
# RESIDENT/FELLOW RESEARCH DAY

**May 16, 2003**

**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 – 4:00 PM**

# RESIDENT/FELLOW RESEARCH DAY - 2003

## DEPARTMENT OF OPHTHALMOLOGY

### PROFESSOR AND HEAD
Thomas A. Weingeist, Ph.D., M.D.

### PROFESSORS EMERITUS
G. Frank Judisch, M.D.
Sohan S. Hayreh, M.D., Ph.D., D.Sc.
Hansjoerg E. Kolder, M.D., Ph.D.
Karl C. Ossoinig, M.D.
Edward S. Perkins, M.D., Ph.D.
William E. Scott, M.D.
H. Stanley Thompson, M.D

### ASSOCIATE EMERITUS
E. Lee Allen

### PROFESSORS
Wallace L. M. Alward, M.D.
Keith D. Carter, M.D.
James C. Folk, M.D.
Gregory S. Hageman, Ph.D.
Ronald V. Keech, M.D.
Jeffrey A. Nerad, M.D.
Edwin M. Stone, M.D., Ph.D.
John E. Sutphin, Jr., M.D.
Michael Wall, M.D.

### ASSOCIATE PROFESSORS
H. Culver Boldt, M.D.
Karen M. Gehrs, M.D.
A. Timothy Johnson, M.D., Ph.D.
Randy H. Kardon, M.D., Ph.D.
Young H. Kwon, M.D., Ph.D.
Andrew G. Lee, M.D.
Thomas A. Oetting, M.D.
Richard J. Olson, M.D.
Stephen R. Russell, M.D.
Mark E. Wilkinson, O.D.

### ASSISTANT PROFESSORS
Hilary A. Beaver, M.D.
Terry A. Braun, Ph.D.
Sara L. Butterworth, O.D.
Ayad A. Farjo, M.D.
Brian R. Kirschling, O.D.
Robert F. Mullins, Ph.D.
Christine W. Sindt, O.D.
Nasreen A. Syed, M.D.

### ASSOCIATE
Todd E. Scheetz, Ph.D.

### ORTHOPTISTS
Pam J. Kutschke, C.O.
Wanda L. Pfeifer, OC(C), C.O.M.T.

### ASSISTANT TO THE CHAIR
Larry W. McGranahan, C.H.E.

### MANAGER, RESEARCH AND DEVELOPMENT
Paul R. Montague, C.R.A.

### FACULTY RESEARCH ADVISOR
Randy H. Kardon, M.D., Ph.D.

# RESIDENT/FELLOW RESEARCH DAY - 2003

## FELLOWS

### CORNEA
Rahul Pandit,, M.D.

### GLAUCOMA
Emily C. Greenlee, M.D.

### NEURO-OPHTHALMOLOGY
Steven L. Goldin, M.D.

### OCULOPLASTICS
Alice Song, M.D.

### PEDIATRIC OPHTHALMOLOGY
David B. Petersen, M.D.
Scott A. Larson, M.D.

### VITREORETINAL DISEASE
Esther M. Bowie, M.D.
Denise L. Kayser, M.D.
Karin R. Sletten, M.D.
Matthew H. Wood, M.D.

# RESIDENT/FELLOW RESEARCH DAY - 2003

## THIRD-YEAR RESIDENTS

Michael A. Grassi, M.D.
Michael G. Hunt, M.D.
John W. Kitchens, M.D.
Susan J. Quick, M.D.
Russell B. Warner, M.D.

## SECOND-YEAR RESIDENTS

William J. Dupps, M.D., Ph.D.
John F. Fingert, M.D., Ph.D.
Erin L. Holloman, M.D.
Jennifer J. Lee, M.D.
Judy C. Liu, M.D.

## FIRST-YEAR RESIDENTS

Michael V. Boland, M.D., Ph.D.
Andrew P. Doan, M.D., Ph.D.
Lynn E. Fraterrigo, M.D.
James G. Howard, M.D.
Sudeep Pramanik, M.D.

