dB, and the ZEST is terminated when the standard deviation falls below 1.5 dB.

<u>Results</u>: When there is no change in field from test to retest, the retest algorithms (Z-GAUSS, Z-CONT and REMU) are all at least one presentation per location faster than the test algorithms, on average, and at least 0.5 dB more accurate. When fields change from test to re-test, REMU is faster and more accurate than the other two retest approaches.

Conclusions: The new retest algorithms are as fast and more accurate than current goldstandard test algorithms such as SITA, and REMU is more accurate than Z-CONT and Z-GAUSS when fields change from one visit to the next.

[1] McKendrick & Turpin. "Combining Perimetric Suprathreshold and Threshold Procedures to Reduce Measurement Variability in Areas of Visual Field Loss", OVS Jan 2005. p43-51.

THE EFFECT OF STIMULUS ORIENTATION, LEARNING AND CENTRAL REFRACTION ON A NEW MULTI-LOCATION MOTION DISPLACEMENT TEST FOR THE DETECTION OF GLAUCOMA

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Purpose: To investigate the effect of stimulus orientation, learning and central refraction on a new multi-location motion displacement test (Moorfields MDTTM) for the detection of glaucoma.

Method: A 32-location MDT was presented on a 20-inch flat screen monitor, under PC control, at a test distance of 30 cm. The MDT threshold was determined as the last seen response on the second reversal of a staircase (3-30 min arc displacement). 16 glaucoma patients (33-76 years), with reproducible focal Humphrey defect (MD -1.58 to -7.69), and 17 perimetrically experienced, aged-matched controls (27-75 years) were tested. Near refractive correction [median (range)] was 1.9 (+6.0 to -3.0) DSph for patients and 1.8 (+6.0 to -4.0) DSph for controls. A baseline MDT was done with all line stimuli vertically aligned, with near correction, followed by four randomised tests: (i) repeat baseline (ii) repeat baseline, unaided (iii) stimuli orientated with the retinal nerve fibre layer (RNFL), with correction (iv) stimuli orientated perpendicular to the RNFL, with correction. Statistical evaluation was by nonparametric tests.

<u>Results</u>: Patient MDT thresholds were significantly elevated compared to controls for all stimulus orientations (p < 0.001). For patients and controls: there was no significant difference in thresholds between the baseline and repeat baseline; thresholds were elevated for peripheral locations (> 9° eccentricity) with central correction, compared to unaided (p < 0.001), with no significant difference within 3° of central fixation; thresholds of stimuli orientated with the RNFL were elevated when compared to vertical and perpendicular (p < 0.001).

Conclusion: All variations of stimulus orientation showed good separation of control with glaucoma. MDT thresholds are robust to central refractive error and learning for perimetrically familiar subjects. The Moorfields MDTTM therefore offers potential as a screening device for the detection of glaucoma. Supported by an unrestricted grant by Pfizer.

QUANTIFYING "SECOND-EYE2 SENSITIVITY LOSS IN FREQUENCY-DOUBLING PERIMETRY

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Purpose: Previous studies have shown that the second eye tested on the Matrix perimeter has elevated thresholds (reduced sensitivity) relative to the first, and that this elevation is not uniform across the visual field. Our study investigated how this "second-eye effect" evolves over time at various visual field locations.

Method: We measured psychophysical thresholds in 4 subjects for 5° square, 0.5 c/° sine wave gratings counterphase flickered at 18Hz and presented in a raised cosine temporal envelope of 600ms. Stimuli appeared in one of five interleaved locations (18° nasal, 9° nasal, central, 9° temporal & 18° temporal). Subjects adapted binocularly (background= 45cd/m²) for five minutes before performing a five minute test with one eye (the "first-eye") followed immediately by the other (the "second-eye"). We used an opaque occluder for monocular testing. Subjects repeated the test series 12 times, allowing us to use a version of the "method of a thousand staircases" (Mollon & Polden, 1980. *Nature* 286: 59-62) to track changes in thresholds at 10s intervals throughout the course of the first- and second-eye tests. These results were compared to baseline monocular thresholds after binocular light adaptation, measured over the course of 3.5 minutes using a conventional ZEST procedure.

<u>Results</u>: All subjects showed a second-eye effect. On average, second-eye thresholds were raised by 0.3 log at the beginning of the test, reducing to 0.2 log towards the end. There was little change in the magnitude of the second-eye effect as a function of eccentricity. We also found a significant "first-eye effect", where thresholds increased by approximately 0.1 log as the first-eye test progressed.

<u>Conclusions</u>: The second-eye effect is not constant, but rather decreases as a test progresses. In contrast, thresholds in the first-eye progressively increase with time. It is likely that light adaptation differences between the two eyes, due to opaque monocular patching, are partly responsible for these effects.

ASSESSING VISUAL FIELD CLUSTERING SCHEMES USING MACHINE LEARNING CLASSIFIERS IN STANDARD PERIMETRY.

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Purpose: To compare machine learning classifiers (MLCs) trained on 3 clustering schemes to determine: (1) if categorizing healthy and glaucomatous optic neuropathy (GON) eyes can be optimized by training with clustered data, and (2) how structurederived schemes [Garway-Heath et al., (G-H); Glaucoma Hemifield Test Sectors (GHT)] compare to a mathematically-derived scheme (variational Bayesian independent components analysis, ICA).

Methods: Raw thresholds from the standard Humphrey full-threshold 24-2 field locations were averaged within each cluster ("cluster thresholds") within each map. Two MLCs [constrained Mixture of Gaussian (cMoG) and Support Vector Machines with Gaussian kernel (SVMg)] were trained separately using cluster thresholds plus age on a training data set (156 eyes/156 glaucoma patients with GON; 189 eyes/189 normal controls). Trained MLCs were then applied to an independent data set containing 73 eyes of 73 GON eyes with early visual field loss and 95 eyes of 95 normal controls. Sensitivity and specificity were compared using the McNemar statistic. Two control conditions were included – unclustered data¹ and a random map.

<u>Results:</u> For 96% specificity cutoff: Sensitivity of GHT/cMoG (77%) was equivalent to unclustered/cMoG and both G-H/cMoG (63%) and ICA/cMoG (62%) were significantly lower than unclustered/cMoG (77%). No effect of clustering type using SVMg. Sensitivity was significantly higher with GHT/cMoG than ICA/cMoG. For 90% specificity cutoff: Sensitivity of GHT/cMoG (92%) was significantly higher than unclustered/cMoG (79%). G-H/SVMg (64%) and ICA/SVMg (67%) were significantly lower than unclustered/SVMg (77%). Sensitivities were higher using cMoG than SVMg regardless of specificity cutoff and clustering method.

<u>**Conclusions:**</u> cMoG performed better with the early glaucoma data set than the SVMg. The structurally-derived clustering (G-H and GHT) showed a small advantage over the mathematically-derived (ICA) clustering, though it depended on specificity. Clustering may be advantageous when data-dimension reduction is needed, for example when combining field results with other high-dimensional data (e.g., HRT data).

WHY ARE SITA-SWAP SENSITIVITIES HIGHER THAN THOSE FROM FULL THRESHOLD SWAP?

