

S15 FREE PAPER SESSION

THE VELOCITY OF VISUAL FIELD PROGRESSION IN EYES WITH OPTIC DISC HEMORRHAGES IN THE OCULAR HYPERTENSION TREATMENT STUDY

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Purpose: To determine rates of visual field (VF) change in eyes with and without optic disc hemorrhage (DH) detected on stereophotographs and to determine whether the rate of VF change is influenced by DH recurrence.

Methods: We included OHTS participants with ≥ 10 reliable VF tests and ≥ 5 years of follow-up. Eyes reaching endpoints considered non-glaucomatous by the OHTS endpoint committee were excluded (261 eyes of 202 participants). Optic disc stereophotographs were reviewed for the presence of DH. VF progression was assessed using 2 methods of trend-analyses: 1) regression of mean deviation over time to determine its rate of change (MDR), and 2) pointwise linear regression (PLR) in which the sensitivity at each VF location (30-2 pattern) was regressed over time. For PLR, a progression endpoint was defined as a slope ≤ -0.5 dB/yr with $p \leq 0.01$ at ≥ 1 location, ≥ 2 locations or ≥ 2 neighboring locations.

Results: Data from 2,607 eyes of 1,378 participants were included. The mean number of VF tests in a test sequence was 23.7 ± 4.9 spanning an average of 12.2 ± 2.0 years. At least one DH was detected in 187 eyes (7.2%). 135 eyes had 1 DH and 52 eyes had >1 DH. The MDR was significantly worse in DH compared to non-DH eyes (-0.17 ± 0.19 vs. -0.07 ± 0.27 dB/yr, $p < 0.01$). Eyes with a single DH and eyes with recurrent DH were not significantly different in their MDR (-0.16 ± 0.29 dB/yr vs. -0.20 ± 0.18 dB/yr, $p = 0.29$). There was a significant association between DH and progression endpoints determined using PLR by all three criteria described above (Odds ratios = 3.6, $p < 0.01$; 2.8, $p < 0.01$; 2.5, $p < 0.01$ respectively (logistic generalized estimating equations)). In contrast to the MDR results, eyes with ≥ 2 DH were significantly more likely to display PLR progression by all 3 criteria described above than eyes with only 1 DH (Odds ratios = 4.2, $p = 0.01$; 3.4, $p < 0.01$; 3.6, $p < 0.01$ respectively).

Conclusions: Eyes with one or more DH during follow-up had more rapid VF deterioration when assessed by global (MDR) or local (PLR) methods when compared to eyes without DH. Eyes with recurrent DH had statistically similar rates of global VF change (MDR) when compared to eyes with a single DH, but reached PLR endpoints more often.

CORNEAL SENSITIVITY IN PATIENTS TREATED FOR GLAUCOMA OR OCULAR HYPERTENSION

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Background: The use of topical IOP-lowering medications is associated with numerous ocular surface changes. Previous studies have suggested that topical antiglaucoma treatments may affect corneal sensitivity. The purpose of this study was to evaluate the corneal sensitivity in patients treated with IOP-lowering medications and the influence of preservatives.

Methods: Thirty nine patients treated for glaucoma or ocular hypertension (OHT) and 9 untreated patients were included in this study. Patients treated with intraocular pressure-lowering medications were divided in 3 groups according to the number of instillations of preserved eyedrops (0, 1 and ≥ 2). Corneal sensitivity was assessed using the Cochet-Bonnet esthesiometer. Then, all patients underwent a complete examination of the ocular surface including Schirmer test, tear film breakup time (TBUT) and, corneal and conjunctival fluorescein staining. The Ocular Surface Disease Index (OSDI) questionnaire was used to evaluate symptoms.

Results: The corneal sensitivity was 58.8 ± 2.8 mm, 56.2 ± 5.2 mm, 50.3 ± 12.5 mm and 44.3 ± 13.6 mm in untreated patients, in patients treated with 0, 1 and ≥ 2 instillations of preserved eyedrops, respectively. The corneal sensitivity of patients treated with preserved eye drops was significantly lower as compared to untreated patients ($p < 0.001$) and patients treated with preservative-free eyedrops ($p = 0.012$). The corneal sensitivity of patients treated with intraocular pressure-lowering medications was negatively correlated to the number of instillations of preserved eyedrops ($r = -0.390$; $p < 0.001$) as well as to the duration of treatment ($r = -0.357$; $p = 0.001$).

Conclusion: The chronic administration of eyedrops containing preservatives may decrease corneal sensitivity. These results could explain the absence of correlation between symptoms and signs sometimes observed in patients treated for glaucoma or OHT.

Key words: Glaucoma, corneal sensitivity, treatment, preservatives.

MITOCHONDRIAL DAMAGE IN THE TRABECULAR MESHWORK OF GLAUCAMATOUS PATIENTS

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Oxidative damage to the trabecular meshwork is a pathogenic mechanism contributing to glaucoma. The source of this oxidative stress still remains to be identified. Since no environmental risk factors for glaucoma is recognised, we focused our attention on mitochondria, the main endogenous source of reactive oxygen species. Mitochondrial damage was evaluated analysing the common mitochondrial DNA (mtDNA) deletion by real-time PCR in the trabecular meshwork of 79 primary open-angle glaucomatous patients and 156 unaffected controls collected at surgery. Glaucomatous patients included patients affected by various glaucoma types: primary open-angle, pigmented, juvenile, congenital, pseudoexfoliative, acute, neovascular, and chronic closed-angle glaucoma. MtDNA deletion was dramatically increased in trabecular meshwork of glaucomatous patients *versus* controls. This finding was paralleled by a decrease in the number of mitochondria per cell and by cell loss. Only primary open-angle glaucoma (3.0-fold) and pseudoexfoliative glaucoma (6.3-fold) showed significant increases in the amount of mitochondrial DNA deletion. In all other cases, deletion was similar to controls. The results obtained indicate that the mitochondrion is a target for the glaucomatous degenerative processes selectively involved in the pathogenesis of primary open-angle glaucoma and pseudoexfoliative glaucomas.