## ORTHOPTIC STUDENT

Sara Downes

# RESIDENT/FELLOW RESEARCH DAY
# SCHEDULE OF EVENTS

**Friday, May 16, 2003**



**10:00** **BREAK**

# RESIDENT/FELLOW RESEARCH DAY
# SCHEDULE OF EVENTS

**Friday, May 16, 2003**



**12:00** **LUNCH**
Blodi Conference Room
11131 PFP



**2:30** **BREAK**

# RESIDENT/FELLOW RESEARCH DAY
# SCHEDULE OF EVENTS

**Friday, May 16, 2003**



## Manuscripts Submitted

# Improved Estimation of Nerve Fiber Layer Thickness in Patients With Optic Neuropathy Using Optical Coherence Tomography

Michael V. Boland, MD, PhD
Dr. Randy H. Kardon, sponsor

**Background**: It has been observed in some patients with severe visual field loss from glaucoma and other optic neuropathies that the OCT estimate of the retinal nerve fiber layer is thicker than expected. In these patients, the correlation between retinal nerve fiber layer thickness and visual field sensitivity is poor. For example, patients with longstanding no light perception may have retinal nerve fiber layers that are similar in thickness to seeing patients with mild to moderate damage. Patients with acute optic neuropathy followed over time show thinning of the retinal nerve fiber layer, followed by some degree of re-thickening. One explanation for these findings is that the retinal nerve fiber layer thickness as measured by OCT may not always correlate with the number of axons and may be measuring gliotic replacement of the nerve fibers.

**Purpose**: To determine whether there are features of retinal optical coherence tomography (OCT) that can be used to differentiate a healthy nerve fiber layer from the damaged and paradoxically thickened ones described above. Once identified, such features will be used to improve the estimate of retinal nerve fiber layer thickness in patients with neuropathy.

**Methods**: Patients with known, unilateral optic neuropathy and available OCT of the retina will be studied. The pattern of reflectivity of the retina in the diseased eye will be compared to the same region in the normal, fellow eye of each patient. This comparison will be done using graphical and statistical methods with the goal of finding features of the reflectivity that discriminate between the two eyes. Once such features have been found, similar analysis will be performed in patients with two normal eyes in order to confirm specificity of the approach. Similar analysis will also be performed in a small number of patients with acute optic neuropathy that have been followed over time with OCT. Data from these patients will allow for analysis of the nerve fiber layer at the time of injury, at the time of maximal thinning, and during re-thickening. Again, features of nerve fiber reflectivity will be analyzed as to their ability to distinguish healthy from diseased nerve fiber layer. Finally, the above analyses will be used to estimate the "true" nerve fiber layer thickness in patients with optic neuropathy. The revised thickness estimate will then be correlated with available visual field results.

## Evaluation of Intravitreal Triamcinolone Acetonide in Macular Edema Secondary to Nonischemic Central Retinal Vein Occulsion

Esther M. Bowie, MD
Drs. James C. Folk and Stephen R. Russell, sponsors

**Purpose**: To determine if intravitreal injection of triamcinolone acetonide is safe and effective in treating macular edema in nonischemic central retinal vein occulsion (CRVO).

**Methods**: Thirty patients (15 subjects and 15 controls) with a diagnosis of nonischemic central retinal vein occulsion will be identified. Entry criteria will include nonischemic central retinal vein occulsion with macular edema involving the fovea for at least 2 months. The best corrected visual acuity will be 20/50 or worse with no explanation apparent for decreased visual acuity except central retinal vein occulsion. Exclusion criteria include a diagnosis of glaucoma/ glaucoma suspect, ocular hypertension, or a history of elevated intraocular presure following steroid use. Patients with diabetes mellitus or concurrent active ocular diseases associated with macular edema will be excluded. The patients will be randomly assigned to receive intravitreal triamcinolone acetonide 4 mg or sham injection. A complete eye examination, macular photocoagulation study (MPS) refraction, fluorescein angiography, ocular coherence tomography (OCT) and visual field will be obtained on the initial visit. Patients will be evaluated on the day of enrollment, day one, four to six weeks, three months and six months post injection. On day 1 post injection the patients will have their visual acuity, intraocular pressure and slit lamp evaluation. At all subsequent visits they will have visual acuity measurement with MPS refraction, intraocular pressure measurement, pupillary, slit lamp, fundus examination and ocular coherence tomography. In addition at the final visit (6 months) they will have fluorescein angiography and visual field. Repeat injections will be offered to patients if macular edema returns following initial injection. Final outcome measures visual acuity, extent of leakage on fluorescein angiography and retinal thickness on OCT will be evaluated by masked observers.