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Purpose: When the commercially-available SITA algorithm for Short Wavelength Automated Perimetry (SWAP) was introduced (IOVS 2003, 44:1388-1394), the authors stated that mean sensitivities using SITA were on average 4.3dB higher than using Full Threshold (FT) in the same subjects. 1dB of this difference is because FT defines threshold as the 'last seen stimulus', rather than averaging the last seen and last unseen stimuli. However, the remaining discrepancy is unexplained.

Methods: Results were analyzed from 74 eyes of 37 early glaucoma subjects tested with FT and (one year later) SITA; and from 50 normal and glaucoma subjects tested (within one week) using FT and the SITA-like ZEST algorithm (Turpin et al, Perimetry Update 2000/2001:139-147). To test whether adaptation over time produces the discrepancy, 9 subjects were tested with SITA twice after 10-minutes pre-adaptation (simulating adaptation levels as FT concludes), and twice without.

<u>Results:</u> Sensitivities using SITA within the inner 10° averaged 3.8dB higher than those using FT; the difference increased to 4.5dB outside 20°. Sensitivities estimated by ZEST were 2.8dB greater than FT within 10°, and 3.6dB greater outside 20°. Since outer locations are tested last by FT, it seems FT underestimates sensitivities increasingly as the test proceeds in time. Pre-adaptation increased sensitivities by 1.1dB, so cannot account for FT results being lower than SITA.

Conclusions: A large fatigue effect, decreasing sensitivities by around 1.5dB from beginning to concluding FT, plus the 1dB 'last seen' effect, would explain most of the discrepancy between algorithms. However, even at the four locations tested first at $\pm 9^{\circ}$ (so having no difference in adaptation or fatigue levels), there is still 3dB difference between FT and SITA. We conclude that in SWAP, FT is underestimating sensitivities especially at greater eccentricities, principally because of increasing fatigue as the test proceeds. This large fatigue effect has implications for frequency-of-seeing curves, hill-of-vision estimates, and variability. However, using SITA SWAP instead cannot be completely recommended as a solution until the remaining 1-2dB of difference can be satisfactorily explained.

STABILIZATION AND COMPARISON OF TOP AND BRACKETING PERIMETRIC STRATEGIES USING A THRESHOLD SPATIAL FILTER

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Purpose: To evaluate a new perimetric spatial filter that takes into account relations of dependence between regions of the glaucomatous visual field. We investigated its capacity to reduce threshold fluctuation and compared its effect on the results of TOP and Bracketing (BRA) strategies.

<u>Methods</u>: 51 glaucoma patients and 30 controls were examined using the Octopus 1-2-3 on four occasions using program 32; two with TOP and two with BRA. Each threshold was replaced by a filtered threshold, calculated as the mean of its own value and the four points best correlated with it, weighted with the correlation coefficient (r) that relates them.

<u>Results:</u> Application of the filter had minimal effect on the absolute mean defect (MD) but reduced the square root of loss variance (sLV) by 17.75% in TOP and 28.69% in BRA, increasing the similarity between their results. Filtered TOP and BRA thresholds were more similar than those obtained in the two unfiltered BRA examinations. Filtering reduced the value of short fluctuation by 28.8% in TOP and 45.3% in BRA and reduced sLV fluctuation by 15.3% in TOP and 26.3% in BRA, thus harmonizing the two strategies for these two parameters (p>0.05). The influence of filtering on MD fluctuation was minimal (p>0.05). In normal subjects the number of points beyond 5 dB of normality (false scotomas) reduced by 85.6% in TOP and 66.0% in BRA, while in glaucoma patients it was reduced less than 5%.

<u>Conclusions</u>: The proposed spatial filter stabilized perimetric results, acting with greater effect on BRA than on TOP, and approximated their results except for MD.

SPATIAL CHARACTERISTICS OF VISUAL FIELD PROGRESSION DETERMINED BY MONTE CARLO SIMULATION: DIAGNOSTIC INNOVATIONS IN GLAUCOMA STUDY (DIGS) JP Pascual¹, U Schiefer², J Paetzold², LM Zangwill¹, I Tavares¹, RN Weinreb¹, PA Sample¹. Hamilton Glaucoma Center, University of California at San Diego, La Jolla, CA¹, University Eye Hospital, Department II, Tuebingen, GERMANY²

<u>Purpose:</u> To determine the spatial characteristics of glaucomatous visual field progression in persons with glaucomatous appearing optic neuropathy (GON) from the Diagnostic Innovations in Glaucoma Study (DIGS).

Methods: Progression in pattern deviation (PD) plot p-values were evaluated in test locations from the first and last eligible, full-threshold, pattern 24-2, standard automated perimetry (SAP) exams (Humphrey Field Analyzer II) in a visual field series (median follow-up = 3.0 years) from 314 patients with GON confirmed on two occasions by stereophoto review. The proportion of patients exhibiting PD plot p-value progression was determined at each of 52 locations for patients with a baseline abnormal p-value (p < 5% or worse) in one or more of 52 PD locations in the first test for a total of 2704 location pairings. Progression was defined as any worsening of PD plot p-value in the last test relative to the first test. Monte Carlo simulation was employed to determine the significance of the observed patterns of PD plot p-value progression.

<u>Results:</u> Changes in PD p-values were dependent on their location relative to abnormal PD locations in the first test. The proportion of patients progressing ranged from 0 to 0.35 (mean = 0.13). These proportions and the associated p-values for each of 2704 location pairings are reported (52 possible abnormal locations in the first test X 52 locations in the last test).

<u>Conclusions</u>: Visual field progression occurs in retinotopically constrained patterns consistent with changes along the nerve fiber bundle.

COMPARISON OF CENTRAL CONTRAST RESPONSES TO LUMINANCE INCREMENTS AND DECREMENTS IN GLAUCOMA

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Purpose: Previous studies have demonstrated contrast processing abnormalities in paracentral regions of the visual field in glaucoma, including in subjects where white-onwhite perimetry indicated no functional loss in these regions. We aimed to investigate proposed differences between para-central response to luminance increments and decrements (presumed to represent separate on and off pathway responses) in both magno-cellular (M) and parvo-cellular (P) pathways.

<u>Methods</u>: Thirteen subjects with early glaucoma and fourteen (approximately agematched) controls performed luminance discrimination experiments using a pedestal of four squares (subtending approximately 2 degrees) on a 30 cd/m² background. Detection thresholds were measured separately for luminance increments and decrements using continuously presented pedestals (24, 30 and 38 cd/m²), or pulsed (29ms) pedestals (using the same pedestal array and luminance series). In each case the subject was required, while fixating at the centre of the array, to determine the location of a briefly presented (29ms) luminance increment or decrement target square, using a forced-choice response method. The steady and pulsed pedestal paradigms are presumed to measure contrast processing within M and P pathways respectively [1].

<u>Results</u>: The glaucoma group required significantly larger increments and decrements to detect the target from the pedestal luminance for both the steady (F(107, 1) = 6.35, p<0.05) and pulsed (F(107, 1) = 6.78, p<0.05) tasks. Increments and decrements revealed deficits of similar magnitude.

Conclusions: Contrast processing deficits were found within the central 2 degrees of visual field in individuals with early glaucoma who had normal visual acuities and paracentral white on white perimetry measures. These deficits were not selective for presumed M or P processing and were of equivalent size for increment and decrement stimuli. Study of glaucomatous performance on these tasks in the mid-peripheral visual field is ongoing within our laboratory.