ASSESSMENT OF RETINAL AND OPTIC NERVE HEAD BIOMARKERS FOR PREDICTION OF THE CIRCUMPAPILLARY RETINAL NERVE FIBER PROFILE

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Background: To define an accurate normative database for glaucoma detection based on the correlation of TSNIT profiles with putative morphological biomarkers.

Methods: A sample of 120 healthy volunteers underwent complete ophthalmologic examination, including HR-OCT scanning (Cirrus ® Carl Zeiss Meditec Inc.) and RNFL Assessment (GDx-ECC ® Carl Zeiss Meditec Inc.). The direction of the major retinal vessels near the optic nerve head was proven to be a good predictor of the TSNIT profile. To confirm this and establish retinal and optic disc parameters as biomarkers for the TSNIT profile, SLO-OCT images centered at the optic disc will be processed for automatic segmentation of vessels and optic disc. All extracted putative biomarkers will be analysed to determine their relevance for the TSNIT profile. To test this model, a preliminary analysis was performed using a subsample of 79 subjects. TSNIT profiles from GDx were parameterized using Discrete Wavelet (DWT) and Discrete Fourier Transforms (DFT). The results were correlated with the major superior and inferior vessel angles (manually segmented).

Results: A good correlation was obtained between retinal vessel angles and DWT coefficients. The 2nd and the 5th detail coefficients present better correlation with the superior major vessel ($R = -0.47$, $R = -0.48$, $p < 0.05$), while 8th and the 10th approximation coefficients present a better correlation with the inferior major vessel ($R = -0.38$, $R = -0.40$, $p < 0.05$). The 2nd and 4th values of amplitude of the DFT coefficients present good correlations with the superior and inferior vessel angles ($0.38 < R < 0.55$, $p < 0.05$), as well as the 2nd and 4th values of power ($0.35 < R < 0.50$, $p < 0.05$).

Conclusions: The results confirm a relation between the angles of the retinal blood vessels and TSNIT profile. This validates Wavelet and Discrete Fourier transforms as approaches to determine possible morphological biomarkers for the prediction of the TSNIT profile. This study is considered a step forwards on individualized normative data concerning RNFL. Determining independent biomarkers may compensate for the intersubject variability of RNFL measurements and might render the normative values of retinal nerve fiber measurements more accurate.

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NON-INVASIVE THREE DIMENSIONAL (3D) SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY (SDOCT) CASTING OF THE AQUEOUS OUTFLOW SYSTEM

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Purpose: Aqueous exiting the eye via the trabecular meshwork/Schlemm's canal (SC) passes through the deep and intrascleral venous plexus (ISVP) or directly through aqueous veins. The purpose of this study was to visualize the human aqueous outflow system 360 degrees in 3D during active aqueous outflow.

Methods: During perfusion at different pressures, the outflow pathways of 7 donor eyes were imaged with a modified SDOCT system (Biotigen Inc, USA; SuperLum LTD, Ireland). Thirty-six scans (3 equally distributed in each clock hour), each covering a 2 x 3 x 2 mm volume (512 frames, each 512 x 1024 pixels), were obtained from each eye (Figures A and B). All image data were black/white inverted, and the background subtracted (Subtract Background algorithm, ImageJ 1.40g, <http://rsb.info.nih.gov/ij/>). Contrast was adjusted to isolate the ISVP.

Results: SC, collector channels, the deep and ISVP, and episcleral veins were observed in different regions of limbus. Aqueous veins could be observed extending from SC towards the ISVP (B). Individual scan ISVP castings were rendered (C) and assembled in 3D space (D) in Amira 4.1 (Visage Imaging Inc. USA). A 360-degree casting of the ISVP was obtained in all perfused eyes. The ISVP tended to be dense and overlapping in the superior and inferior quadrants, and thinner in the lateral quadrants.

Conclusions: The human aqueous outflow pathway can be imaged using SDOCT. The more superficial structures of the aqueous outflow pathway present with sufficient contrast as to be optically isolated and non-invasively cast in-situ 360 degrees in cadaver eye perfusion models. This approach may be useful in future studies as a model of human aqueous outflow.

SOCIODEMOGRAPHIC FACTORS THAT IMPACT ON COST OF CARE FOR INCIDENT OPEN-ANGLE GLAUCOMA

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Background: Little is known about the cost of treating newly-diagnosed open-angle glaucoma. Most information on cost has been based on prevalent glaucoma, and the capture of costs was confined to one point in time. The purpose of our study was to identify enrollees in a large health care plan who had newly diagnosed OAG, obtain costs of their glaucoma care over a two-year period, and evaluate sociodemographic factors that impacted on cost of care.

Methods: We identified patients with incident OAG from a large, national, managed care network in the US (the i3 InVision Data Mart dataset; Ingenix, Eden Prairie, MN). The dataset contains fully de-identified records of all beneficiaries. We had access to data for a subset of beneficiaries who had any form of eye care from January 1, 2001 through December 31, 2009. Incident glaucoma was identified by identifying enrollees who had no coding for OAG from eye care visits during a one-year look-back period preceding the first diagnostic coding for OAG. Resource use for glaucoma care over the two year post-diagnosis period included glaucoma-related medication, surgery, office visits, and diagnostic testing. Socio-demographic variables (age, sex, race, education level, household net worth and region of residence) were associated with total glaucoma charges by a multivariable linear regression model. An estimate of glaucoma severity and systemic co-morbidity burden were included as covariates in the model.