**Results**: Not yet available.

**Conclusion**: Not yet available.

## Comparison of Wavefront Analysis using the Tracey Visual Function Analyzer and VISX Wavescan

Rahul T. Pandit, MD,
Dr. John E. Sutphin and Ayad A. Farjo, sponsors

**Purpose**: To compare results of wavefront analysis using the Tracey Visual Function Analyzer (Tracey VFA), based on a ray-tracing method, and the VISX Wavescan, based on Hartmann-Shack aberrometry, in a clinical practice setting.

**Methods**: Wavefront analysis was performed on 262 eyes of 135 consecutive patients with various ocular diagnoses using both the Tracey VFA and the VISX Wavescan. Scans were performed on undilated eyes and on automatic settings under identical mesopic conditions. Data obtained from both machines were compared looking for differences in refraction and individual and total amounts of zernike aberrations as measured by root mean square (RMS).

**Results**: Eight of 262 eyes (3%) were excluded because data could not be obtained from the VISX Wavescan. Of the remaining 254 exams on each machine, 109 (43%) were performed on male patients, 145 (57%) on female patients, 133 (52%) were performed on the right eye, and 121 (48%) on the left eye. There was no statistically significant difference between scan diameter as measured on the Tracey VFA and pupil diameter as measured on the VISX Wavescan ($p<0.0001$). The Intraclass Correlation Coefficient (ICC), measuring strength of agreement between the two machines, was statistically significant ($p<0.05$) for refraction (sphere, cylinder, and axis expressed as a dioptric power matrix), spherical equivalent, total RMS, and lower order aberrations Z2-2, Z20, and Z22 (astigmatism, defocus, astigmatism). Though statistically significant, agreement was low (ICC <0.5) for three of 22 higher order aberrations, Z3-3, Z3-1, and Z33 (trefoil, coma, trefoil). No statistically significant agreement was found for the remaining 19 of 22 sequential higher order aberrations assessed by each machine. The mean intermachine differences in spherical equivalent and refraction (sphere, cylinder, and axis expressed as a dioptric power matrix) were statistically significant, with the Tracey VFA measuring more myopic values than the VISX Wavescan. The mean intermachine difference in total RMS was 0.666 (95% confidence interval 0.328 to 1.011), with the Tracey VFA resulting in lower values.

**Conclusion**: Statistically significant agreement between measurements on the Tracey VFA and VISX Wavescan was found for refraction, total RMS, lower order aberrations, and only three of 22 higher order aberrations. Agreement was high, however, only for refraction, total RMS, and lower order aberrations. The Tracey VFA measured more myopic refractions and lower RMS values than the VISX Wavescan. This data carries important implications for the interchangeability of different wavefront methods and machines, as well as the application of wavefront analysis in customized refractive procedures.

## Central Retinal Vein Occlusion With Cilioretinal Artery Occlusion

Lynn Fraterrigo, MD.
Dr. Sohan Singh Hayreh, sponsor

**Background**: Central retinal vein occlusion (CRVO) is often associated with cilioretinal artery occlusion. In cases of non-ischemic CRVO, cilioretinal artery occlusion may be the primary cause of severe visual loss. Case reports/series describing this clinical entity are rare. No large study has been performed which defines the clinical presentation and prognosis of CRVO with cilioretinal artery occlusion.

**Methods**: We will perform a detailed review of the medical record of all patients with the diagnosis of CRVO with cilioretinal artery occlusion that presented to the vascular clinic at University of Iowa Hospitals and Clinics between 1974 and 2002. Co-morbidities including systemic medications, systemic disease and tobacco use will be investigated. Demographic data will be recorded, including age and sex of affected patients. These data will be compared to available population controls. The frequency of presenting clinical symptoms and signs will be determined. The area of the retina affected by cilioretinal artery occlusion will be recorded for those cases with flourescein angiograms. Collected data will be examined for prognostic value.

