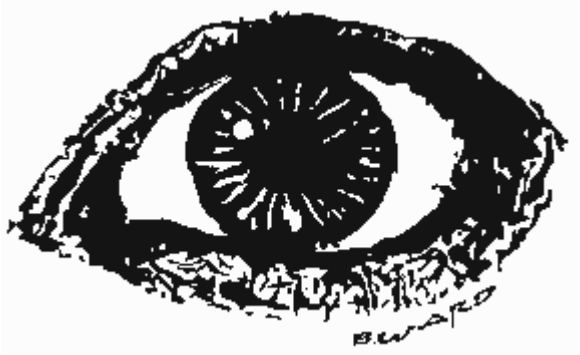

RESIDENT/FELLOW
RESEARCH DAY

May 19, 2006

DEPARTMENT OF OPHTHALMOLOGY
AND VISUAL SCIENCES

UNIVERSITY OF IOWA
ROY J. AND LUCILLE A. CARVER
COLLEGE OF MEDICINE

UNIVERSITY OF IOWA
HOSPITALS & CLINICS

IOWA CITY, IOWA

Braley Auditorium
01136 Lower Level
Pomerantz Family Pavilion
8:00 AM – 5:00 PM

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IOWA CITY, IOWA

RESIDENT/FELLOW RESEARCH DAY - 2006

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OPHTHALMOLOGY RESIDENT/FELLOW RESEARCH DAY
SCHEDULE OF EVENTS

Friday, May 19, 2006

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OPHTHALMOLOGY RESIDENT/FELLOW RESEARCH DAY
SCHEDULE OF EVENTS

Friday, May 19, 2006

Presented at Morning Rounds

Manuscripts submitted for publication (excused from presenting)

Recurrence of Amblyopia following Occlusion Therapy

Rahul Bhola, MD,
Ronald V. Keech, MD, Pamela Kutschke, CO, Wanda Pfeifer, COMT, William E. Scott, MD, sponsors

Purpose: To determine the stability of visual acuity following a standardized occlusion regimen in children with strabismic and/or anisometropic amblyopia.

Methods: We performed a retrospective chart review of all patients treated by occlusion therapy for strabismic and/or anisometropic amblyopia at our institution over a 34-year period. Of the 1621 patients identified in our database, 449 patients met the eligibility criteria and were included in this study. Patients having at least 2 logMAR level improvements in visual acuity by optotypes or a change from unmaintained to maintained fixation preference during the course of occlusion therapy were included. A recurrence of amblyopia was defined as two or more logMAR levels of visual acuity reduction or reversal of fixation preference within one year after a decrease or cessation of occlusion therapy.

Results: Of 653 occlusion trials 179 (27%) resulted in recurrence of amblyopia. The recurrence was found to be inversely correlated with patient age. There was no statistically significant association between the recurrence of amblyopia and the visual acuity of the amblyopic eye.

Conclusion: There is a clinically important risk of amblyopia recurrence when occlusion therapy is decreased before the age of 10 years. The risk of recurrence is inversely correlated with age ($p<0.0001$).

Long-term Outcomes of Strabismus Surgery in Thyroid Ophthalmopathy

Erin O'Malley, M.D.
Pam Kutschke, CO, Ronald Keech, M.D. Richard Olson, M.D., sponsors

Purpose: Thyroid ophthalmopathy is one of the most common causes of adult strabismus. This restrictive strabismus results from inflammatory infiltration and fibrosis of the extraocular muscles, most commonly the inferior and medial rectus. Although some patients achieve functional benefit from non-surgical modalities such as prisms, often surgical intervention is necessary. This study will examine the long-term functional and motor outcomes of extraocular muscle surgery in patients with strabismus secondary to thyroid dysfunction.

Methods: We have identified 181 patients with strabismus secondary to thyroid dysfunction treated at the University of Iowa Hospitals and Clinics. We performed a retrospective chart review of all thyroid patients with strabismus and identified 127 who had surgery as part of their treatment. We are studying the type and number of strabismus surgeries performed over the course of follow-up as well as the long-term functional and motor outcomes.

Results/Conclusions: Pending.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Clinical Characterization and Blepharoptosis Surgery Outcomes in Hispanic New Mexicans With Oculopharyngeal Muscular Dystrophy

Richard C. Allen, MD, PhD
Jeffrey A. Nerad, MD and Keith D. Carter, MD, sponsors

Purpose: To clinically characterize blepharoptosis in Hispanic New Mexicans with oculopharyngeal muscular dystrophy (OPMD) and to examine eyelid surgery outcomes.

Methods: A retrospective noncomparative case series and retrospective, nonrandomized, comparative interventional case series was performed on 86 patients with OPMD.

Review of medical records was performed to obtain the following: preoperative levator function (LF), pre and postoperative margin reflex distance (MRD) and palpebral fissure height (PF), patient age and gender, type of eyelid surgery, and dates of surgery.

Results: Preoperative measurements between the right and left eye were symmetrical with respect to MRD (-0.40 +/- 1.34 mm OD, -0.38 +/- 1.49 mm OS), PF (4.80 +/- 1.50 mm OD, 4.64 +/- 1.71 mm OS), and LF (9.2 +/- 2.9 mm OD, 9.3 +/- 2.9 mm OS) by paired t-tests (all $p>0.2$). There were correlations between age and MRD ($r=-0.75$, $p<0.001$), age and PF ($r=-0.45$,$p=0.001$), and age and LF (-0.32, $p=0.02$). There was no difference detected between males and females with respect to age, MRD, PF, and LF ($p>0.39$). 83 of 86 patients underwent eyelid surgery. As initial surgery, 15 underwent blepharoplasty, 17 levator advancement, and 51 frontalis suspension. 93.3% of blepharoplasty patients, 47.1% levator advancement patients, and 7.84% undergoing frontalis suspension went onto additional surgery for recurrent ptosis (rates differed, $p<0.001$). There was no statistical difference in time to re-operation [4.9 +/- 4.0 years for levator advancement, 9.5 +/- 3.3 years for frontalis suspension, and 8.8 +/- 6.4 years for blepharoplasty ($p>0.08$)]. Post-operative change for PF was 0.33 +/- 1.83 mm OD and 1.1 +/- 0.86 mm OS for levator advancement and 2.63 +/- 1.34 mm OD and 2.68 +/- 1.47 mm OS for frontalis suspension ($p=0.03$, OD and $p=0.004$, OS).

Conclusion: OPMD in Hispanic New Mexicans is a symmetrical, progressive disease that affects males and females similarly. Frontalis suspension correction of ptosis is a more effective primary surgery with respect to upper lid elevation, need for re-operation, and time to re-operation in this patient population.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

The D658G Variation In The WDR36 Gene Is Not Associated With Open Angle Glaucoma In A Large Cohort Of Patients From Iowa.

J.H. Fingert, MD, PhD
W.L.M. Alward, MD, Y.H. Kwon, MD, PhD, S.P. Shankar, PhD, P.A. Moore, B.R. Roos, V.C. Sheffield, MD, PhD
E.M. Stone, MD, PhD, sponsor

Purpose: An open angle glaucoma locus (GLC1G) on chromosome 5q22 was recently identified and the WDR36 gene was reported to be the glaucoma gene in this locus. One mutation in the WDR36 gene (D658G) was identified in glaucoma patients at a significantly higher frequency than in control subjects. We attempted to confirm this finding by screening a large population of primary open angle glaucoma (POAG) patients and control subjects from Iowa for WDR36 mutations.