[1] Pokorny & Smith, 1997, Vision Res. 14(9), 2477-2485.

ESTIMATING SENSITIVITY TO CHANGE FROM SIGNAL-TO-NOISE ANALYSIS OF TEST-RETEST DATA

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<u>Purpose:</u> It is problematic to compare variability between visual field tests that use different sensitivity scales. As an alternative, we propose a new methodology based on signal/noise (S/N) ratios to quantify how well measurements from two visual field locations are distinguishable from each other. We apply this method to data from standard automated (SAP) and Humphrey Matrix Frequency-Doubling perimetry (HM).

Methods: Fifteen patients with open-angle glaucoma (MD, mean -4.0 dB; range +0.2 to - 16.1 dB) were examined with SAP (24-2 Sita-Standard) and HM (24-2 ZEST). During 3 sessions, each patient underwent 6 visual field tests with both techniques (12 tests in total). S/N-ratios were established by calculating Mann-Whitney U statistics, a non-parametric measure of separation, for superior-inferior pairs of test locations. Pairwise comparisons between the S/N-ratios of SAP and HM were then carried out.

<u>Results:</u> Over the entire dynamic range of the instruments the S/N ratios of SAP and HM were similar (p>0.43, Wilcoxon). While the S/N-ratios of SAP appeared slightly larger at the high end of the sensitivity spectrum, this finding did not reach statistical significance (p>0.15).

<u>Conclusions</u>: Analyses of signal-to-noise ratios provide a simple and intuitive first approximation to a test's sensitivity to change that can be compared between different psychophysical tests. Our analyses indicate that, over a large part of their dynamic range, HM and SAP may have similar power to detect visual field progression.

LINEAR REGRESSION ANALYSIS OF THE CUMULATIVE DEFECT CURVE BY SECTORS AND OTHER CRITERIA OF GLAUCOMATOUS VISUAL FIELD PROGRESSION

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<u>Purpose</u>: To analyze the capacity to detect the progression of visual field loss using a sector analysis of cumulative defect curve, in association with other procedures of lineal regression.

<u>Methods</u>: Visual field of 260 glaucomatous eyes was analyzed during a mean period of 2.8 years (SD = 1.2) with at least 5 examinations (mean 6.9; SD = 2.0). We applied Threshold Noiseless Trend (TNT) program, which performs local filtering of threshold to reduce fluctuation, and five criteria were analyzed: A.- A score based on significant progression of eight sectors of the cumulative defect curve (CD). B.- A score based on the presence of points (PO) with progression. C.- Global progression (GL) of all local deviations. D.- Progression of mean defect (MD). E.- Progression of the square root of loss variance (sLV). We estimated false diagnoses (FD) randomly reordering examinations of each patient. An index of focality of the progression (FOC) was obtained from CD analysis.

<u>Results:</u> Since sLV presented low sensitivity and GL low specificity, they were excluded from the study. CD and PO presented twice the sensitivity of MD, often proving earlier indicators. We observed significant progression of some of the three criteria in 17.5% of the cases when MD<6dB and in 20.7% when MD>6dB, with FD of 5.7%. Agreement between two criteria occurred in 6.8% of cases with MD<6dB and in 11.6% when MD>6dB, with FD of 1.9%. Result reproducibility in successive examinations was observed in 9.9% of cases, with FD of 1.3%. Focality of progression increased with the value of MD.

<u>Conclusions</u>: PO and CD indicate suspected progression earlier than MD. Reproduction of results in successive examinations or agreement between criteria allow confirmation of the progression.

PERIMETRIC PROGRESSION DETECTION IN GLAUCOMA STUDIED WITH EVENT-DETECTION ALGORITHMS APPLIED TO LINEAR DETERIORATION: ADAPTIVE INTER-TEST INTERVALS ARE MORE EFFICIENT THAN FIXED-SPACED INTER-TEST INTERVALS

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<u>Purpose</u>: To determine the optimal spacing in time of visual field tests for progression detection in glaucoma.

Methods: Three perimetric strategies for progression detection, two with fixed-spaced inter-test intervals and one with adaptive inter-test intervals, were compared by means of simulation experiments in a theoretical cohort. In strategy I, visual field testing is performed with fixed-spaced inter-test intervals at a frequency of four tests per year. In strategy II, testing is performed with fixed-spaced intervals at a frequency of two tests per year. In strategy III, the frequency of testing is set to one test per year as long as the fields are apparently unchanged, whereas as soon as progression is suspected, confirmation or falsification is performed within a short time span. A single visual field test result was summarized as a single real number, and a series of visual field test results was represented as a sequence of numbers with normally distributed random fluctuations around a linear decrease in time at various rates (including no decrease). Follow-up fields were compared to two baseline fields using various criteria. For definite progression, two confirmations of a suspected progression were required, i.e., three consecutive follow-up fields had to be worse than a predefined level.

<u>Results</u>: Strategies II and III had a higher specificity than strategy I, i.e., a lower incidence rate of definite progression in the case of stable fields. Strategies I and III detected progression earlier than strategy II for all realistic conditions. The total number of visual field tests to be performed in a four-year period was lowest in the case of strategy III in all situations.

Conclusions: Perimetry in glaucoma can be optimized by postponing the next test in the case of an apparently stable field and accelerating the next test in the case of a suspected progression.

INFLUENCE OF AGEING ON VISUAL FIELD DEFECTS DUE TO STABLE LESIONS

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<u>Purpose:</u> To examine the effect of ageing on visual field defects due to stable lesions.

Methods: We followed 28 patients with light to moderate visual field defects remaining after surgery for pituitary tumors. None had tumor recurrence or complicating disorders. Hence, all had stable lesions of the chiasm. Follow-up periods ranged over 4 - 18 years (median 9). Using high-pass resolution perimetry, we analysed results from the centermost test locations in the upper temporal and upper nasal quadrants. The former bear the brunt of damage whereas the latter are least affected. Each patient contributed results from one eye only. Fixation stability and reproducibility were uniformly good. Measuring values were expressed in minutes of arc.

<u>Results:</u> Measuring values from the nasal quadrants remained essentially constant throughout the follow-up periods, for all age groups. Results from the temporal (T) quadrants were contrasted with those from the nasal (N) quadrants by calculating the T/N ratios, which were then individually regressed over follow-up periods. Hence, each patient was his or her own control. Most regression coefficients (25 out of 28) did not significantly differ from 0.

<u>Conclusions</u>: The rate of age-related loss of neural channels appears to be identical in normal and abnormal visual field areas in subjects with stable mid-chiasmal lesions.

CHANGE DETECTION BASED ON AN INDIVIDUAL PATIENT'S VARIABILITY

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Purpose: This study uses clinical data to examine the effectiveness of a theoretical technique we have previously published for incorporating an individual patient's variability information into estimates of probability of change in visual fields [1].

Methods: The clinical data set consisted of 9 primary open-angle glaucoma patients with fields measured twice a year for 5-12 years (mean 8.3 years) with 30-2 Full Threshold (Humphrey Field Analyzer). These patients also had frequency-of-seeing (FOS) curves measured with the same stimuli using a short MOCS procedure in six locations of their fields at their first visit. A cumulative Gaussian curve was fitted to each FOS, and fits with a correlation coefficient less than 90% were discarded. From the remaining FOS curves, linear regression on log-slope and threshold was used to elicit a slope-threshold relationship similar to that published by Henson et al. [2]. False response rates were determined from the average of the asymptotes of the FOS curves for each patient. Using this variability information for each patient, and specific knowledge of the Full Threshold algorithm, we derived individual probability of change (IPoC) maps similar to GCP maps, and also performed a pointwise linear regression (PLR) weighted by variability information (WPLR) for each patient. We compared these customised methods for determining change with standard techniques [3,4].