Results: A total of 19,927 enrollees met our definition of incident OAG. These patients had a mean (standard deviation) age of 60.2 (11.0) years and were more likely to be female (55.2%). Most people with incident OAG were white (81.4%) followed by Blacks (8.3%), Latinos (6.5%), and Asians (3.0%). Almost all were high school graduates (98.3%) and 24.7% had graduated from college. The majority of the enrollees with incident OAG (75.4%) had household net worth levels of > \$150,000. Over the first two years after OAG diagnosis, a total of \$42.3 million was spent on glaucoma-related care. The median cost of care was \$1,516, with an inter-quartile range from \$801 to \$2,547. Factors strongly predictive of two year cost of care (all p-values <0.0001) included age (lower costs among the youngest and oldest), sex (females > males), region of country (NE highest), and expected increases with worsening glaucoma severity and more systemic co-morbidities. Household net worth, education, and race were also significantly associated with two-year costs. The regression model predicted that two-year cost of care for a 60 year-old with incident OAG would vary from \$1762 for a black male to \$2139 for an Asian female, with other race/sex combinations falling between these estimates.

Conclusions: Sociodemographic factors impact strongly upon cost of care for incident OAG, even after adjusting for the severity of glaucoma and systemic co-morbidities. Knowledge of these associations may lead to identifying underlying factors that create discrepancies in not only cost but also effectiveness of care.

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MORPHOLOGICAL CHANGES OF LATERAL GENICULATE NUCLEUS IN PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA: A 3.0T MAGNETIC RESONANCE IMAGING STUDY

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Background: Recently, more and more studies indicate that the glaucomatous damage not only occurred to retinal ganglion cells in the eyes, but went across optic nerves, visual chiasm, lateral geniculate nucleus (LGN) and finally the visual cortex, similar to the neurodegenerative disease, such as Alzheimer's disease. LGN works like a relay station in the visual nerve system. Results from previous experiments on the primates (pressure-induced glaucoma monkey models) have shown the atrophies and the shrinkage in both LGNs. In this report, morphological changes of LGN in patients with moderate to severe primary open-angle glaucoma (POAG) were investigated by 3.0-Tesla magnetic resonance imaging.

Methods: Eighteen patients with moderate to severe POAG, and eighteen age and gender matched healthy subjects underwent MRI examinations. LGN was identified and manually extracted by two experienced neuroradiologists. The maximum height and volumes of the bilateral LGNs were measured. The patients and controls were compared with *t* test

Results: Bilateral LGNs could be visualized clearly by 3.0T MRI. The mean maximum height of the right LGN was 4.18 ± 0.53 mm for patients and 5.01 ± 0.40 mm for controls, while that of left LGN was 4.15 ± 0.55 mm for patients and 4.96 ± 0.40 mm for controls. The combined LGN height was 8.33 ± 1.05 mm for patients and 9.97 ± 0.73 mm for normal subjects. For volumes, the mean right LGN was 86.6 ± 15.0 mm³ in patients whereas it was 148.4 ± 19.5 mm³ in controls, the left one was 83.4 ± 17.9 mm³ in patients and 149.3 ± 13.5 mm³ in controls, the combined LGN volumes of patients and controls were 169.9 ± 29.0 mm³ and 297.7 ± 29.2 mm³ respectively.

Conclusions: Bilateral LGNs could be clearly visualized by 3.0T MRI, both the heights and volumes of LGN decreased significantly in patients with POAG than the normal subjects. The morphological changes, especially changes in the LGN volumes, provided an efficient and reliable biomarker for the clinical observations on central nerve system damages in glaucoma.

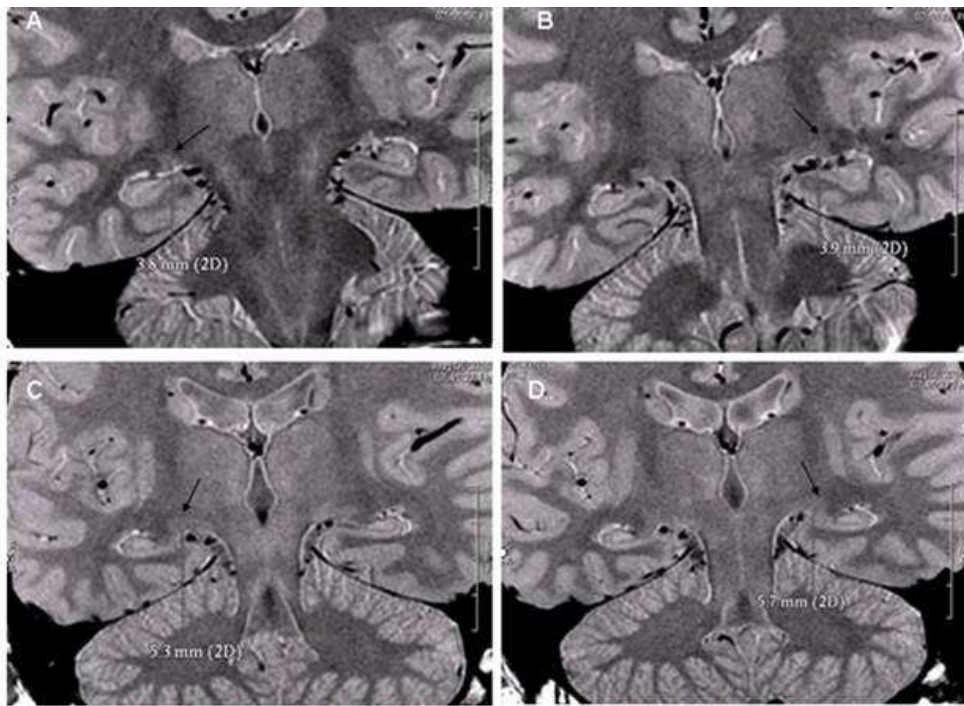


Figure 1 Representative lateral geniculate nucleus (LGN) images of the maximum height in control(A,B) and glaucoma subjects(C,D). The arrows indicate right and left LGNs. Minimum scale of the calibration bar indicates 10.mm.↵