Methods: A total of 393 POAG patients and 365 control subjects from Iowa were screened for mutations in the WDR36 gene. Single strand conformation polymorphism (SSCP) analysis and automated DNA sequencing were used to detect mutations in the 4 exons of WDR36 that contain previously identified mutations (exons 8, 11, 13, and 17).

Results: The D658G mutation was identified in 5 of 393 POAG patients (1.3%) and in 5 of 365 control subjects (1.4%) in our Iowa cohort (p=1). Other WDR36 variations were also detected in patients and controls at the same frequency.

Conclusion: Mutations in the WDR36 gene (including D658G) were not associated with POAG in our study of a large cohort of patients and controls from Iowa.

Complement Factor H Polymorphism Tyr402His and Cuticular Drusen

Michael A. Grassi, MD
James C. Folk, MD; Todd E. Scheetz, PhD; Nicole C. Phillips, BA; Edwin M. Stone, MD, PhD.

Purpose: Previous studies have demonstrated that the Tyr402His polymorphism in the complement factor H (CFH) gene is associated with an approximately 3-fold increased risk for age-related macular degeneration (AMD). AMD subtypes evaluated to date have not revealed a specific phenotypic correlation with this variant. Due to the high prevalence of the histidine allele in patients with membranoproliferative glomerulonephritis type II, we hypothesized that the histidine variant might be associated with the fundoscopically similar cuticular drusen phenotype.

Methods: 50 individuals with cuticular drusen were ascertained at the University of Iowa and graded based on a threshold image by two retina specialists. DNA samples were genotyped using a PCR based NIaIII restriction digest assay. The frequency of the histidine allele at position 402 of the CFH gene was determined. In addition, 700 individuals with AMD and 252 controls were genotyped at this locus. Fisher's exact test was used to analyze the significance of both genotype and allele frequency between these groups.

Results: The histidine allele was present in 70% (0.70+/-0.05) of the cuticular cohort ; 55% (0.55+/-0.01) of the AMD cases; and 34% (0.34+/-0.02) of controls. The association between cuticular drusen and the histidine allele was highly significant [p=0.0034; OR 2.0 (1.3-3.1) vs. AMD cases; OR 4.54 (2.85-7.24) vs. controls]. Genotype distribution between the three groups was similarly significant [p=0.0004].

Conclusion: Distribution of the Tyr402His polymorphism in the Iowa AMD cohort supports previously published findings. The cuticular drusen phenotype is highly associated with the histidine allele at position 402 of the CFH gene and is over four times more prevalent in individuals with cuticular drusen as compared to controls. To our knowledge the cuticular drusen phenotype is the first AMD subtype to be definitively associated with the CFH Tyr402His polymorphism.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Photographic and Angiographic Changes After Iodine-125 Brachytherapy for Choroidal Melanoma: Findings From the Collaborative Ocular Melanoma Study (COMS): COMS Report

The Collaborative Ocular Melanoma Study Group*

*Prepared by: H. Culver Boldt, MD[1], B. Michele Melia, ScM[2], **Judy Liu, M.D**.[1], Sandra M. Reynolds[3], MA. Lists of members of the COMS Group can be found in references.

[1]University of Iowa Hospitals and Clinics, Department of Ophthalmology, Iowa City, IA; [2]Jaeb Center for Health Research, Tampa, FL; [3]Department of Ophthalmology, Johns Hopkins University, Baltimore, MD.

Objective: (1) To describe the protocol used for grading features of radiation retinopathy from fundus photographs and fluorescein angiograms of patients enrolled in the Collaborative Ocular Melanoma Study (COMS); (2) to characterize the natural history of photographic and angiographic changes in the posterior pole of eyes with choroidal melanoma treated with iodine 125 brachytherapy in the COMS, and (3) to investigate baseline patient, tumor, and treatment characteristics associated with posterior pole changes.

Design: Observational case series within a randomized, multi-center clinical trial.

Participants: Six hundred fifty patients who were assigned to and received iodine 125 brachytherapy in the Collaborative Ocular Melanoma Study randomized trial for medium-sized tumors were included in this report. All patients had choroidal melanoma of at least 2.5 mm but no more than 10.0 mm in apical height, and no more than 16.0 mm in largest basal dimension.

Methods: Color fundus photographs and fluorescein angiograms were taken at baseline (prior to treatment), and 2, 5, and 8 years later and graded according to a standard protocol on 30 features.

Results: The most common features overall in the macular field were microaneurysms, macular edema, capillary non-perfusion, telangiectasias, retinal hemorrhages, and hard exudates. In the peripapillary field, optic disc hyperfluorescence, microaneurysms, telegiectasias, vascular sheathing, capillary non-perfusion, and retinal hemorrhages were most common. The least common findings were peripapillary preretinal hemorrhage, peripapillary subretinal hemorrhage, macular preretinal hemorrhage, and peripapillary vitreous hemorrhage (observed in 2% or less of all follow-up visits). Macular and peripapillary vascular sheathing, macular microaneurysms, and foveal RPE atrophy increased with each successive follow-up examination. The only feature that was most common at baseline compared with follow-up was foveal retinal detachment. Mean number of features per subject increased with time from 2.1 features at baseline to 7.8 features at the 8 year follow-up examination. Prevalence of neovascularization of the disc (indicating proliferative retinopathy) ranged from 0.3% at baseline to 5.2% at year 5 follow-up. Prevalence of features indicative of optic neuropathy ranged from <1% at baseline to 26% at year 5 follow-up. The presence of diabetes at baseline was associated with more prevalent and more severe features of retinopathy and neuropathy at both baseline and follow-up examinations until the year 2 follow-up, while hypertension was

not. Patients with tumors that were close to the fovea and nerve had a greater number of and more severe findings in the posterior pole at follow-up than patients with tumors farther away from these structures.

Conclusions: Features of retinopathy and neuropathy were often already present at baseline, the most common of which was optic nerve hyperfluorescence (26.7%). The most common feature overall was macular microaneurisms (90.7%) at the year 8 follow-up. Mean number of features increased with time. The maximum prevalence of radiation retinopathy was at least 5.2% and the maximum prevalence of optic neuropathy was at least 26% in this series at the year 5 follow-up. Presence of diabetes, tumor distance closer to the optic nerve and foveola, and greater radiation dose to these structures was associated with more prevalent and more severe features. Patient age, gender, smoking status, presence of hypertension and tumor size and shape were not generally associated with number and severity of posterior pole findings.

Automatic Cup-To-Disc Segmentation From Stereo Color Fundus Photographs Using Pixel Feature Classification Algorithm

Young H. Kwon, MD, PhD, Michael D. Abramoff MD, PhD.,

Wallace LM Alward, MD, Emily C Greenlee, MD, Lesya M Shuba, MD, PhD, Chan Y Kim, MD, PhD, and John H. Fingert MD, PhD

Purpose: To evaluate a novel computer image processing algorithm for cup-to-disc (C/D) segmentation from stereo color fundus photographs

Methods: 101 stereo color optic disc photographs taken by a fixed stereo-base fundus camera (Nidek 3Dx) from 70 consecutive patients from the Univ of Iowa Glaucoma Service were studied. Cases were chosen based on image quality of the photographs. Each set of stereoscopic photographs was digitized, viewed stereoscopically using hand-held stereoscope, and computer-aided planimetry was performed to delineate disc and cup margins by 3 glaucoma faculty experts and 3 glaucoma fellows in a masked fashion. The *reference standard* for cup and disc boundaries was determined from the 3 glaucoma faculty drawings using a "majority win" strategy for each pixel. Linear C/D ratio (square root of area cup-to-disc ratio, or LCDR) was calculated from the each of the optic discs based on the reference standard. Categorized pixels and LCDR from the fellows were compared to the reference standard.