<u>Results</u>: The IPoC maps generally agreed with GCP on the classification of patients as progressing or stable, but discovered progression on average 2 visits earlier than GCP. IPoC flagged significantly less points than GCP. WPLR, however, classified all 9 patients as progressing almost immediately after their two baseline measurements, which disagreed with the PLR two-omitting criteria [3] and the GCP methods.

Conclusions: IPoC compared favourably to GCP because both used the same definition of baseline (average of first two fields). WPLR, however, suffered from the error characteristics of the Full Threshold algorithm used to gather the data, not allowing a solid baseline estimate from the first two fields. More work is required to integrate customisation of PLR using individual's variability data.

[1] Turpin & McKendrick. Vis Res 45, 2005.

[2] Henson et al. IOVS 41(2), 2000.

[3] Gardiner & Crabb, IOVS 43(5), 2002.

[4] Vesti et al IOVS 44(9), 2003.

Miscellaneous

RELATIVE RISK OF PROGRESSIVE GLAUCOMATOUS VISUAL FIELD LOSS IN PATIENTS ENROLLED AND NOT ENROLLED IN A PROSPECTIVE

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<u>Purpose</u>: To establish the relative risk of progressive visual field loss in a sample of glaucomatous eyes enrolled in a prospective longitudinal study versus those not enrolled in a study.

Methods: The first visual field records of 66 glaucomatous eyes enrolled in a prospective longitudinal study were matched to 66 eyes from patients not enrolled in any studies. Eyes were matched on the basis of 1) time of enrollment, 2) length of follow-up and 3) the extent and spatial pattern of visual field loss. Both samples were drawn from the same longitudinal study outpatient population of Manchester Royal Eye Hospital. Linear regression of global visual field indices was used to measure change and the relative risk of progression for a series of progression criteria.

<u>Results:</u> The risk of progressive visual field loss was approximately 4 times higher in the eyes not enrolled in a prospective longitudinal study. This difference is believed to be due to selection bias. Those patients voluteering to participate in longitudinal studies are more engaged with their condition and are likely to be more compliant with their therapy.

<u>Conclusions:</u> Selection bias reduces the risk of progressive visual field loss in patients enrolled in a longitudinal studies. Improved compliance with therapy is likely to have significant effects upon the extent of progression in glaucoma. Longitudinal studies of glaucoma underestimate the extent of progression in unselected glaucoma populations.

GLAUCOMA AND FITNESS TO DRIVE: PREDICTING A 'MILESTONE TO BLINDNESS'

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Purpose: To determine which patients with normal tension glaucoma (NTG) would lose their driving licence because of progressive visual field (VF) defects after 8 years of follow-up, using binocular Integrated Visual Field¹ (IVF) indices as early predictors. **Methods:** All patients with at least 8 years of follow-up were selected from the Moorfields NTG clinic. For each patient, binocular IVFs were constructed by taking the maximum left-right sensitivity at each location in the 24-2 VF. Using these IVF sensitivities, binocular VF criteria used by the UK Driver and Vehicle Licensing Agency (DVLA) were applied. Patients were excluded if they had already failed these criteria at the beginning of follow-up. VF loss was estimated from linear regression slopes of mean IVF sensitivities over time. Logistic regression analyses were performed to predict DVLA failure at 8 years using average IVF slopes at 3 years as predictors, controlling for initial sensitivity and treatment.

<u>Results:</u> Of the 153 eligible patients, 27 (18%) failed the DVLA VF criteria at 8 years, 95% confidence interval (CI) (12, 25%). Patients who failed the DVLA criteria at 8 years were more likely to (i) be using topical treatment, estimated odds ratio (OR) 1.4, 95% CI (1.2, 1.7); (ii) have lower initial average sensitivity, OR 3.3, 95% CI (1.0, 10.8); (iii) have more steeply deteriorating mean IVF sensitivity over time, OR 6.1, 95% CI (2.7, 13.8) than patients who passed the DVLA criteria at 8 years. The slope of mean IVF sensitivity over time was a better predictor of DVLA failure than the slope of mean sensitivity for the eye deteriorating fastest, OR 3.6, 95% CI (1.9, 6.9).

Conclusions: Driving licence loss is a significant life event, representing a 'milestone to blindness'. A substantial proportion of patients with NTG would lose their driving licence after 8 years of follow-up. Analysis based on rates of binocular IVF sensitivity loss at 3 years of follow-up may help identify patients that might benefit from intervention.

1.Crabb DP, Viswanathan AC, McNaught AI, Poinoosawmy D, Fitzke FW, Hitchings RA.

Simulating binocular visual field status in glaucoma. Br J Ophthalmol. 1998;82:1236-41.

TO WHAT EXTENT DOES SIZE AND LOCATION OF HOMONYMOUS SCOTOMAS INFLUENCE THE FREQUENCY OF TRAFFIC ACCIDENTS? – A STUDY BASED ON VIRTUAL REALITY DRIVING TASKS

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<u>Purpose</u>: To assess the influence of the size and location of homonymous visual field defects (HVFDs) on the frequency of traffic accidents under standardised virtual reality (VR) conditions.

Methods: Size and location of absolute HVFDs were assessed by binocular semiautomated kinetic perimetry within the 90° visual field (stimulus III4e [26', 320 cd/m²], angular velocity 3°/s, background luminance 10 cd/m²) with the OCTOPUS 101 perimeter (HAAG-STREIT Inc., Koeniz, Switzerland). For further analysis perimetric results could be digitally superimposed onto standardized VR driving tasks presented on a projection screen covering a viewing angle of 160° (30 sequences of approaching an intersection with two levels of cross-traffic density) under continuous recording of head and gaze position. Correlations of the number of accidents (NA) with the individual reaction time (RT), with the area of the HVFDs (A-HVFD), and with the area of sparing within the affected hemifield (A-SPAR) were estimated by Spearman's r_s . Eleven patients (4 females, 7 males; age range 21 to 70 years) with HVFDs due to unilateral vascular brain lesions with a minimum visual acuity of 16/20 participated in this study. **Results:** The number of accidents was positively correlated with reaction time ($r_s =$ 0.61). There was no correlation between NA and A-HVFD ($r_s = 0.02$) and likewise between NA and A-SPAR ($r_s = -0.12$).

<u>Conclusions</u>: Global perimetric findings per se seem to be inadequate in predicting driving performance of patients with HVFDs under VR conditions. It may be necessary to consider compensation via exploratory eye and head movements additionally.

RESEARCH ON THE APPLICATION OF OPTIC NERVE FIBER MAP TO FUNDUS PERIMETER

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Purpose: The visual field has disability and some scotomata if the optic nerve fiber has disability around the optic disc. Some paracentral scotomata or an arcuate scotoma appear in the Bjerrum area. The perfect defects of the visual field have a series of scotomata from the optic disc to the nasal longitude with detouring around the fovea centralis. The perimetry can detect many scotomata efficiently if some perimeters show stimuli along the optic nerve fiber, because the arcuate scotoma has a series of scotomata along the optic nerve fiber.