## The Threshold for the Detection of Strabismus

Scott A. Larson, MD
Dr. Ronald V. Keech, sponsor

**Purpose**: To identify threshold at which horizontal or vertical strabismus becomes reliably detectable by observers and determine the effects of interpupillary distance, age, gender and observer experience.

**Methods**: Six models of different gender, age, and interpupillary distance were digitally photographed in several predetermined gaze positions off axis in the horizontal and vertical planes. Standardized distance, zoom factor and lighting were used. The images were digitally altered to exactly superimpose one eye deviated and one eye aligned with the axis of the camera. The images were arranged in random order and presented to groups of lay and professional observers and their responses recorded.

**Results**: The statistically significant threshold for detecting esotropia, exotropia and hypertropia was found to be 12.5 prism diopters. Hypotropia had a higher threshold of 20 prism diopters. Observer experience and model age each had a significant effect on the ability to detect strabismus.

**Conclusions**: Our study demonstrates a unique method for assessing the significance of different types and degrees of strabismus. Our findings may be used to help patients with strabismus as they consider others' perception of their ocular misalignment. Physicians can also use this information in surgical decision making.

This study was supported in part by the University of Iowa Department of Ophthalmology Resident and Fellow Research Fund

# Photodynamic Therapy of Juxtafoveal Choroidal Neovascularization With Verteporfin in Ocular Histoplasmosis Syndrome and Idiopathic Choroidal Neovascularization: Retrospective Case Series

Judy C. Liu, MD
Drs. H. Culver Boldt and Karen Gehrs, sponsors

**Purpose**: To evaluate the safety and effect on visual acuity of photodynamic therapy (PDT) with verteporfin in patients with juxtafoveal choroidal neovascular membranes in ocular histoplasmosis syndrome (OHS) and idiopathic choroidal neovascularization.

**Methods**: Retrospective case series. The visual outcome of eight patients with OHS (6 patients) or idiopathic choroidal neovascularization (2 patients) with juxtafoveal choroidal neovascular membranes (CNVM) treated with PDT was reviewed. Mean follow-up time was 8.9 months, mean patient age was 41.3 years, and mean length of time of symptoms until presentation was 38.9 days.

**Results**: 50% of patients had improved final vision (improvement of 2 or more lines), 37.5% were stable (final vision within 1 line of initial visual acuity), and 12.5% were worse (decrease by 6 or more lines). 12.5% had a final visual acuity of 20/20 or better, 50% between 20/25-20/40, 12.5% between 20/50-20/100, and 25% between 20/125-20/200. There were no patients with final vision worse than 20/250. Patients received an average of 2.6 treatments with an average of 46.3 days between treatments. 50% of patients received retreatments. Younger age and fewer number of treatments were associated with visual improvement. No clear association between change in visual acuity was found with the following variables: length of symptoms prior to first treatment with PDT, hypertension, smoking, prior therapy, and initial lesion size.

**Conclusion**: Given the small number of subjects no statistically significant conclusions can be made. However, the results of this study compare favorably with the results of the Macular Photocoagulation Study for krypton laser photocoagulation of choroidal neovascular membranes from ocular histoplasmosis (subgroup with CNVM within 200 microns of the FAZ center). 50% of patients had improvement of 2 or more lines treated with PDT compared with 17% of those treated with krypton laser. A comparable proportion experienced no change in vision (37.5% in the PDT group vs. 42% in the krypton laser group). 12.5% in the PDT group vs. 8% in the krypton laser group experienced a greater than 6 line decrease in vision. Initial worsening in vision and eyestrain were the most commonly reported adverse effects.

## Medial and Lateral Orbital Wall Surgery for Balanced Decompression in Thyroid Eye Disease

Alice Song, Scott M. Graham, Christopher L. Brown, Alice Song, Keith D. Carter, Jeffrey A. Nerad,

**Purpose:** To examine the effect of medial and lateral wall surgery with sparing of the orbital floor on the incidence of postoperative diplopia in orbital decompression.