Feature vectors were calculated for each pixel in the image, including color-opponency at multiple scales, Gabor and Gaussian wavelet filters, and mathematically simulated simple and complex cells (derived from primate visual cortex). Optimal set of features was selected by calculating the accuracy of various combination of features against the reference standard using 51 randomly selected stereo images as training, and the remaining 50 as testing set. Using the optimal features, the algorithm then classified all pixels in each stereo image into cup, rim, or background (outside disc margin). LCDR was calculated from each classified image and was compared to that of the reference standard.

Results: The LCDR correlations between the 3 fellows and reference standard were 0.74 (95% CI: 0.67-0.84), 0.84 (CI: 0.77-0.89), and 0.90 (CI: 0.85-0.93). The LCDR correlation between the pixel feature classification algorithm and reference standard was 0.92 (CI: 0.88-0.94). In general, there was good agreement of the C/D boundaries determined by the algorithm and reference standard.

Conclusions: The performance of the disc segmentation and LCDR calculation of the algorithm was comparable to glaucoma fellows. Pixel feature classification of stereo optic disc photographs can be optimized to detect disc and cup margin without human input, and holds promise as a clinical tool for *objective*, *quantitative* optic disc analysis.

Diurnal Fluctuation and Concordance of Intraocular Pressure in Glaucoma Suspects and Normal Tension Glaucoma Patients

L.M. Shuba, MD, PhD
M.K. Maley, MD, M.B. Zimmerman, PhD,
A.P. Doan, MD, PhD, R.B. Dinn, MD,
E.C. Greenlee, MD, W.L.M. Alward, MD, Y.H. Kwon, MD, PhD,
sponsors

Purpose: The one-eye drug trial for intraocular pressure (IOP) lowering medications assumes the concordant fluctuation of the IOP between the fellow eyes. Our objective was to determine the diurnal variation and concordance of IOP in glaucoma suspects (GS) and normal tension glaucoma (NTG) patients.

Methods: A retrospective review was performed on GS and NTG patients with diurnal curves performed at the University of Iowa. No subject had IOP greater than 21 mmHg. We defined GS patients as having suspicious optic nerves (ON) with normal visual fields (VF), and NTG patients as having glaucomatous ON with associated VF loss. Subjects were excluded with: glaucoma surgery, trauma, use of anti-glaucoma or steroid medications, uveitis or secondary glaucoma. The IOPs were measured using Goldmann applanation tonometry at 10:00, 13:00, 16:00, 19:00, 22:00 and 07:00. The linear association of OD and OS IOP over the 6 time points was estimated using the average Pearson correlation coefficient (r). Linear mixed model analysis for repeated measures, with Eye and Time as the within subject fixed effects, was used to test if the mean change in the IOP over time differs between OD and OS. For the analysis of concordance, the diurnal period was divided into seven time intervals of 3, 6, 9, 12, 15, 18 and 21 hours and the *absolute difference in change* in IOP between fellow eyes and probability that it was within 3 mm Hg were calculated.

Results: Sixty eight GS subjects (29 males and 39 females; age 56.8±18.5 (SD), range 12-86 years) and 95 NTG subjects (32 males and 63 females; age 62.2±14.9 (SD), range 27-89 years) were included in the study. In GS subjects, the pooled mean IOP was 14.9 mmHg with the inter-eye SD of 1.4 (95% CI: 1.4, 1.6) and coefficient of variation (CV) of 9.7% (95% CI: 9.1, 10.4). In NTG subjects, the pooled mean IOP was 15.5 mmHg with the inter-eye SD of 1.3 (95% CI: 1.2, 1.4) and CV 8.3% (95% CI: 7.8, 8.8). The average correlation of OD and OS IOP over the six time points was r=0.8 (95% CI: 0.7, 0.8) for GS, and r=0.8 (95% CI: 0.8, 0.8) for NTG subjects. The mean absolute difference in IOP change between OD and OS over the six time intervals ranged between 1.4 and 1.9 mmHg for GS, and 1.3 and 1.5 mmHg for NTG subjects. The probability that this difference was within 3 mmHg ranged between 87% and 94% for GS, and 86% and 93% for NTG subjects.

Conclusions: We observed high correlation and similarity of the mean IOP diurnal curves of fellow eyes in GS and NTG subjects. The current results show that the diurnal variation in IOP between the fellow eyes is mostly concordant within the limits of measurement variability in GS and NTG patients. Assuming no cross-over effect, we

conclude that the one-eye therapeutic trial should help determine the effectiveness of a topical agent in approximately 90% of the time in GS and NTG patients.

Support: Residents and Fellows Research Program, Research to Prevent Blindness, Lew Wasserman Award, McLaughlin Fellowship.

Horner's Syndrome Without Anisocoria: How It Can Happen

S. Randhawa, MD
R.H. Kardon, MD, PhD, sponsor

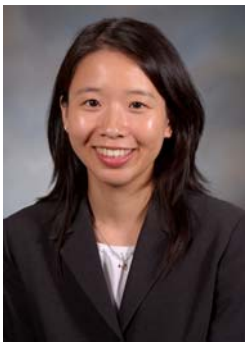
Introduction: Four patients with sympathetic palsy and no miosis of the pupil demonstrated unequivocal pharmacologic evidence of Horner's syndrome. 3 patients initially had miosis but recovered, and 1 patient had a larger pupil in the eye with Horner's.

Methods: Four patients were referred for a diagnosis of Horner's syndrome. In 3 patients (pituitary apoplexy, carotid dissection, and carotid cavernous occlusion), the miosis and anisocoria resolved over time. The fourth patient presented with a *larger* pupil in the eye with ptosis and pain following cluster headaches. All patients underwent computerized pupillography (to demonstrate "dilation lag") and pupil photography before and after pharmacologic testing (10% cocaine) to confirm a Horner's syndrome. After resolution of miosis in three patients, they underwent repeat cocaine testing and pupillography; in addition, adrenergic supersensitivity testing (at a separate visit) was performed in all patients.

Results: Three patients in whom miosis resolved had unequivocally positive cocaine testing at the first test and even after its resolution. The fourth patient with cluster headache, who presented with a larger pupil in the ptotic eye, also had positive cocaine testing. All four patients localized to the post-ganglionic neuron with hydroxyamphetamine. In all patients, the pupil on the side of the lesion demonstrated supersensitivity to adrenergic testing (in the absence of miosis) on a separate visit.

Conclusion: In Horner's syndrome, development of adrenergic supersensitivity may occasionally lessen/reverse the typical miosis expected in oculosympathetic paresis. This compensatory change may cause a patient with Horner's syndrome to not be diagnosed, even though there is subnormal sympathetic discharge at the dilator muscle.

The OCT Hills Are Alive: The Effect of Refractive Error on OCT Retinal Nerve Fiber Layer Analysis



Paula Wynn, MD
Randy H. Kardon, MD, PhD, sponsor

Problem: The variation in the sector location at which the major arcuate bundles of RNFL come together to enter the nerve can cause false positive results on the Stratus probability plots. This appears to be due to the maximum peak of the superior and inferior arcuate bundles being displaced toward the maculo-papillary sector in high myopes; the peaks in the TSNIT plot are spread more apart. In the case of high hyperopes, the opposite occurs; the peaks are closer together. This is easily seen if one looks at the reference TSNIT plot for normative data in the print-outs. This effect can cause one to either under or over-estimate the probability of abnormality compared to the normal TSNIT configuration.