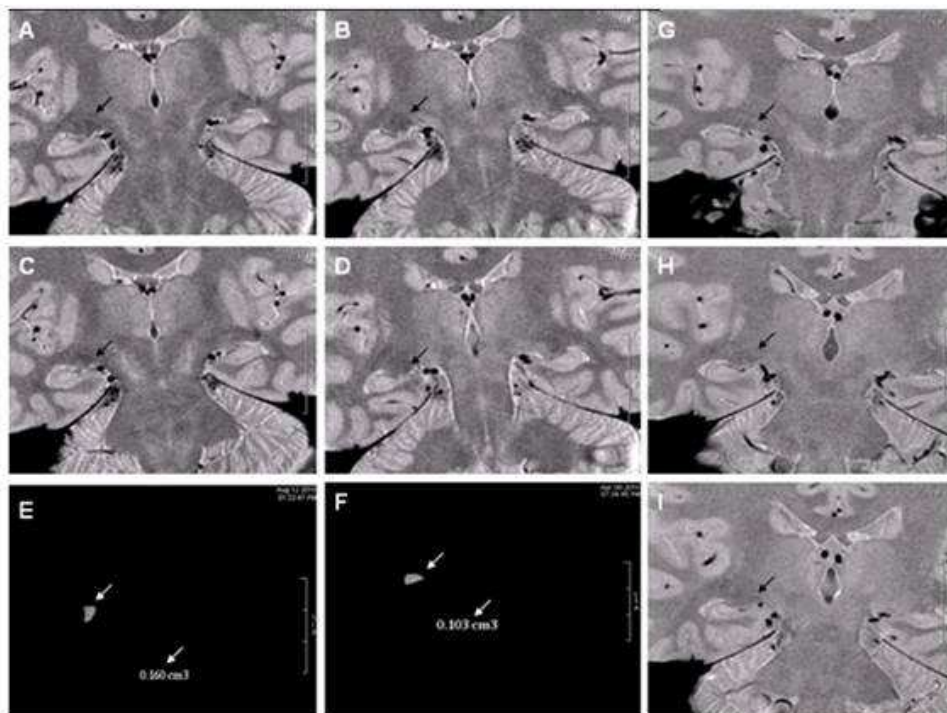


Figure 2 Representative lateral geniculate nucleus (LGN) images of the volume measurement in control(A-E) and glaucoma subject(F-I). The black arrows indicate the outlined LGNs of every slice of one subject, the white arrows indicate last slice(cut down) of LGN and the volume value obtained from the processing software. Minimum scale of the calibration bar indicates 10mm.↵

OCULAR SURFACE CHANGES IN GLAUCOMA PATIENTS TREATED WITH FIXED COMBINATIONS OF PROSTAGLANDINES/TIMOLOL 0.5%H. Russ¹, P.A. Nogueira Filho¹, F. Montiani-Ferreira², P.A. Arruda Mello¹, J.A. Pereira Gomes¹¹Universidade Federal de São Paulo, São Paulo - Brazil; ²Universidade Federal do Parana, Curitiba - Brazil

Purpose: To compare ocular surface changes induced by glaucoma treatment in patients using fixed combination of prostaglandine analogues (latanoprost, travoprost and bimatoprost) and timolol maleate 0.5%.

Methods: 33 patients with ocular hypertension or open angle glaucoma not receiving treatment were included in the investigation. Exclusion criteria: previous ocular surgeries, ocular inflammation, dry eye or multiple glaucoma treatment. Ocular surface evaluation was done before and 3 months after fixed combination treatment with Xalacom (XC), Duo-Travatan (DT) and Ganfort (GF). Slit lamp biomicroscopy, break up time (BUT), Schirmer Tear Test (STT) and Lisamine Green Test 1% (LGT) quantified by the Bijsterveld scale were performed in all patients, who also answered the OSDI form. After the ophthalmic examination, impression cytology was done and the samples underwent HE, PAS and immunohistochemistry staining with antibodies against IL-6 and HLA-DR.

Results: All drugs induced a STT reduction, but it only was significantly different in the groups DT ($p < 0.0001$) and XC ($p < 0.0007$). Comparing all drugs, DT induced greater reduction compared to GF ($p = 0.0034$) and XC ($p = 0.04$). BUT decreased in the DT group ($p = 0.0125$) and in the XC group ($p = 0.035$), and the difference of DT group was significant when compared to GF ($p = 0.0007$) and XC ($p = 0.0008$). LGT score increased significantly in DT ($p = 0.9999$) and GF ($p = 0.0063$), and it was also significant comparing DT to GF ($p = 0.0001$), DT to XC ($p = 0.0001$) and GF to XC ($p = 0.0001$). OSDI Scores increased in all treatment groups, but only with DT it was significantly different (higher) ($p = 0.02$). XC presented the lowest scores. The OSDI Scores for DT were worse than for GF ($p = 0.0095$) and XC ($p < 0.0001$) and XC scores were better than GF ($p < 0.0001$). All drugs induced a significant IOP reduction ($p < 0.0001$). GF ($p = 0.013$) and XC ($p = 0.0021$) demonstrated a greater reduction comparing to DT. Immunohistochemistry results showed an over-expression of inflammatory cells (IL-6 and HLA-DR) in all treated groups. After treatment DT presented a higher HLA ($p = 0.0184$) and IL-6 ($p = 0.0023$) expressions. Comparing groups for HLA expression, in the DT group it was significantly higher than in the XC group ($p = 0.0036$) and in the GF group it also was significantly higher than in the XC group ($p = 0.007$). For IL6 expression, the GF group presented more positive cells than the XC group ($p = 0.0132$) post-treatment. Total impression cytology scores showed a deterioration of ocular surface conditions in all groups post-treatment (54.54% to XC and DT, and 45.45% to GF) with no significant difference among drugs. Other specific parameters changed as cellularity, which was considered *borderline* or *abnormal* in all groups (DT $p = 0.0008$; GF $p = 0.008$ and XC $p = 0.0022$), with a significant difference when comparing GF (which was worse) to DT ($p = 0.0486$). Cell-to-cell contact decreased significantly only in DT group ($p = 0.0005$). Nucleus-cytoplasm ratio tended to increase in all groups but it was only significantly different when comparing DT to GF ($p = 0.0131$) and to XC ($p = 0.0483$). Goblet cells density increased in all groups, being significantly higher in the DT group ($p = 0.0012$) and XC ($p = 0.0186$). Comparing drugs, GF significantly increases this cells comparing to XC ($p = 0.0425$). There were no signs of inflammatory cells or keratinization.