Methods: We sketched many optic nerve fibers and created an optic nerve fiber map. We took 27 color fundus photographs (12 left eyes and 15 right eyes) of 16 ophthalmologic disease patients (6 AMD, 1 macular hole and 9 retinal disease) between the ages of 37 and 82 (66.1 \pm 16.1 ages), and 6 photographs (3 right and left eyes) of 4 normal persons between the ages of 31 and 56 (39.8 \pm 11.4 age), and used the fundus perimeter. We measured the distance between the fovea centralis and the center of the optic disc. The optic nerve fiber map could be shown on the fundus photograph.

<u>Results:</u> We measured the distance between the fovea centralis and the center of the optic disc, and the ratio of the distance and angle of view, patient 0.379 ± 0.024 and normal 0.359 ± 0.016 . We were able to put both the fovea centralis of the map and the center of the optic disc of the map on the fundus photograph precisely. On the other hand, we developed the software to enable simulation of the optic nerve fiber curves, if an inspector selects certain some points on the fundus photograph.

<u>Conclusions:</u> We applied the optic nerve fiber map to the fundus perimeter, and developed the simulation software. We showed the efficacy of the software when an inspector determines certain stimuli points.

AUTOMMATED STAGING OF VISUAL FIELD DEFECTS IN GLAUCOMA

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Purpose: To introduce a new software, based on the Glaucoma Staging System 2 (GSS 2) formulas, for automatically classifying both the severity and the characteristics of glaucomatous visual field defects assessed by the Oculus Easyfield 30-2 fast threshold test.

<u>Material and methods</u>: The GSS 2 uses both the MD and CPSD/PSD (or CLV/LV) indices to classify the visual field defects into 6 stages and in 3 different types (generalized, localized, and mixed). The lines that separate the different stages and defect types were determined mathematically. The formulas have been introduced in the new software of the Oculus Easyfield perimeter. Forty-five patients with primary open angle glaucoma (POAG) at various stages of severity were examined both with the HFA 30-2 SITA standard test and with the Oculus 30-2 fast threshold test. The visual field defects were classified using a clinical method, based on the probability maps and Bebie curve analysis, and with the GSS 2, automatically supplied in the Easyfield output. The level of correlation between these two methods was measured.

<u>Results</u>: The GSS 2 showed a high level of association with the clinical classification method (P<0.0001) both in staging the severity and differentiating the characteristics of the defects.

Conclusions: The GSS 2 was able to correctly stage the visual field defect severity of the sample studied. It was also able to accurately distinguish the defects into three groups (generalized, localized, and mixed). The new Oculus Easyfield software allows the staging to be both automatic and easier, without the need of having to manually use the GSS charts.

PULSAR PERIMETRY IN THE DETECTION OF EARLY GLAUCOMATOUS VISUAL FIELD LOSS

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Purpose: to assess the ability of Pulsar perimetry in detecting early glaucomatous visual field (VF) damage.

Methods: one eye of 49 controls, 52 patients with ocular hypertension (OHT), 97 patients with primary open-angle glaucoma (POAG) was considered. The POAG group was divided into 47 patients with early VF defects (perimetric-POAG) and into 50 patients with glaucomatous optic neuropathy and normal VFs (pre-perimetric-POAG). VFs were assessed using standard automated perimetry (SAP) SITA standard HFA 30-2 test and Pulsar perimetry (Haag-Streit International) T30W test. The Pulsar stimulus consists of a circular sinusoidal pattern, 5° in diameter and 500 msec in duration, shown with a pulse motion at 30 Hz. Spatial resolution and contrast of the stimulus are simultaneously modified during the test using TOP strategy. The stimulus is presented in 66 test locations within the central 30 degrees. Pulsar test mean deviation (MD), loss variance, number of significantly abnormal points on the Deviation Probability plot, and testing time were evaluated. Sensitivity and specificity of Pulsar perimetry in detecting glaucomatous damage were calculated using different algorithms.

<u>Results</u>: Sensitivities at specificity $\geq 90\%$ ranged from 53.2% to 93.6% in the perimetric-POAG-group and from 36% to 54% in the pre-perimetric-POAG group. The percentages of abnormal OHT eyes ranged from 11.5% to 40.4%. The best discriminating parameter was the Pulsar MD, with sensitivity at specificity $\geq 90\%$ of 93.6% and 52% in the perimetric-POAG and pre-perimetric-POAG groups, respectively, with 36.5% of abnormal OHT eyes. Pulsar test was significantly shorter than SAP test (P<0.001).

Conclusions: The Pulsar T30W test appeared to be a rapid and easy perimetric test, showing high sensitivity and specificity in detecting early glaucomatous functional defects, and providing a higher ability than SAP in detecting VF damage in patients at risk of developing glaucoma. The Pulsar test required 60% time than SAP.

REPEATABILITY OF AUTOMATED PERIMETRY USING STIMULUS SIZE V IN NORMAL SUBJECTS: A COMPARISON WITH SIZE III

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Purpose: To describe the visual field of normal subjects using Humphrey perimetry with size V stimuli and to compare size V thresholds and retest variability with perimetry using size III stimuli.

Methods: We tested one eye of 58 normal subjects with the Humphrey full threshold algorithm using size V stimuli and with SITA standard using size III stimuli. The patients were retested 1-4 weeks later. We compared the mean scores, concentric zones, and point-wise sensitivities between the sizes and their retest variability within sizes. A two-factor, repeated ANOVA was performed with the dependent variable as sensitivity (dB) at each location.

<u>Results</u>: The sensitivities were on average 3.93 dB higher for size V and were different for the two tests (p < 0.001). The sensitivity of size V ranged from 3.47 dB more at the fovea to 4.30 dB in the periphery. The mean difference on retest across test locations was 1.58 dB \pm 0.39 for size III and 1.42 dB \pm 0.37 for size V. The difference in variability between size III and size V increased with eccentricity (interaction was significant: p<.001), with size III having slightly higher variability (Figure).

Conclusion: The retest variability in normal subjects is slightly less for size V full threshold testing compared with size III SITA standard results and increases with eccentricity.

Concentric Zone Analysis



RETINOTOPIC ORGANIZATION OF HUMAN PRIMARY VISUAL CORTEX CORRELATES WITH THE PATTERN OF VISUAL FIELD THRESHOLDS RO Duncan¹, PA Sample¹, RN Weinreb¹, LM Zangwill¹. Hamilton Glaucoma Center, University of California, San Diego, USA.

<u>Purpose</u>: To quantify the relationship between the pattern and magnitude of visual field loss in human primary open-angle glaucoma (POAG) and the functional organization of primary visual cortex (V1).

Methods: Six subjects with asymmetric POAG were recruited from the Diagnostic Innovations in Glaucoma Study (DIGS) to participate in this functional magnetic resonance imaging (fMRI) experiment. Visual field defects were measured using standard automated perimetry (SAP), short-wavelength automated perimetry (SWAP), and frequency doubling technology (FDT) perimetry. A retinotopic map of visual space was obtained for V1 in each subject using fMRI, and the retinotopy data was fit with a template. The template was used to project regions within the visual field onto a computationally flattened representation of V1. Subsequently, cortical responses to viewing through the glaucomatous vs. fellow eye were compared by alternately presenting each eye with a flickering checkerboard pattern. The resulting blood oxygen level dependent (BOLD) fMRI response was compared to interocular differences in thresholds from the visual function tests. Specifically, interocular differences between pattern deviation (PD) values were computed for 12 test locations, and the resulting difference scores were compared on a "pointwise" basis to fMRI responses at corresponding locations of V1.