Purpose: The location of the peak RNFL thickness for the superior and inferior arcuate bundles will be studied as a function of axial eye length and refractive error to understand how common this occurs and at what range of refractive errors, or whether it is a continuous function of eye length (refractive error). In addition, there may be some pseudophakic patients that have this phenomenon and are not suspected of it due to their corrected vision after cataract surgery.

Once we identify the frequency of the shift in RFNL peak thicknesses and possible correlation to refractive error, we will also attempt to devise mathematical methods of correcting for it, to shift the RNFL thickness in location towards a template that signifies normal eyes.

Methods: We will review the Stratus RFNL analyses conducted at the University of Iowa Department of Ophthalmology and generate a frequency distribution curve for the arcuate peak-to-peak distances measured on the TSNIT plot. We will then randomly sample patients from each part of the frequency distribution curve, and refractive error and axial eye length data will be retrospectively gathered for these subjects. Peak-to-peak distances will then be plotted against refractive error to evaluate if there is any quantitative relationship between the two variables.

Results/Conclusion: Pending.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Correlation of OCT Retinal Nerve Fiber Layer Thickness (RNFL) and Visual Threshold in Optic Nerve Hypoplasia

Reid Longmuir, MD
Randy Kardon, MD, PhD, sponsor

Purpose: To determine the structural-functional correlation between retinal nerve fiber layer thickness and optic nerve function (automated visual threshold perimetry) in adults with optic nerve hypoplasia.

Methods: 23 patients were studied with a diagnosis of optic nerve hypoplasia based on disc appearance (fundus photography) and who also had retinal nerve fiber layer (RNFL) and optic disc analysis by optical coherence tomography (OCT) as well as visual field testing (HVF n=14, GVF n=19).

Results: A significant correlation was found between RNFL thickness and disc area (correlation coefficient $R=0.51$, $p<0.001$), RNFL thickness and vertical neuroretinal rim volume ($R=0.50$, $p<0.001$), and between disc and cup area ($R=0.429$, $p=0.004$). A significant linear and non-linear relationship between RNFL and average visual field threshold was also found (linear $R=0.425$, $p=0.038$, non-linear $R=0.53$, $p=0.053$). Two eyes had significantly more visual field loss than would be predicted from their RNFL thickness. Qualitatively, there was a very good correlation between nerve fiber layer sectoral analysis and the area of the corresponding visual field defect.

Conclusions: Optic nerve hypoplasia shows significant relationships between disc morphology as measured by optical coherence tomography and RNFL thickness. Segmentally thinned RNFL from developmental causes correlates well with the location of visual field defect.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Segmental Inner Retinal Layer Analysis of Macular OCT Scan Detects Damage in Unilateral Optic Neuropathy

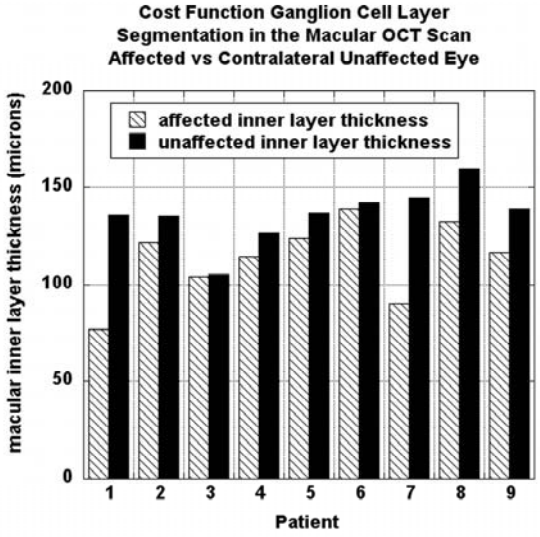
V.A. Shah, MD
M. Haeker, PhD., M.D. Abramoff, PhD, M. Sonka, PhD,
R. Kardon, MD, PhD, sponsors

Purpose: 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. Layer segmentation of the macular scan by optical coherence tomography (OCT) may help to better define ganglion cell (RGC) loss.

Methods: Nine patients with chronic unilateral optic neuropathy were tested by Stratus OCT (circular and macular fast scans) and analyzed by both Stratus algorithm and by a novel segmentation image analysis technique to determine layers of the retina. Boundaries were automatically determined using a graph-based cost function approach that utilized edge/regional image information and a priori-determined constraints. Layer analysis was also performed along the vertical meridian scan at the macula in four patients with altitudinal visual field loss.

Results: Significant differences between the affected and unaffected eyes were found with the cost function layer OCT macular analysis (p=0.013) but not with total retinal thickness (p=0.111). Significant altitudinal differences in macular inner layer thickness (p=0.046) were found in eyes with corresponding field loss. The most significantly affected layer corresponded to the expected location of the RGC. There was significant linear correlation between the Stratus derived retinal layers (retinal nerve fiber layer and total retinal thickness) and our new segmenting algorithm.

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



Comparative Effects of Switching from Latanoprost to Travoprost: A Retrospective Study Population Study

Edward Hu, MD, PhD,
Robert Shaw, MPH, PharmD,
Thomas Oetting, MD, Emily Greenlee, MD, sponsors

Purpose: To evaluate the effects of switching prostaglandin analogues (Latanoprost to Travoprost) in the treatment of glaucoma

Methods: This Iowa City VA medical center-based retrospective cohort study will examine the effects of switching prostaglandin analogues (Latanoprost to Travoprost). The VA administration decided to switch patients from latanoprost to travoprost for cost considerations in 2003. We believe this change was well tolerated by our patients but would like to examine this set of patients to ensure that the administrative change led to reasonable control of glaucoma and limited side effects. VA patients with at least a two year history of latanoprost use from Jan 2001 who were unilaterally switched to travoprost will be included. The following outcome measures will be analyzed: 1) intraocular pressure measurements before and after the switch of prostaglanin analogues 2) side effect profiles attributed to travaprost 3) documented intolerance to travaprost requiring discontinuation. Patient data will be censored at the termination of the study period.

Results: Pending

Conclusions: Pending

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Edwin M. Stone, MD, PhD

To be announced

Evidence Of Drusen Cores Among Patients With High-Risk Drusen in Age-Related Macular Degeneration

James M. Coombs, MD
Steve Russell, MD, sponsor

Purpose: To evaluate whether patients with bilateral, high risk drusen (HRD) from age-related macular degeneration (ARMD) demonstrate coaxial, central hyperfluorescent cores (CCHC) based upon the difference of visible (color) and fluorescein angiographic image size.

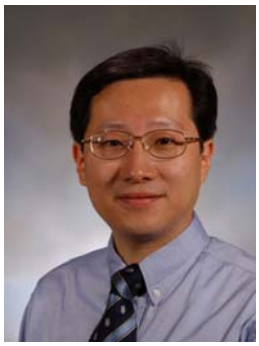
Methods: CAPT participants, enrolled with HRD associated with ARMD, underwent color fundus photography and fluorescein angiography as part of a multi-center prospective photocoagulation choroidal neovascularization risk-reduction trial. For this analysis, the green channel (RGB) color and angiographic images were scanned on a Nikon Super Coolscan 4000 at 4,000 pixels per inch^2 for both eyes at the entry and exit (4 year) visit. The scanned images were normalized and registered utilizing Adobe PhotoShop 7.0. A difference image was created by subtracting, pixel-by-pixel, the angiographic value from the green channel value. The resulting images were evaluated for the presence or absence of characteristic halo pattern of drusen substructure. Permission from the CAPT was preceded this ancillary study.