Conclusions: All drugs induced a significant IOP reduction. Fixed combinations increase expression of inflammatory markers such as HLA-DR and IL-6. Some drugs may induce fewer changes than others in some parameters but all of them worsened ocular surface conditions during glaucoma treatment.

MEASUREMENT OF TNF-ALPHA, INTERLEUKIN-6, FASL, INTERLEUKIN-1 ALPHA AND INTERLEUKIN-1 BETA IN THE AQUEOUS HUMOR OF PATIENTS WITH OPEN ANGLE GLAUCOMA USING MULTIPLEX BEAD ANALYSIS

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Background: Various cytokines have been demonstrated to contribute to the pathogenesis of glaucomatous damage. Upregulation of TNF- α in optic nerve heads and retina sections of glaucomatous eyes has been shown in ex vivo studies, while an in vitro study provided evidence that glial cells exposed to elevated hydrostatic pressure or stimulated ischemia secreted increased amounts of TNF- α . Endothelial leukocyte adhesion molecule-1 (ELAM-1) is a cell-adhesion molecule consistently present in the outflow region of glaucomatous eyes, while being absent in the outflow region of normal eyes. Expression of ELAM-1 has been suggested to be under control of interleukin-1 α (IL-1 α), interleukin-1 β (IL-1 β), and interleukin-6 (IL-6). Furthermore, in an in vitro study using co-cultured retinal astrocytes, microglia and RGCs, IL-6 has been shown to counteract pressure-induced apoptotic death of RGCs. Decreased cellularity of the trabecular meshwork has been reported in glaucomatous eyes and this cell loss has been suggested to be due to apoptotic death via the Fas/FasL pathway. Multiplex bead analysis has the advantage of measuring a large number of analytes in parallel in relatively small volumes, as they are typically provided in ophthalmologic samples from the aqueous humor, vitreous or tear fluid. The present study was set to investigate concentrations of the aforementioned cytokines (TNF- α , FasL, IL-1 α , IL-1 β and IL-6) in the aqueous humor of patients with POAG using a multiplex bead analysis.

Methods: 25 patients with POAG and 29 control subjects were enrolled in this case-control study. The study was approved by the Institutional Review Board of the Medical University of Graz. Prior to enrollment, written informed consent was obtained from all participants. POAG was defined by an open anterior chamber angle, optic disk changes characteristic for glaucoma, visual field defects characteristic for glaucoma and absence of conditions leading to secondary glaucoma. The control group consisted of 29 unrelated patients with no morphological or functional damage indicative for primary or secondary open angle or angle closure glaucoma. Aqueous humor was collected via limbal paracentesis using a blunt 30 gauge canula at the beginning of the surgery, and was placed immediately on ice. Determination was done using BDTM CBA Flex Set System. The assay sensitivities were as follows: IL-1 α 6.54 pg/ml, IL-1 β 1.74 pg/ml, IL -6 1.87 pg/ml, FasL 2.05 pg/ml, and TNF- α 1.95 pg/ml.

Results: Concentrations of IL-1 α , TNF- α , and FasL were below limits of detection. IL-1 β was detected in 6 patients and 5 controls with mean concentrations of 0.5 and 0.4 pg/ml, respectively ($p = 0.72$). IL-6 was detected in 10 (out of 25) patients and 22 (out of 29) controls. The mean concentration was 9.3 pg/ml in patients and 55.9 pg/ml in controls, respectively ($p = 0.003$). No significant correlation was found between IL-6 and age, duration of disease, cup/disk ratio, or mean deviation.

Conclusion: We observed significantly lower concentrations of IL-6 in the aqueous humor of patients with POAG compared with control subjects. As studies provided evidence that IL-6 protects RGC's from pressure-induced apoptotic death and after ischemia/reperfusion injury, lower intraocular concentrations of IL-6 may increase the likelihood of RGC damage.

EFFECTIVITY OF THE BAERVELDT GLAUCOMA IMPLANT IN PATIENTS WITH SECONDARY GLAUCOMA DUE TO UVEITIS

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Background: Patients with secondary glaucoma due to uveitis are at high risk of failure after conventional glaucoma filtering surgery and usually require more interventions to maintain adequate intraocular pressure (IOP). The objective of this study was to evaluate the effectivity of the Baerveldt glaucoma implant in patients with secondary glaucoma due to uveitis.

Methods: Case series in which we prospectively studied uveitis patients who underwent Baerveldt glaucoma implant surgery due to refractory secondary glaucoma. In all cases a Baerveldt 350 mm² glaucoma implant was placed in the anterior chamber. Twenty-eight eyes of 26 patients were included. Pre-operatively, an extensive ophthalmologic examination was performed including endothelial cell density (ECD) count and OCT Visante imaging of the anterior eye segment. The ECD was compared with a group of 20 POAG patients for all follow-up moments. Follow-up visits were scheduled 1, 3, 6 and 12 months post-operatively.

Results: The mean age of the included patients was 51 ± 19 years, 50% were male. The causes of uveitis were diverse: 4 patients suffered from sarcoidosis, 5 patients had Fuchs' heterochromic uveitis, 2 patients had HLA-B27 positive uveitis and 2 patients suffered from juvenile idiopathic arthritis. Four of the 26 patients were treated with adalimumab, 3 patients with methotrexate and 2 patients used oral prednisone. Mean IOP was 28.1 ± 8.7 mmHg pre-operatively. After one month follow-up mean IOP was 17.8 ± 9.6 mmHg; after 3 months 12.7 ± 5.1 mmHg; after 6 months 12.3 ± 5.3 mmHg and after 1 year 10.8 ± 4.8 mmHg. The mean ECD was 2216 ± 541 pre-operatively. After three months of follow-up the mean ECD was 2147 ± 627 ; after 6 months 1874 ± 510 and after 12 months the mean ECD was 2112 ± 644 . There was no statistically significant difference in ECD count between the uveitis patients and the POAG patients at all follow-up moments. After one year, the mean ECD in POAG patients was 2340 ± 713 . One eye developed a late hypotony (3 mmHg after a year follow-up) but without hypotonic maculopathy. In one eye, the tube was reinserted into the pars plana because of tube-corneal touch 12 months post-operatively.