<u>Results</u>: The spatial pattern of activity observed in the flattened representation agreed with the pattern of visual field loss for all three tests of visual function. Furthermore, the amplitude of the BOLD response was correlated on a pointwise basis with the difference in sensitivity thresholds between the glaucomatous and fellow eyes (all p < 0.05). **<u>Conclusions</u>**: The BOLD signal in human V1 is altered for POAG patients in a manner consistent with the loss of visual function. FMRI of visual brain areas is a potential means for quantifying the neurodegeneration in glaucoma.

RELATIONSHIP BETWEEN FIXATION STATUS EVALUATED WITH SLO MICROPERIMETRY AND CRITICAL PRINT SIZE BEFORE AND AFTER PHOTODYNAMIC THERAPY

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<u>Purpose</u>: To evaluate the relationship of the position and light sensitivity of the fixation area with critical print size before and after photodynamic therapy (PDT) in patients with age-related macular degeneration (AMD).

Patients and methods: Seven eyes with AMD were studied. Before and 1 year after PDT, the position of fixation area and light sensitivity were determined using scanning laser ophthalmoscopic microperimetry and critical print size was measured using MNREAD-J.

<u>Results:</u> The position of fixation area was unchanged in 5 eyes and was shifted in 2 eyes 1 year after PDT. Pre-PDT light sensitivity was 15 dB in 4 eyes, 20 dB in 2 eyes, and 25 dB in 1 eye; while post-PDT light sensitivity was less than 0 dB in 2 eyes, 0 dB in 1 eye, 10 dB in 1 eye, 25 dB in 2 eyes, and 35 dB in 1 eye. In 2 eyes with less than 0 dB sensitivity, the fixation area was shifted toward the peripheral visual field. The change of light sensitivity in the fixation area before and after PDT was evaluated in 5 eyes, excluding 2 eyes that showed a shift in fixation area after PDT. Light sensitivity was improved in 3 eyes and worsened in 2 eyes. Critical print size (logMAR) was 0.40-1.20 (mean: 0.71 ± 0.28) before PDT and 0.30-1.40 (mean: 0.93 ± 0.41) 1 year after PDT. Critical print size was improved in 3 eyes, unchanged in 1 eye, and worsened in 3 eyes. Improved light sensitivity after PDT was associated with improved or unchanged critical print size. Worsened light sensitivity after PDT was associated with worsened critical print size, and shift of fixation area toward peripheral visual field was associated with worsened critical print size.

<u>Conclusions</u>: The position of fixation area and light sensitivity at 1 year after PDT correlate with critical print size.

CENTRAL MEAN SENSITIVITY AND NON-PENETRATING TRABECULECTOMY

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<u>Purpose</u>: The aim of this study is to evaluate the central mean sensitivity (MS) in open angle glaucoma patients with the central impairment of visual field, in order to prevent the loss of central visual acuity after surgical procedure.

<u>Methods</u>: Material was comprised of 85 eyes in 70 patients (POAG, 56 eyes in 46 patients, NTG 29 eyes in 24 patients). An average age was $50.2\pm11.7(26-78)$ years. In all patients MSs were examined by Octopus (201), program M2, and Delta analysis was performed for the calculation of MS in each quadrant. In this study non-penetrating trabeculectomy (NPT) was employed. The mean follow-up period was 60 months (range 24-115).

Results: In 21 eyes (24.7%), MS within 5 degrees decreased over 2dB. Subgroup analysis was performed on two groups: 1) MS within 5 degrees decreased over 2dB (21 eyes), 2) MS did not change before and after surgery (64 eyes). In group 1, MS within 5 degrees, MSs of upper temporal and lower nasal before surgery was lower than group 2 (p<0.05). The patients, who had visual field defect in 2 or more quadrants before surgery, decreased MS after surgery (P<0.01).

Conclusion: Central MS was decreased after NPT in the advanced glaucoma patients who have visual field defect 2 or more quadrants within 5 degrees. A detail visual field measurement within 5 degrees was useful for the judgment of NPT in the advanced glaucoma patients.

COMPARISON OF FREQUENCY DOUBLING TECHNOLOGY PERIMETER, OFF- PERIMETER, AND ON-PERIMETER IN EYES WITH GLAUCOMA. S Kogure¹, H Iijima¹, K Kashiwagi¹, S Tsukahara¹ Department of Ophthalmology, Faculty of Medicine, University of Yamanashi, Yamanashi, Japan¹

<u>Purpose</u>: To compare the threshold of frequency doubling technology (FDT), OFF perimeter, and ON perimeter in eyes with glaucoma.

<u>Methods:</u> In ordinary perimetry, the visual stimulus is luminance changes in the test target projected on to the background screen. In order to assess the difference of the stimulus effects between light-on and light-off, we developed an OFF-perimeter and ON-perimeter. The temporal aspect of the test target luminance is an abrupt reduction to 3 cd/m² followed by a gradual recovery to the background luminance of 150 cd/m² in our OFF-perimeter. We also developed an ON-perimeter in which the test luminance is abruptly increased to 150 cd/m² followed by gradual decrease to the background luminance of 3 cd/m². Three different perimetry including the OFF-perimeter, ON-perimeter and frequency doubling technology (FDT) were tested in eyes with glaucoma and their results were compared. Both the OFF-perimeter and the ON-perimeter have19 test target locations as in the FDT N-30 program. Ten glaucoma eyes of 10 patients were examined using FDT, OFF-perimeter, and ON-perimeter.

<u>Results</u>: The mean threshold of 190 test points of 10 eyes for FDT, OFF perimeter, and ON perimeter were 14.4dB (range, 0 - 31dB), 19.6dB (range, 0 - 35dB), 24.9 dB (range, 0 - 40), respectively. The Pearson's correlation coefficients between FDT-OFF, FDT-ON, and OFF-ON were 0.620, 0.550, and 0.413, respectively.

Conclusion: The sensitivity of frequency doubling illusion, light-off and light-on differed in glaucomatous eyes. These results suggest that there is some type of functional disorder in eyes with glaucoma. Although the clinical meaning of these tests is unknown, further investigation will show the usefulness of these tests.

PUPIL PERIMETRY IN GLAUCOMA

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Purpose: To evaluate our newly developed pupil perimeter in glaucoma patients. **Methods:** Our new pupil perimeter consists of a 19 inch liquid crystal display and an infrared CCD camera. The diameter of the pupil is measured in a darkened room, and the pupillary contraction ratio is analyzed. The stimulus parameters were an intensity of 300 cd/m^2 , a diameter of 4.0 degrees, a duration of 400 ms with flickering in 10 Hz and a background intensity of 0.50 cd/m^2 . Twenty-one points on the meridians of 45, 135, 225, and 315 degrees were stimulated (each direction 0, 5, 10, 15, 20, and 25 degrees). Three pupillary responses were averaged at each point.