Results: One hundred two eyes from fifty one patients were evaluated for drusen cores. Fifty one (51) of 102 eyes showed evidence of at least one druse possessing coaxial, central hyperflourescent cores (CCHC). Forty five (45) eyes did not show CCHC . Six eyes could not be evaluated properly due to poor contrast of photographic images. Of the 45 participants for which bilateral difference images were available, concordance was 91%.

Conclusion: This is the first study to show that patients with age related macular degeneration with high risk drusen show clinically detectable drusen sub-structure. Further studies are underway to determine whether CCHCs are present over the duration of the study and/or have correlation with the genotype and development of choroidal neovascular membrane formation.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Laser Capture Microdissection and Microarray Analysis of the Human Retinal Ganglion Cell Layer



Chan Y. Kim, MD, PhD
Markus H. Kuehn, PhD, Wallace L. M. Alward, MD, Edwin M. Stone, MD, PhD, and Young H. Kwon, MD, PhD, sponsors

Purpose: Cell death in the retinal ganglion cell layer (GCL) is a prominent feature in glaucoma. The purpose of this study was to identify and catalogue the genes whose expression is restricted to the GCL in the human retina.

Methods: Laser capture microdissection (LCM) technology was used to isolate tissue from the perimacular region of three normal human donor retinae. The tissue was preserved within four hours postmortem. Material was isolated from the (1) retinal ganglion cell layer and (2) the inner and outer nuclear layers of the same retina. RNA was extracted, amplified, and the gene expression profiles of both fractions were determined using Affymetrix Hu133Plus 2.0 GeneChips. Data were evaluated by two-class paired statistical analysis to identify those genes whose expression is considerably substantially more prevalent in the GCL when compared to the outer retinal layers.

Results: The results show that mRNA levels of previously described ganglion cell markers were highly enriched in the isolated GCL fraction. Examples include neurofilament genes (NEFH, NEF3 or NEFL), the Brn3b transcription factor (POU4F2) and the beta 3 subunit of the nicotinic cholinergic receptor (CHRNB3). In contrast, transcripts for genes associated with phototransduction (PDE6A, RDH12 or OPN1SW), photoreceptor development (NRL) or interphotoreceptor matrix constituents (IMPG1) were nearly absent from the GCL fraction. Approximately 30 genes were identified whose expression in the human retina appears to be limited to the GCL.

Conclusion: We have successfully used LCM technology to generate gene expression profiles of highly enriched GCL as well as outer retinal fractions of the normal human retina. The results will serve as a resource in the development of ganglion cell specific markers or transfection vectors and the identification of candidate genes for hereditary forms of glaucoma.

A comparison of the Femtosecond Laser (Intralase®) versus Manual Microkeratome (Moria ALTK®) in Dissection of Donor Tissue for Posterior Lamellar Keratoplasty. Initial Studies in Eye Bank Eyes

Y. Jin Jones, MD
K .Goins, MD, N. Syed, MD, G. Locke, MBA, G. Schmidt,
C. Reed, RN, PhD,
J.E. Sutphin, MD, sponsors

Purpose: To compare and evaluate the safety and efficacy of the Intralase® and the Moria ALTK® in creating pre-cut endothelial keratoplasty donor tissue

Methods: Ten fresh human cadaver corneoscleral buttons were used in creating endostromal lenticles. Five were created using Intralase®, while the other five were created using the Moria ALTK® microkeratome. The donor buttons were secured onto the Moria ALTK® artificial anterior chamber infused with Optisol GS. After ultrasonic corneal pachymetry, the Intralas® was used to make the posterior corneal lamellar interface (lamellar cut) and trephine (side) cut with the goal of 150 microns of residual posterior stroma after keratectomy. The laser parameters were energy 7.4 ± 0.1 uJ (lamellar cut) and 5.5 ± 0.1 uJ (side cut), spot size 10 uM, firing rate 30 kHz, trephination diameter 9.0 to 9.5, depth 400 microns, and spiral pattern. The Moria ALTK® 350-micron head was used. Lamellar dissection depth was dependent on surgeon hand speed and preoperative corneal thickness. For preoperative pachymetry measurements less than 500 microns, Intralase® and Moria ALTK® parameters were altered to prevent damage to the endothelium (i.e. reduction in attempted lamellar depth). After the lamellar keratectomy, ultrasonic pachymetry was repeated on the stromal bed and endothelial disc thickness was determined. Endothelial cell count, observation of cell morphology and measurement of disc pachymetry were done before and after the lamellar keratectomy as well as after 48 hours to evaluate the stability of the endostromal lenticle. The cut surfaces were examined by scanning electron microscopy to examine the surface architecture.

Results: The resultant change in total donor corneal pachymetry, endothelial disc pachymetry, and endothelial cell count/morphology were evaluated. Both the femtosecond laser and Moria ALTK systems produced safe and effective means of creating endostromal buttons for posterior lamellar keratoplasty. Scanning electron microscopy evaluation of the stromal surface of the endothelial discs revealed that the femtosecond laser keratectomy interface is not as smooth as that seen with the Moria ALTK.

Conclusions: The preliminary studies show that the Intralase® and the Moria ALTK® are safe and effective in creating pre-cut endothelial keratoplasty donor tissue. The Intralase may have an advantage over the Moria ALTK by creating an endothelial disc of more uniform thickness and a more rough surface, which may reduce hyperopia shift and improve disc adherence postoperatively.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Evaluation Of Changes in Intraocular Pressure and Incidence of Glaucoma Following Endothelial Keratoplasty

C. Robinson, MD
S. Pramanik, MD, K.M. Goins, MD, J.E. Sutphin, MD, W.L. Alward, MD, E.C. Greenlee, MD, Y.H. Kwon, MD, PhD, sponsors

Purpose: To report the changes in intraocular pressure (IOP) and incidence of new or worsened ocular hypertension (OHTN) or glaucoma following endothelial keratoplasty. Secondary measures included BSCVA and central corneal pachymetry (CCT).

Methods: A retrospective, consecutive review of all patients undergoing DLEK and DSEK between 12/03 and 9/05, with a minimum of 3 months of postoperative follow-up was done. Baseline data included age, gender, BSCVA, preoperative IOP, preoperative CCT, preoperative diagnosis of OHTN or glaucoma, preoperative IOP medication regimen and preoperative glaucoma surgical history. IOP and other clinical outcome measures were collected at 1, 3, 6 and approximately 12 months postoperatively. All IOP measurements were collected with a Tono-pen. The development or worsening of OHTN or glaucoma was defined as the need for medical or surgical intervention for the treatment of elevated IOP.

Results: 57 eyes of 57 consecutive patients were evaluated with a mean age of 70.0±10.4 years. 34 (59.6%) were female and the average follow-up time was 8.0±4.0 months with a range of 3 to 16 months. Preoperatively, the mean BSCVA was 0.70±0.47 LogMAR (20/100), mean IOP was 15.7±4.0 mmHg, and mean CCT was 736.1±113.7µm. 13 (23%) of patients carried a diagnosis of OHTN or glaucoma: 9 required preoperative glaucoma medication and 6 had prior filtering surgery. There were 39 endothelial keratoplasties (38 DLEK, 1 DSEK) and 18 combined phacoemulsification cataract surgery with IOL and DLEK. The mean IOP difference from preoperative measurements was -0.6±5.1 mmHg at 1 month, 1.9±6.6 mmHg at 3 months, 1.2±7.5 mmHg at 6 months and -0.3±5.3 mmHg at 1 year. The mean CCT was 573.8±124.1 µm, 559.9±122.4 µm, 578.0±115.0 µm, and 587.4±143.0 µm at 1, 3, 6 and 12 months. The mean BSCVA was 0.55±0.29 LogMAR (20/70) at 1 month, 0.41±0.22 LogMAR (20/50) at 3 months, 0.34±0.19 LogMAR (20/44) at 6 months and 0.29±0.15 LogMAR (20/40) at 12 months. 16 (28%) patients developed or worsened pre-existing OHTN or glaucoma at the time of last followup; 7 out of 13 patients with a pre-existing diagnosis worsened and 9 out of 44 patients without a pre-existing diagnosis required treatment. Only 12 (23%) patients required an increased number of glaucoma medications from baseline or surgical intervention at the time of last follow-up.