Conclusion: The Baerveldt glaucoma implant is an effective and relatively safe procedure for the treatment of refractory secondary glaucoma due to uveitis.

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MULTICENTER GLAUCOMA SCREENING IN ISRAEL DURING THE 2010 WORLD GLAUCOMA DAY

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Background: Early detection of glaucoma enables beginning of therapy at an earlier stage, and may improve outcome. Screening of large populations at risk is likely to help in achieving this goal.

Methods: Public awareness campaign was carried out in electronic and paper media in Israel during the 2010 World Glaucoma Week, culminating in a one-day, free-of-charge screening of individuals in 12 outreach locations throughout Israel. Cases with a prior diagnosis of glaucoma or ocular hypertension were excluded. Screening was performed by 30 ophthalmologists, members of the Israel Glaucoma Screening Group, and included medical history, slit-lamp exam, including gonioscopy and intraocular pressure (IOP), and fundus exam with evaluation of cup/disc ratio. When necessary, further evaluation at an ophthalmology clinic was recommended.

Results: 1296 individuals were screened, 702 females and 594 males. All were older than 30, mean age was 60 ± 12 . The table shows the number of eyes and cases with elevated IOP and with enlarged cupping.

	Eyes (%)	Individuals (%)
IOP ≥ 21 mmHg	94 (3.6)	57 (4.4)
IOP ≥ 24 mmHg	19 (0.7)	15 (1.2)
Cupping ≥ 0.5	291 (11.2)	173 (13.3)
Cupping ≥ 0.7	97 (3.7)	65 (5.0)
Cupping = 0.9	14 (0.5)	10 (0.8)
IOP ≥ 21 and Cupping ≥ 0.5	27 (1.0)	20 (1.5)

The number of cases with both IOP ≥ 21 **and** cupping ≥ 0.5 , apparently suggestive of preperimetric glaucoma, increased with age: it was found in 20 cases aged ≥ 50 years (1.9%), compared to none among younger individuals ($p = 0.04$). Likewise, cupping ≥ 0.7 was observed in 5.6% of those aged ≥ 50 , compared to only 1.8% of younger individuals ($p = 0.02$). The combined IOP ≥ 21 **and** cupping ≥ 0.5 was significantly more common in women compared to men (2.4% and 0.5% respectively, $p = 0.01$). Further ophthalmological evaluation was recommended to 185 of the screened individuals (14.2%).

Conclusion: Outreach screening for glaucoma is a valuable tool for detecting glaucoma or ocular hypertension in a meaningful number of previously undiagnosed cases. The yield of such screening is increased in those older than 50 and in women.

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COMBINING STRUCTURAL AND FUNCTIONAL MEASUREMENTS TO IMPROVE DETECTION OF GLAUCOMA PROGRESSION USING BAYESIAN HIERARCHICAL MODELS

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Purpose: To present and evaluate a new methodology for combining longitudinal information from structural and functional tests to improve detection of glaucoma progression and estimation of rates of change.

Methods: This observational cohort study included 434 eyes of 257 participants followed for an average of 4.2 ± 1.1 years and recruited from the Diagnostic Innovations in Glaucoma Study (DIGS). Subjects were followed annually with standard automated perimetry, optic disc stereophotographs and scanning laser polarimetry with enhanced corneal compensation (GDx ECC). Rates of change over time were measured using the visual field index (VFI) and average retinal nerve fiber layer thickness (TSNIT average). A Bayesian hierarchical model was built to integrate information from the longitudinal measures and classify individual eyes as progressing or not. Estimates of sensitivity and specificity of the Bayes method were compared to those obtained by the conventional approach of ordinary least squares (OLS) regression.

Results: The Bayes method identified a significantly higher proportion of the 405 glaucoma and suspect eyes as having progressed compared to the OLS method (22.7% vs. 13%; $p < 0.001$), while having the same specificity of 100% in 29 healthy eyes. In addition, the Bayes method identified as progressing a significantly higher proportion of eyes with progression by optic disc stereophotographs compared to the OLS method (74% vs. 37%; $p = 0.001$).

Conclusion: A Bayesian hierarchical modeling approach for combining functional and structural tests performed significantly better than the conventional OLS method for detection of glaucoma progression and estimation of rates of change over time.

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270° SELECTIVE LASER TRABECULOPLASTY IN PSEUDOEXFOLIATIVE AND PRIMARY OPEN ANGLE GLAUCOMA: A PROSPECTIVE CLINICAL TRIAL

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Background: The purpose of this study was to compare the pressure lowering potential of the 270° selective laser trabeculoplasty (SLT) in patients with pseudoexfoliation (PXF) and primary open angle glaucoma (POAG) with minimum follow-up time of 6 months.

Methods: The study was a single-center, prospective, nonrandomized, interventional case series. All patients were examined, treated and followed-up by one ophthalmologist. The patients received 270° SLT-treatment of 75 nonoverlapping pulses on trabecular meshwork. The patient's medication of glaucoma was not changed within whole time of study. The mean amount of glaucoma medication in PXF-group was 1.63 ± 1.22 and in POAG-group 1.72 ± 1.32 ($p = 0.777$).