Eight glaucoma patients with various visual field disturbances were examined.

<u>Results</u>: One case was not able to evaluate correctly glacomatous visual field defects. In other cases, at the position where the visual field defect existed, pupillary contraction was decreased. In addition, in one case, although no visual field defect compatible to the retinal nerve fiber defect in the Bjerrum area was shown with conventional static perimetry (Humphrey 30-2), pupillary contraction was found to have decreased by pupil perimetry.

<u>Conclusions</u>: Pupil perimetry may be able to objectively detect glaucomatous visual field defects.

CORRELATION OF THE STRUCTUAL AND FUNCTIONAL CHANGES IN THE EARLY AND PREPERIMETRIC STAGES OF GLAUCOMA

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<u>Purpose</u>: To investigate the correlation of structural findings derived from STRATUS OCT with Standard automated perimetry (SAP), FDT and flicker field data in the early and preperimetric stages of open-angle glaucoma (OAG).

<u>Subjects and Methods</u>: Seventy seven eyes of 77 patients with early stage (MD > -6dB) and preperimetric stage of OAG were tested by HFA 24-2 full threshold (SAP), FDT Matrix (24-2-5, 24-2-1), and Flicker perimetry (4-zone 38S) using Octopus 311. The visual fields were divided into 6 sectors and the number of the abnormal points in each sector was evaluated. Correlation of the visual field and visual field sectors was investigated with the average nerve fiver layer thickness (NFLT) and NFLT in 12 clock hour sectors using STRATUS OCT.

<u>Results:</u> In the early stage of OAG, the average NFLT correlated with the number of the abnormal points in the FDT and flicker field except for SAP. In the preperimetric stage of glaucoma, there was no significant correlation between the average NFLT and visual field defects in all the SAP, FDT and flicker perimetry. However, there was significant correlation between two sectors of the NFLT and the anatomically corresponding visual field sectors in the FDT and flicker perimetry.

Conclusion: The functional changes obtained by FDT and flicker perimetry significantly correlated with the structure changes obtained by OCT in the early and preperimetric stages of OAG.

FULL THRESHOLD PERIMETRY IN NORMAL AFRO-AMERICANS AND CAUCASIANS

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<u>Purpose</u>: To determine mean sensitivities (MS) in normal Afro-Americans (AA) and Caucasians (C) in rural North Carolina.

<u>Methods</u>: 110 subjects had full threshold strategy (G1X program) performed using the Octopus 1-2-3 perimeter (Haag Streit, Berne, Switzerland) from June1999 to May 2001. Subjects were identified as normal after complete eye exam (with IOP<22 mmHg) and the exclusion of the complete Metabolic Syndrome (central obesity, hypertension, dyslipidemia, increased fasting glucose and triglycerides). Hypertensive subjects on therapy were included. There were 66 AA (ages 20-29, n=32 and ages 50-59, n=34). There were 44 Caucasians (ages 20-29, n=23 and 50-59, n=21). No subject had been previously tested with full threshold perimetry; hence the Octopus 1-2-3 (TOP) program was used as initial experience to maximize perimetric learning curves. All subjects resided within rural eastern North Carolina (Sampson County).

<u>Results:</u> In AA eyes (n=132) the mean sensitivity (\pm SD) was 28.1 \pm 1.3dB (age 20) and 26.8 \pm 1.4dB (age 60), slope -0.034. The MS in Caucasian eyes (n=88) was 28.1 \pm 1.1dB (age 20) and 27.1 \pm 1.4dB (age 60), slope -0.025. The 95% confidence intervals of these slopes overlap, hence no differences exist. Both groups lose 0.3dB/decade. Test times for the G1X were 10 \pm 0.6 minutes in AA and 10 \pm 0.7 minutes in Caucasians.

<u>Conclusions</u>: The MS is the same in Afro-Americans and Caucasians. Full threshold strategies (G1X program) must become a primary preventive tool to reducing glaucoma blindness in high-risk groups (AA) and to eliminate unnecessary medical, surgical and laser therapies in glaucoma suspects.

DOES THE ENLARGEMENT OF RETINAL NERVE FIBER LAYER DEFECTS RELATE TO DISC HEMORRHAGE OCCURENCES OR VISUAL FIELD LOSS PROGRESSION IN NORMAL-TENSION GLAUCOMA?

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Purpose: To investigate the difference in clinical characteristics {disc hemorrhage (DH), visual field loss progression, and other clinical factors} between the cases of enlargement or non-enlargement of retinal nerve fiber layer defect (RNFLD) during the follow-up. **Methods:** We retrospectively reviewed the charts of 97 eyes of 79 patients with normal-tension glaucoma (NTG) (mean follow-up, 6.2 years). We examined the RNFLD using fundus photographs (including black-white photographs), divided into two groups; one is the enlarged RNFLD cases (enlarged group) and the other is the non-enlarged RNFLD cases (non-enlarged group), and compared the incidence of DH, visual field loss progression, and other clinical factors. The data were analyzed using the Kaplan-Meier life table method to calculate the cumulative probabilities of a stable visual field defined by two different criteria: one by mean deviation (MD, MD deterioration 3dB), and the other by glaucoma change probability analysis (pointwise definition).

<u>Results:</u> We detected the enlargement of RNFLD in 41 of 97 (42.3%) in NTG eyes. The incidence of the DH was significantly higher in the enlarged group (70.7%) than the non-enlarged group (7.1%) (P 0.001). In the enlarged group, mean baseline IOP and mean IOP during follow-up were significantly lower, the variation of MD and CPSD were significantly worse as compared to the non-enlarged group. The cumulative probability of progression of visual field loss was significantly greater in patients with the enlarged group than in patients with the non-enlarged group by either criterion for progression (P .0045, logrank test).

<u>Conclusions</u>: The enlargement of RNFLD seems to be closely associated with disc hemorrhage occurrence and the progression of visual field loss.

DETACTABILITY OF GLAUCOMATOUS CHANGES USING SAP, FDT, SWAP, FLICKER PERIMETRY, AND OCT.

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Purpose: To compare the detactability of glaucomatous functional changes using SAP, FDT, SWAP, flicker perimetry and structural changes using OCT.

<u>Methods</u>: Fifty-five eyes of 55 patients with OAG , glaucoma suspects, and thirty eyes of 30 healthy age matched subjects were tested. All subjects underwent HFA 24-2 full threshold (SAP), SITA SWAP, FDT (24-2-5, 24-2-1, 30-5, 30-1), flicker perimetry (4-zone 38S) using Octopus 311 and Stratus OCT (fast optic disc, fast RNFL thickness). Evaluation of the visual fields was counting the abnormal points. The areas under the receiver operating characteristic (ROC) curves (AUC) and sensitivities at fixed specificities were used to assess the detectability of glaucoma, especially in the early stages of glaucoma and glaucoma suspects. The correspondence of superior, (inferior) RNFL changes to inferior, (superior) visual hemi field was also assessed by complete, partial and no correspondence.