Conclusions: Although endothelial keratoplasty results in a minimal change in IOP there is a moderate risk of the development of OHTN or glaucoma and worsening of pre-existing disease. This risk appears to be lower than the published risk for penetrating keratoplasty.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness and the University of Iowa Department of Ophthalmology Resident Research Fund

One-Year Results After Combined Phacoemulsification and Deep Lamellar Endothelial Keratoplasty (Phaco/DLEK)

Sudeep Pramanik, MD, MBA
Christopher Robinson, MD,
John Sutphin, MD, Kenneth Goins, MD, sponsors

Purpose: To report best spectacle corrected visual acuity (BSCVA) results one year after combined Phaco/DLEK for cataract and Fuchs' dystrophy. Secondary outcomes include postoperative spherical equivalent, endothelial cell counts, keratometric astigmatism, and wavefront aberrations.

Methods: A retrospective, consecutive review of patients with visually significant cataract and Fuchs dystrophy who underwent combined Phaco/DLEK at the University of Iowa and had at least 12 months of postoperative follow-up was performed. Baseline data included age, BSCVA, preoperative keratometric astigmatism, wavefront aberrations, target refraction, and donor endothelial cell counts. Outcome measures were recorded 1, 3, 6, and 12 months postoperatively.

Results: Among the 12 eyes of 12 patients, the mean age at surgery was 70.58 (+/-8.34) years. Preoperatively, the mean BSCVA was 20/70 (range 20/30-20/250), mean keratometric astigmatism was 1.55 D (+/-1.61), mean total wavefront aberration (RMS) was 3.27μm (+/-4.57), mean lower order aberration (LOA) was 2.40 μm (+/-3.11) and mean higher order aberration (HOA) was 1.92 μm (+/-3.41). The mean target spherical equivalent was –0.62 D (+/-0.75) and the mean baseline donor endothelial cell density was 3067 c/mm^2 (+/-389). One year postoperatively, the mean BSCVA was 20/40 (range 20/20-20/100), mean spherical equivalent was 0.25 D (+/-1.47), mean keratometric astigmatism was 1.19 D (+/-0.72), mean RMS was 1.13 μm (+/-0.69), mean LOA was 0.82 μm (+/-0.41), and mean HOA was 0.62 μm (+/-0.7). Endothelial cell counts at one year were 2235 c/mm^2 (+/-410).

Conclusions: Combined Phaco/DLEK offers good visual rehabilitation for patients with Fuchs and cataract. It results in minimal keratometric astigmatism and reduced wavefront aberration with acceptable endothelial levels one year after surgery.

Modified Levator Recession and Muellerectomy for Lid Retraction Secondary to Thyroid Ophthalmopathy

Erin Shriver, M.D.
Keith Carter, M.D., sponsor

Purpose: Eyelid retraction is the most common sign of thyroid ophthalmopathy. Lid retraction results when the horizontal tarsal ligamentous band and vertical eyelid retractors cannot lengthen to accommodate increasing exophthalmos. Upper eyelid retraction has been associated with a startled appearance, ocular discomfort, and keratopathy. Non-surgical treatments have been tried with minimal success. There is no clear agreement on the best surgical lengthening technique for upper eyelid retraction. One popular technique is the levator recession and muellerectomy. This surgery is often successful at restoring the natural lid length, however the upper lid crease is often sacrificed in the process. We are (Instead of Keith Carter is) currently performing a modified version of levator recession and muellerectomy aimed at lengthening the lid while preserving the upper lid crease. The purpose of this study is to assess if the modified levator recession and muellerectomy successfully restores the upper lid crease.

Methods: We will be assessing the prominence of the upper lid crease after modified levator advancement and muellerectomy. The extent of scleral show, palpebral fissure height, margin-reflex distance, and upper eyelid crease (will be determined) from photographs taken before and after the patient's surgery (and review of the patient's chart). The prominence of the upper lid crease will be scored in both pre and post-operative photos.

Results and Conclusions: Pending.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Surgical Planning for Prism Adaptation Non-Responders

Andrew CG Steffensmeier, MD
Richard J Olson, MD, and Pam Kutschke, CO

Background: The Prism Adaptations Study Research Group concluded in a multi-center, prospective, randomized trial in 1990 that prism adaptation results in improved outcomes when surgical correction was directed towards the larger deviation measured following prism adaptation. Several groups have subsequently published data in favor of prism adaptation. To date, no known large series has been published to characterize patients who did not respond to prism adaptation.

Purpose: To evaluate patients treated who failed to respond to prism adaptation preoperatively to identify features of this group of patients that we can use to improve surgical outcomes.

Methods: Retrospective chart review will be used to identify characteristics common to non-responders.

Preliminary Results: The following results are reported from the records of all patients with acquired esotropia who were treated with prism adaptation at the University Of Iowa Department Of Ophthalmology including those in the original prism adaptation study cohort as well as consecutive patients with acquired esotropia treated with prism adaptation having surgery by September of 2003. Of 509 patients listed as prism adapted, 160 were non-responders. Of these, 98 (61%) had deviations greater than 8 prism diopters at either near or distance postoperatively(vs. 73% in the prism adaptation study). 16 (10% of total non-responders) had re-operations. Overall, 254(49.9%) of the 509 patients undergoing prism adaptation had postoperative deviations of greater than 8 prism diopters (vs. 83% in prism adaptation study), and 8.8% of them had secondary surgery to correct the remaining deviation.

Conclusion: The preliminary findings show unexpectedly poor outcomes, with lower success than those originally reported in the Prism Adaptation Study. This may reflect inclusion of patients not originally eligible for the Prism Adaptation Study.

Future plans include detailed analysis of the charts of non-responders with attention to variables including age; gender; initial deviation; course of adaptation; surgical correction made; post operative deviation, fusion testing, visual acuity; and secondary surgeries; and concurrent medical and ophthalmic findings.

Reference: 1. Prism Adaptation Study Research Group, Efficacy of prism adaptation in the surgical management of acquired esotropia. Arch Ophthalmol. 1990 Sep;108(9):1248-56.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Vitreous Sample Analysis After Bevacizumab (Avastin) Injection

James G. Howard, MD
Stephen R. Russell, MD, Gregory S. Hageman, PhD, sponsors

Purpose: Bevacizumab (Avastin) is a humanized murine monoclonal antibody that binds all VEGF-A isoforms. It is FDA approved for the treatment of metastatic colorectal cancer and is widely used as an off label intravitreal agent to treat neovascular age-related macular degeneration (AMD). The pharmacokinetics of bevacizumab following intravitreal injection are not well understood. Whether bevacizumab remains intact or is cleaved into smaller bioactive fragments that are more easily diffusible is not known. A pharmacologic derivative of bevicizumab, ranibizumab (Lucentis) is a VEGF inhibitor that was developed to treat neovascular AMD and is in the final stages of the FDA approval process. Prior studies of retinal permeability suggest that ranibizumab (48 kD) effectively penetrates the retina whereas larger molecules such as HER2 (148 kD) exhibit much poorer penetration. We hypothesize that cleavage of bevacizumab (149 kD) to its Fab fragment enhances its clinical efficacy and can be demonstrated within six weeks of injection.