RESULTS: 66 eyes of 42 patients were treated, 30 eyes in PXF-group and 36 eyes in POAG-group. The SLT-treatment of 66 eyes showed 20% decrease of mean intraocular pressure (IOP) from 23.71 ± 4.53 mmHg to 19.02 ± 4.46 mmHg ($p = 0.000$). The mean IOP drop in the PXF-group was 19% from 22.03 ± 3.95 to 17.80 ± 3.58 mmHg ($p = 0.000$) and in POAG-group comparably 20% from 25.11 ± 4.55 mmHg to 20.03 ± 4.90 ($p = 0.000$). Outcome was defined successful, when IOP was decreased $\geq 20\%$ (definition 1) or ≥ 3 mmHg (definition 2) from baseline and no further need for laser- or incisional surgery and the number of glaucoma medication was the same or less than preoperative. According to definition 1 the over-all success rate was 50% in PXF-group (15 eyes of 30) and 61% in POAG-group (23 eyes of 36); according to definition 2 the success rates were 80% in PXF-group (24 eyes of 30) and 83% in POAG-group (30 eyes of 36). Postoperative inflammatory reaction, cells and flare, was scanty in both groups. There were no intraoperative complications due to SLT.

Conclusion: 270° SLT procedure seems to be a useful glaucoma treatment in both POAG- and PXF-patients.

CHANGES OF INTRAOCULAR PRESSURE AFTER INTRAVITREAL INJECTION OF BEVACIZUMAB (AVASTIN)

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Background: Intravitreal bevacizumab injections have become a widespread treatment for neovascular AMD. Several case reports and a recent study of 101 eyes have described intra-ocular pressure (IOP) elevation after repeated injections. We wanted to study a large group of patients treated in our retina clinic and evaluate the incidence and possible risk factors for IOP elevation after repeated intravitreal bevacizumab injections in neovascular age-related macular degeneration (AMD) patients.

Methods: We reviewed the charts of 203 consecutive patients treated in our retina clinic with intravitreal bevacizumab for AMD. Data collected for each patient included: IOP before the initiation of treatment, before each subsequent injection and at the end of follow up; number of injections; length of follow up and the presence of glaucoma before treatment. Patients with preexisting uncontrolled glaucoma were excluded. Sustained IOP elevation was defined as above 21 mmHg for more than 30 days.

Results: Sustained IOP elevation was observed in 29 of 235(12%) treated eyes. Twenty two eyes required medications to control IOP. At the time of diagnosis, average IOP was 25 mmHg (range 22-36). There was no statistical difference in post-injection IOP elevation between patients with or without preexisting glaucoma. There was no correlation between IOP at the end of follow up or at the time of IOP elevation and: pre-injection IOP; length of follow up and number of injections. The only statistically significant difference was the mean interval between injections: 2.45 months in patients without and 1.9 months in patients with sustained IOP elevation.

Conclusion: AMD patients undergoing repeated intravitreal bevacizumab injections, especially when frequent, are at an increased risk of sustained IOP elevation. Regular IOP measurements and IOP-lowering treatment in patients with persistent elevation are recommended.

THE TRABECTOME. CLINICAL RESULTS AND GLAUCOMA SUBGROUP ANALYSIS

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Background and Purpose: Altered outflow-resistance in the juxtacanalicular trabecular meshwork is responsible for an increased intraocular pressure (IOP) in open angle glaucomas. The Trabectome is a new, minimal invasive surgical option to selectively remove this trabecular meshwork under gonioscopic control.

Methods: Prospective case study. 120 eyes of 115 patients with primary or secondary open angle glaucoma were included. Intra- and postoperative complications were documented, the efficacy of the Trabectome was investigated analysing postoperative IOPs and the number of topical medications needed to reach sufficient IOP control.

Results: Mean preoperative IOP was 25 ± 6 mmHg under mean 2.1 medications. Intraoperatively, trabecular meshwork was removed for 90-120° using the Trabectome. Almost all patients showed mild intraoperative reflux-bleeding from the collector channels in the posterior wall of Schlemm's canal. On postoperative day one, mean IOP dropped to 13 ± 6 mmHg. After a mean follow-up of 313 days, IOP was decreased to a mean of 17 ± 2 mmHg. Mean number of medications was reduced to $n = 1.5$. Subgroup analysis revealed best pressure lowering effect for PEX, Pigmentary glaucoma and Steroid-induced glaucoma (mean -37%), most efficient reduction of topical medications was seen in normal tension glaucoma patients (-58%). No serious intra- or postoperative complications were observed.

Conclusion: The Trabectome is a promising new option in non-filtering glaucoma surgery. Access to the anterior chamber is minimally invasive via a 1.7mm clear-cornea tunnel, the conjunctiva is not altered. Indication for surgery needs to be assessed individually. A larger number of patients and longer follow-up data are necessary to further elucidate the value of this new method in glaucoma angle surgery.

THE CONTRIBUTION OF RETINAL VASCULATURE TO SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY RETINAL NERVE FIBER LAYER SCANS IN NORMAL AND GLAUCOMA EYES

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Background: Measurement of the parapapillary retinal nerve fiber layer (RNFL) provides important information for evaluating the optic nerve in glaucomatous neuropathy. Spectral Domain Optical Coherence Tomography (SD-OCT) is one of several non-invasive scanning technologies often used to assess the RNFL *in vivo*. Assessment of the RNFL thickness is based on B-scans acquired using a 12 degree circular scan path centered on the optic nerve. Current analysis includes TSNIT plots along with average global and sectorial data that are compared to a normative database. However, an accurate analysis of the RNFL requires consideration of ocular biometry, scan path distance from the rim margin and accounting for non-neuronal tissue. The purpose of this study was to investigate the contribution of retinal vasculature to RNFL measures in both normal and glaucomatous eyes using custom scans in non-human primates.

Methods: Cross sectional data from 47 normal rhesus monkeys along with longitudinal data from 5 animals with unilateral experimental glaucoma were used for data analysis. Raster and radial scans centered on the optic nerve were acquired using the Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany). The raw image files were exported for analysis using custom MATLAB (The Mathworks, Inc., Natwick, MA) programs. Prior to analysis, images for each animal were rescaled to 1:1 μm based on transverse scaling computed using ocular biometry measures (IOL Master, Carl Zeiss Meditec Inc., Dublin, CA) and a three surface schematic eye. The neural canal opening (NCO) was identified using the radial scans, and custom B-scans 550 μm from the NCO were interpolated from the raster scans. Retinal vessels were identified by the underlying shadows, and subtracted from the global RNFL measures.