<u>Results:</u> The AUC of FDT 24-2-5, 24-2-1, 30-5, 30-1, SITA SWAP, flicker perimetry were 0.87, 0.91, 0.90, 0.97, 0.87, 0.96 respectively in the OAG group. The AUC of average RNFL thickness and cup/disc vertical ratio were 0.96, 0.94 in the OAG group. In glaucoma suspects group, RNFL thickness had the largest AUC (0.94) compared with cup/disc vertical ratio (0.85) and other functional tests (FDT 24-2-5, 24-2-1, 30-5, 30-1 (0.67, 0.62, 0.69, 0.55), SITA SWAP (0.64), flicker perimetry (0.71)). The percentage of complete and partial correspondence was over 80% in glaucoma suspects and almost 100% in the early stages of glaucoma with all perimeters.

Conclusion: FDT, SWAP, flicker perimetry and OCT are useful procedures for discriminating between healthy eyes and the early stages of glaucoma. Especially, a structural change of RNFL thickness measured by OCT is useful for detecting abnormalities in glaucoma suspects.

MONITORING THE VISUAL FIELD CHANGES USING SEMI-AUTOMATED KINETIC PERIMETRY (SKP) IN PATIENTS TAKING VIGABATRIN.

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<u>Purpose</u>: To assess quantatively the visual field loss in patients taking Vigabatrin during the long-term follow-up

<u>Method</u>: Sixteen epilepsy patients (9 women, 7 men; mean age 40 years, range 23-57 years) under Vigabatrin treatment were examined using semi-automated kinetic perimetry (SKP) implemented in Octopus 101 instrument. Five consecutive examinations of each patient were performed during the 2-years period. The mean time interval between examinations was 6 months (range 3-13 months). Three stimuli (III4e, I4e and I2e) moved with constant angular velocity 3°/s were used to assess the entire 90° visual field of each patient.

<u>Results</u>: The mean isopter area, Mean Radial Degree (MRD), original and modified Esterman grid and Gandolfo score were used to evaluate the visual field loss during the follow-up.

<u>Conclusions</u>: SKP may be a useful tool in detection and monitoring the visual field loss in patients taking Vigabatrin. It enables an examiner-independent examination and quantative analysis of the results.

CLINICAL FOLLOW-UP RETURN RATES AMONG THOSE SCREENING POSITIVELY FOR SIGHT-THREATENING DISEASE IN BEXAR COUNTY, TX Y Trigo, J Hendricks, H Koenig, WE Sponsel.

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Purpose: To determine the return rate of those screening positively for glaucoma or other sight-threatening eye disorders at glaucoma screenings in Bexar County, Texas. Methods: Four-day-long (Sunday - Wednesday) screenings for glaucoma were held monthly at different sites in the parking lot of the region's leading grocery retailer, (HEB stores # 5, 9, 10, 11, 12, 15, 20, 21, 22, 23, 27, 29, 30, 32, 34, and 40) using an airconditioned and heated 60-foot Lions Mobile Eye Screening Unit. Each screening was carried out in two stages: the initial screening by a trained technician who performed history, digital blood pressure, visual acuity using the Optec 2500, and Frequency Doubling Technology (FDT) C-20-5. Those screening positively with > 1 miss on the FDT underwent Humphrey Visual Field (HVF) SITA 30-2, Heidelberg Retinal Tomography (HRT II) scanning laser, and Reichert non-contact tonometry in both eyes by an experienced technician. A slit-lamp exam and ophthalmoscopic exam were performed by an ophthalmologist on the first and final day of each screening (days 1 & 4) in both eyes. Screenees who tested positively on days 2 or 3 were given the option of returning to be seen by the ophthalmologist at the same site on day 4 or to go to a different site the following month on days 1 or 4.

<u>Results</u>: Among 4630 individuals screened during 2 years of Bexar County glaucoma screenings, 454 failed the FDT. Of those that failed, 240 were clinically confirmed as having glaucoma or other sight-threatening eye disorders by an ophthalmologist. Among these 240, 89 were immediately examined on days 1 or 4 of the 4-day screenings. The remainder (151 from days 1-3) returned on day 4. Of the 454 who failed the FDT on the initial screening, 49 made appointments to return on Day 4 for further testing and examination by the ophthalmologist, but did not return. A further 165 chose not to stay for further evaluation.

Conclusion: Follow-up compliance among those at high risk for sight-threatening ocular disease is a critical problem that must be addressed, particularly with screening methods now attaining very high levels of diagnostic sensitivity and specificity. Time and distance between the screening and clinical follow-up site appear to be factors, but economic and sociologic issues yet to be properly identified will inevitably need to be addressed..

THE FREQUENCY-DOUBLING EFFECT FOR VARIOUS SPATIO-TEMPORAL CONDITIONS

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Purpose: The "frequency-doubling" illusion, in which the apparent spatial frequency of a sinusoid grating appears to be doubled, is produced when a low frequency spatial sinusoid grating is counterphased at a high temporal frequency. The current study examines the hypothesis of fractional increases in apparent spatial frequency under particular spatio-temporal conditions.

<u>Methods</u>: Detection contrast thresholds were determined and repeated in two observers for various spatio-temporal combinations of a counterphased sinusoidal grating. The perceived spatial frequency was then determined for each spatio-temporal combination using a matching task, whereby the periodicity of a stationary sinusoid was matched to that of a counterphase flickered grating. The same matching task was repeated under different matching task instructions for five randomly chosen spatio-temporal combinations.

<u>Results</u>: No significant differences were found in test-retest contrast threshold measures and under different matching task instructions. Match ratios were fractional, showing higher or lower apparent spatial frequencies by non-integer multiples.

<u>Conclusions</u>: The appearance of a variety of fractional spatial distortions other than simply doubling provides additional evidence that frequency-doubling illusion in humans is unlikely to be solely generated by spatially nonlinear Y-type magnocellular ganglion (M_y) cells, as previously reported.

PUBLICATIONS ON PERIMETRY LISTED IN THE NATIONAL LIBRARY OF MEDICINE

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Purpose: To evaluate if there is still a scientific interest in perimetry.

Methods: The National Library of Medicine (NLM) was searched for the term 'perimetry' a) in any field stored, b) as MeSH term 'topic', and, c) as MeSH term as 'major topic'. This would render a number or publications where a) the term was at least mentioned b) perimetry was not the main topic of the paper, and, c) the paper focuses on perimetry,.

<u>Results:</u> The number of retrieved articles is 10, 13, 17, 43, 36, 44, 54, 39, and, 54 for the years 1960 - 1969. This sudden increase is probably a sampling error, i.e., not all publications were covered by the NLM in the early 60ties. Furthermore, subject headings (MeSH) are known since 1965. We therefore limit your report on 1965 - 2005 excluding 138 publications published 1960-1964.. For the three groups, a total of 5010, 4233, and, 1882 publications respectively, have been published. Over the years, the numbers increase in strict synchrony. For the sake of simplicity, only the publications averaged 16.6, 23,3, 50,5, 58,9, and, 76.8 per decade, i.e., the rate of publications increased till 1980, remains steady for 20 years and seems to increase lately. For the years 1975 – 2005, it was rather odd to learn, that significantly less 'major topic' research was published in odd than in even years, i.e., 819 versus 874 publications, or, 51.2 versus 58.3 publications / year.

<u>Conclusion</u>: Perimetry as a scientific subject is still of interest. In absolute numbers, this interest is increasing. Further studies will have to compare the presented number of publications on perimetry to all clinical papers published. The observed biannual fluctuation of the rate of publications may reflect the important of our meetings. However, the increase in publications is not related to the number of IPS members