Methods: Six pseudophakic patients who have been treated with bevacizumab (Avastin) for the first time within the previous six weeks and who are in need of an additional intravitreal injection will undergo a vitreous tap of 0.1 cc at the same time as injection. The samples will be subjected to Western blot analysis to determine whether the bevacizumab molecule has remained intact or if it has been proteolyzed into smaller fragments.

Results and conclusions are pending.

Treatment of Visual Loss in Glaucoma and Ischemia with Neurotrophic Growth Factors

Sinisa Grozdanic DVM, Iowa State University
Don Sakaguchi Ph.D., Erin Lavik Ph.D., Markus Kuehn Ph.D., Young Kwon M.D. Ph.D, Randy Kardon M.D. Ph.D

Purpose: This study seeks to show that slow release of growth factors injected into the vitreous will reduce the progression of damage and in some cases, reverse visual loss in rats with induced glaucoma/ischemia, in dogs with spontaneous glaucoma and in dogs with acutely induced ischemia from raised intraocular pressure.

Methods: Rats and dogs with acute ocular ischemia and spontaneous glaucoma were divided into groups treated with growth factors or placebo and the effects on visual function and structure were assessed by pupillography and electroretinography over time to determine if slowly released growth factors in the vitreous improved visual outcome, compared to placebo

Results: Our preliminary results in rats with induced glaucoma and retinal ischemia demonstrated a therapeutic effect of growth factor treatment. We found that the intrinsically increased production of ciliary neurotrophic factor (CNTF) was temporally correlated with recovering visual function (pupil light reflex and electroretinogram) in rats affected with glaucoma or retinal ischemia. This effect was further improved by exogenous supplementation with glial derived neurotrophic factor (GDNF) and brain derived neurotrophic factor (BDNF).

Conclusions: The therapeutic effect of exogenous growth factor therapy could be achieved only if: a) exogenously supplemented growth factor was not already up-regulated as a response to the disease process; b) if receptors for the supplemented growth factors were present in the diseased retina. In order to translate the potential of this new form of treatment to human glaucoma and other forms of ocular ischemia, including diabetes, ongoing studies are extending our findings to dog glaucoma, which is likely to have more relevance toward treatment in humans, a necessary step preceding human treatment trials.

Supported by a Merit Review Grant from the Veterans Administration Rehabilitation Division

The Effect of Viewing 3-D Ophthalmology Movies on Ophthalmic Education when compared to traditional 2-D Viewing

J.C. Friedrichs, MD
M. Abramoff, PhD, and A.G. Lee, MD, sponsors

Purpose: Understanding the three dimensional (3-D) nature of ocular pathology and of ophthalmic surgery is essential for training in ophthalmology for residents and medical students. Ophthalmologists almost exclusively use stereo-slitlamps, -fundoscopes, -angiograms, and –surgical microscopes. Nevertheless, during training, students and residents are only rarely exposed to 3-D viewing. This makes it much more difficult to understand the three-dimensional relationships of structures such as the optic nerve head in glaucoma, ocular tumors, cataract, cornea, macular edema, retinal detachments, thickened and thinned retina, retinal scars and retinal blood vessels. It also steepens the learning curve for ophthalmic surgery, because in almost all surgery, depth vision is required. This is especially the case for the surgical procedures commonly performed by residents, including cataract surgery, strabismus surgery and glaucoma surgery.
The reasons for this lack of exposure are mostly due to technological limitations: because of the nature of optics, additional sets of binocular oculars on any diagnostic imaging device such as a surgical microscope means substantially less light is available for the primary set of oculars that is used by the clinician - leading to unacceptable darkening of the image. In addition, recording and viewing of stereo movies has until recently been both prohibitively difficult because of the synchronization required between two cameras, the low contrast by stereo cameras, and it is prohibitively expensive. This is not withstanding the fact that almost all ophthalmic images are acquired in stereo format – so far there has just not been a way to conveniently view these images in a group. New digital stereo acquisition and display technology that have recently become available hold the promise to improve this situation.

As faculty, we have recently started to use high resolution, flicker-free stereo videoprojection (DepthQ, Lightspeed Inc, CA) with LCD shutter glasses for research and for clinical discussions during rounds for collaborative viewing. We have developed the software to display these images and image sequences in various ways. We have also successfully acquired digital stereo movies of cataract, glaucoma , retinal and strabismus surgery.

Though it may be expected that viewing stereo movies of surgical procedures may better prepare residents for wet-lab and real surgical procedures, and that viewing of stereo images of diverse pathology may help medical students and residents better understand those pathologies, no evidence is currently available in the literature.

We propose to utilize the LCD shutter glasses technology to enable all students and residents to view stereo images of ocular pathology, angiography and stereo movies of surgical procedures. We propose to then evaluate the effect of the addition of stereo viewing on the education and understanding of students, residents and fellows.

Methods: We will use an established stereo viewing technology, using a flickerfree stereo high quality video projector and LCD shutter glasses, to allow medical students and residents to see ophthalmic images and surgical movies in stereo. This is especially

attractive for stereo viewing of images and surgical movies during rounds and clinical conferences.

We propose to then evaluate the effect of the addition of stereo viewing on the understanding of students, residents and fellows by using a questionnaire. The questionnaire will be administered to all participants prior to the educational intervention and after. All participating medical students and residents will receive the standard format presentation followed by the 3-D presentation. After each presentation, the questionnaire will be completed. The questionnaire includes statements about perception and understanding of the three dimensional nature of the eye. After each statement, the learner will indicate her or his level of agreement by means of a 5-point Likert scale, with possible responses ranging from "completely agree" to "completely disagree.

The data will then be collected and analyzed by statistical analysis to see if a difference exists between traditional image viewing and 3-D image viewing when used in the teaching of ophthalmic surgical techniques, pathology and anatomy.

Hypothesis: We expect that medical students will better understand ocular pathology and surgical procedures by three-dimensional viewing. We also expect that ophthalmology residents and even fellows will be better prepared for wet-lab surgical training and hands-on surgery by viewing stereo movies of surgical procedures.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness and the University of Iowa Residents Research Fund

Concordance of Diurnal Intraocular Pressure Between Fellow Eyes in Primary Open Angle Glaucoma

Robert B. Dinn, MD
M. Bridget Zimmerman, PhD; Lesya M. Shuba MD, PhD; Andrew P. Doan, MD, PhD; Michael K. Maley, MD; Emily C. Greenlee, MD; Wallace L. M. Alward, MD; Young H. Kwon, MD, PhD, sponsors

Support: Resident and Fellow Research Program, Research to Prevent Blindness

Purpose: This study examined the concordance of diurnal intraocular pressure (IOP) between fellow eyes in primary open-angle glaucoma (POAG) in order to better assess the validity of the one-eye drug trial for intraocular pressure lowering medications.

Method: An IRB approved retrospective chart review of diurnal curves in patients with POAG was performed on 291 subjects identified through the Glaucoma Service computer database. Subjects were excluded from the study if they previously underwent any intraocular surgical procedure (laser or incisional), used asymmetric glaucoma medications, had a previously diagnosed vascular eye disease (e.g. vein occlusion), or had incomplete diurnal curves. Patients were included only if 1) at least one IOP measurement was greater than 21 mmHg in one eye prior to or during the diurnal curve, 2) optic nerve cupping (as determined by a glaucoma faculty member) was present, and 3) visual field deficits consistent with glaucoma (as determined by a glaucoma faculty member) were present. Measurements were obtained at 10:00, 13:00, 16:00, 19:00, 22:00, and 7:00 using a Goldmann applanation tonometer.