Results: In non-glaucomatous eyes, the average RNFL thickness, after vessel compensation, for scans 550 μm from the NCO measured $111.9 \pm 9.1 \mu\text{m}$. Retinal vasculature accounted for $9.4 \pm 1.3\%$ of the global RNFL thickness ($123 \pm 9.3 \mu\text{m}$). For animals followed longitudinally, the percentage vascular contribution to the RNFL increased with decreasing RNFL thickness ($R^2 = 0.58$, $p < 0.01$). However, the overall vessel thickness contribution to the RNFL decreased with increasing disease severity ($R^2 = 0.21$, $p < 0.01$). There was no significant relationship between RNFL thickness and vessel thickness contribution in the non-glaucomatous eyes ($R^2 = 0.02$, $p = 0.18$).

Conclusions: The retinal vasculature within the RNFL accounts for a large proportion of the RNFL thickness measures in both normal and glaucomatous eyes. With disease progression, although the proportion of retinal vasculature increases, the overall thickness contribution decreases. The decrease in vessel thickness contribution reflects 1) vessels falling outside the RNFL segmentation, and 2) a decrease in vessel caliber with disease progression.

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THE INTRAOCULAR PRESSURE-REDUCING EFFECT OF ORAL PARACETAMOL – A PILOT STUDY

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Background: Several studies have confirmed the ability of cannabinoids to reduce intraocular pressure (IOP). Experimental data recently unequivocally demonstrated that the analgesic effect of paracetamol is due to its indirect action on cannabinoid CB₁ receptors. The question then arises as to whether paracetamol can reduce IOP via its effect on intraocular cannabinoid receptors.

Methods: A two-week, prospective, randomized, controlled, single centre, parallel group pilot study was carried out to determine the efficacy and safety of orally administered paracetamol 1g every 6 hours in adult patients with primary or secondary open angle glaucoma as compared to topical levobunolol 0.5% twice a day. Patient well-being was closely monitored throughout the study and focused on hepatic safety in accordance with the Drug Induced Liver Injury (DILI) Network Criteria.

Results: Eighteen adult patients were enrolled in the study, nine in the topical levobunolol group and nine in the oral paracetamol group. In the levobunolol group the mean IOP reduction at day 7 was 7.5 mmHg ($p < 0.008$) and at day 14 was 9.1 mmHg ($p < 0.005$) from a mean IOP baseline of 29.6 mmHg. The corresponding figures for the paracetamol group were 8.8 mmHg ($p < 0.0004$) at day 7 and 6.5 mmHg ($p < 0.004$) at day 14 from a mean IOP baseline of 29.4 mmHg. A mean IOP reduction of 20% or more from baseline was achieved in 78% of patients in the levobunolol group compared with 63% of patients in the paracetamol group at week 2 of the study. Both study regimens were well tolerated. No serious treatment-related adverse events were reported in either of the two treatment groups. Liver function tests, systolic/diastolic blood pressures and heart rates remained unchanged during the two weeks of the study in both groups.

Conclusion: The results of this study suggest that paracetamol taken orally, 1 g every 6 hours, reduces IOP in patients with open angle glaucoma and/or angle recession glaucoma in a comparable way to a topical beta-adrenergic receptor antagonist.

TEMPORAL RELATIONSHIPS OF CLINICAL SIGNS OF GLAUCOMATOUS NEUROPATHY

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Background: The clinical signs of glaucomatous neuropathy include 1) losses in visual sensitivity (localized or diffuse), 2) increased cupping of the optic nerve head (ONH) with a thinning of the neuroretinal rim, and 3) localized or diffuse loss in circumpapillary retinal nerve fiber layer (RNFL) thickness. However, the clinical signs do not occur simultaneously and it is important to define the temporal relationships for these features of the pathology of glaucoma.

Methods: Rhesus monkeys with unilateral experimental glaucoma were followed by subjective and objective measurements over the course of induced optic neuropathy. Visual fields were obtained by behavioural methods using standard automated perimetry (SAP). Spectral domain optical coherence tomography (SD OCT) using the Spectralis HRA+OCT (Heidelberg Engineering), was used for scanning the optic nerve head (ONH) and the circumpapillary retinal nerve fiber layer (RNFL). The SD OCT raw image files were exported for analysis using custom MATLAB programs to 1) rescale the images to a 1:1 aspect ratio using transverse scaling based on each animal's ocular biometry, 2) acquire circumpapillary RNFL thickness and area data from interpolated raster scans after removal of blood vessels, and 3) derive ONH cup volume parameters from contour maps interpolated from radial scans centered on the ONH and referenced to the surface of the retina or to the level of the neural canal opening (NCO). In order to present the data from these different measurements on a common scale, the data were converted to Z-scores based on standard deviation (SD) units derived from repeated measures of each animal's control eye.

Results: Preliminary data have been collected for two monkeys, each followed for about 8 months after their intraocular pressures (IOP) were elevated. For both subjects, clinically significant ($p < .05$) ONH cupping and global thinning of the RNFL had occurred within 1 month of IOP elevation, while significant mean deviation (MD) loss of visual sensitivity did not occur until 4 - 6 months. The significance of ONH cupping and RNFL thinning progressed rapidly, with differences exceeding 10 SD units within 2 - 4 months, while the visual field losses did not exceed 4 SD units at the end of 8 months of experimental glaucoma. The different temporal relationships for the clinical signs of glaucomatous neuropathy are partially explained by differences in the precision of objective and subjective measurements. The coefficients of variation (CV) for the repeated measurements of the control eye were much smaller for the objective measurements (1-2% for RNFL thickness, 2-8% for cup volume below the NCO) compared to a CV of 22-30% for SAP measurements.

Conclusions: Quantitative assessments of the clinical signs of glaucoma that are caused by biomechanical stresses and neuronal losses demonstrated different time-courses of progression which, in part, reflects differences in precision of subjective and objective measures. Further analyses are required to determine whether there are also neuronal components underlying the different temporal relationships.

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