Results: A total of 93 of the 291 subjects met criteria for inclusion. 37 were on no glaucoma medications (Group A). 56 were on symmetric glaucoma drops (Group B). The average IOP (in mmHg) ranged from 21.4 (7am) to 17.9 (10pm) in Group A and 18.9 (10am) to 17.8 (10pm) in Group B. The IOP correlation (r) between eyes was 0.84 for Groups A (CI:0.78-0.88) and B (CI:0.80-0.88). The probability that the difference in change in IOP between eyes was less than 3 mmHg was 78-95% for Group A and 83-93% for Group B. The mean difference in diurnal variation of IOP between fellow eyes for all individuals ranged from 1.4-2.2 mmHg in Group A and 1.5-2.0 mmHg in Group B.

Conclusion: The diurnal variation in IOP in POAG is concordant (to within 2.2mmHg) between fellow eyes.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Internet Use Among Ophthalmology Patients: Search Modalities For Eye Information

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P.G. Duffel, MA, A.P. Doan MD, PhD,
T.A. Oetting MD, T.A. Weingeist, PhD, MD, sponsors

Purpose: The Internet provides a potentially powerful tool for patient education. Surveys of patients in other fields of medicine generally reveal that a majority of patients are now using the Internet to search for information related to their medical conditions, though this is not universally the conclusion. There has been no formal study of internet use and search modalities among ophthalmology patients in the United States. We seek to describe the use of the Internet to search for eye and health related information in this population.

Methods: Cross-sectional survey administered in ophthalmology waiting rooms of university-based health care center. Anonymous survey of at least 250 patients will be obtained.

Results: To be discovered.

Conclusions: We hypothesize that a high percentage of Midwestern ophthalmology patients use the Internet to search for information related to their eye care. We also hypothesize that the majority of these patients are likely to employ broad-based, commercial search engines to find this information. Whether or not this is true will be discovered.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Adjustment of IOL power for Ciliary Sulcus position of MA60BM Intraocular Lens

Jeff Maassen MD,
Luis C. Omphroy, MD,
Thomas A. Oetting, MS MD, sponsor

Abstract: We reviewed 726 consecutive phacoemulsification procedures over a 3 1/2 year period (07/27/97 – 12/31/00) and found 48 cases where the intraocular lens (IOL) (Alcon Acrysof MA60BM) was placed in the ciliary sulcus. We also reviewed a representative sample of IOLs placed in the capsular bag. We calculated the difference in A constant and error in spectacle spherical equivalent from predicted between the sulcus and the capsular bag IOL groups.

Method: Retrospective chart review of 48 consecutive IOLs placed in the ciliary sulcus. Thirty five cases met the inclusion criteria of visual acuity 20/40 or better. A representative control group was selected using IOLs placed in the capsular bag on the same date. We used the Holladay IOL Consultant program (http://www.docholladay.com/iolprogram.htm) to calculate the A-constant for the sulcus and bag groups.

Results: 48/729 (6.6%) of the IOLs were placed in the ciliary sulcus. The post operative spectacle deviation from the target spherical equivalent for the MA60BM IOL was –0.22 +/- 0.55D (SD) and –0.76 +/- 0.81D (SD) when placed in the capsular bag and ciliary sulcus respectively (p=0.0020). This difference of 0.54 diopters at the spectacle plane would roughly correspond to 0.8 diopters at the IOL plane. With our data using the Holliday consultant the A-constant for bag placement was 118.6 and the A-constant for sulcus placement was 0.9 diopters less at 117.7.

Conclusion: When placing the Acrysof MA60BM IOL in the ciliary sulcus, the surgeon should lower the IOL power by 0.8 to 0.9 diopters in order to compensate for the more anterior placement of the sulcus based IOL.

Support: Supported in part by an unrestricted grant from Research to Prevent Blindness.

Clinically Detectable Drusen Substructure in Fibulin-5 Associated Age-Related Macular Degeneration

Chetankumar B. Patel, MD
Edwin M. Stone, MD, PhD, Patricia G. Duffel, RPh, MA, Stephen R. Russell, MD, sponsors

Purpose: To evaluate whether drusen from fibulin-5-associated age-related macular degeneration eyes demonstrate clinical drusen substructure based upon the difference between the visible and fluorescein angiographic size.

Design: Retrospective case series.

Methods: Of the seven patients known to have age-related macular degeneration associated with missense mutations in the fibulin-5 gene, five had undergone color fundus photography and fluorescein angiography on a prior visit. The green channel (RGB) color and angiographic film-based images were scanned on a Nikon Super Coolscan 4000 at 4,000 pixels per inch^2. The scanned images were normalized and registered utilizing Adobe PhotoShop 7.0. A difference image was created by subtracting, pixel-by-pixel, the angiographic value from the green channel value. The resulting images were evaluated for the presence or absence of characteristic halo pattern of drusen substructure. In addition, drusen and hyperfluorescent core sizes were measured by overlaying the Zeiss 30° fundus images with the Age Related Eye Disease Study (AREDS) template.

Results: All five patients displayed coaxial central hyperfluorescent cores (CCHC) associated with a subset of drusen ranging in size from 63 to 180 µm. CCHC were not evident in any drusen larger than 180 µm. CCHC were found in several fibulin-5 phenotypic backgrounds such as scattered small macular drusen, near-confluent macular drusen, and associated with occult choroidal neovascularization.

Conclusion: Patients with missense mutations in the fibulin-5 gene harbor drusen with clinically evident substructure. Further evaluation of this phenotype in additional patients with fibulin-associated-age-related macular degeneration will be necessary to clarify the pathophysiologic mechanisms, natural history, and prognostic significance of this feature. **Brief Summary Statement:** Patients with missense mutations in the fibulin-5 gene harbor drusen with clinically evident substructure. The nature and prognostic significance of coaxial central hyperfluorescent cores (CCHC) associated with fibulin-5-associated AMD will require further study.

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Anesthesia Monitoring by Registered Nurses During Cataract Surgery: Assessment of Need for Intraoperative Anesthesia Consultation

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Purpose: The purpose of this study is to assess the frequency and risk factors for intraoperative anesthesia consultation when performing cataract surgery monitored by registered nurses.

Setting: Iowa City Veterans Affairs Medical Center, Iowa City, Iowa.

Methods: Retrospective review of 270 cataract surgeries performed under local anesthesia from April 1, 2002 to April 1, 2003.

Results: The ASA (American Society of Anesthesiologists) classification of each patient was determined: 1 patient was classified as ASA 1. 150 patients were classified as ASA 2. 119 patients were classified as ASA 3. Anesthesiology was consulted 24 times. 19 consultations involved patients who were ASA 3, while 5 consultations involved patients who were ASA 2 ($p < 0.001$). In most cases, (23/24) anesthesia provided a consultation (e.g. increase oxygen flow rate, clarification of EKG, start IV, equipment repair) and left to allow the nurses to continue to monitor the patient. In only 1 case, (ASA 3) the anesthesia service converted the case to monitored anesthesia care and relieved the nurse to monitor the patient.

Conclusions: In our study, monitoring of routine cataract surgery by registered nurses is associated with a low rate of intraoperative anesthesia consultation. Most consultations resulted in little intervention. ASA classification appears predictive of need for intraoperative anesthesia consultation.

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