**Methods:** Retrospective chart review of 63 consecutive medial and lateral orbital wall surgeries (40 patients) performed between 12/96 and 5/02 for orbital decompression for thyroid ophthalmopathy.

**Results:** The average patient age was 50.9 years (range 14-83), and the mean follow-up time was 31.5 months (3-69). The female: male ratio was 36:4. Indications for surgery were compressive optic neuropathy (34 eyes), exposure keratopathy (25 eyes), and aesthetic concerns (4 eyes). Two patients had cerebrospinal fluid leaks during lateral wall surgery. These were repaired during surgery without complications. Five patients had preoperative diplopia that persisted after surgery. No patient complained of worsening of double vision. Three of the 40 patients had new-onset persisting diplopia. The mean duration of diplopia in these 3 patients was 10.2 months (range 6-16). Two patients had complete resolution of diplopia without intervention; one patient underwent eye muscle surgery with resolution of diplopia.

**Conclusions:** The diplopia rate of 7.5% is less than in other series for orbital decompression. Medial and lateral wall surgery with sparing of the orbital floor may reduce diplopia after orbital decompression surgery for thyroid ophthalmopathy.

## Outcome of Pediatric Aphakic Glaucoma

David Petersen, MD
Drs. Richard Olson and Ronald Keech, sponsors

**Purpose**: To determine the long term outcome of eyes with aphakic glaucoma following pediatric cataract extraction.

**Methods**: The records of all patients with the diagnosis of aphakic glaucoma at the University of Iowa Hospitals and Clinics were reviewed retrospectively. 124 patients with this diagnosis were identified. Of these, 59 were excluded for cataract extraction after age 10, and 19 were excluded for syndromic conditions (Lowe, Reiger, Peter, etc.), traumatic cataracts, congenital glaucoma, no documented IOP increase, or inadequate follow-up (less than one year). 46 patients were included in the study, including bilateral and unilateral aphakia, for a total of 68 eyes. Outcome measures were visual acuity, number of medication changes required over the course of the follow-up, and surgical interventions required. Average follow-up was 9.8 years (range 1.5-23.7 years).

**Results**: Visual acuity outcomes: 59% were 20/40 or better, 21% were 20/50 to 20/200, and 20% were worse than 20/200. The average maximum intraocular pressure recorded was 39 mmHg (range 26-56 mmHg). Medical intervention: 33% required 1-2 medication changes over the course of the follow-up, 34% required 3-5 medication changes, and 33% required 6-12 medication changes. These outcomes were used as a surrogate to roughly estimate the difficulty of controlling the glaucoma: 1-2 changes is easy to control, 3-5 changes is moderate difficulty, and 6-12 changes is significant difficulty. Of the 68 total eyes, 36% required surgical intervention (15% with 1 surgery, 16% with 2-3 surgeries, and 5% with 4-6 surgeries).

**Conclusions**: Based on these results, the final visual outcomes of eyes with aphakic glaucoma are comparable to those with pediatric aphakia without glaucoma. Roughly 1/3 are easy to control with medications, 1/3 are moderately difficult, and 1/3 are very difficult. Also, roughly 1/3 of the patients with aphakic glaucoma will require surgical intervention, often multiple procedures.

## The Design of Contact Lenses That Predictably Induce Spherical Aberration in Similar Quantities and Zones to Eyes That Have Undergone Myopic Photorefractive Keratectomy or Laser Epithelial Keratomileusis

Jennifer J.Y. Lee, MD
Drs. Ayad A. Farjo and Christine Sindt, sponsors

**Purpose**: To design contact lenses that predictably induce spherical aberration in similar quantities and zones to eyes that have undergone myopic photorefractive keratectomy or laser epithelial keratomileusis.

**Methods**: The material used for the contact lenses was Hioxifilcon A, which is 59% H20 and non-ionic. Contact lenses were designed with a standard base curve of 8.6mm and with a central optical zone of 6.0mm. The central power ranged from -5.00 to -8.00 in 0.5 diopter increments. A hyperopic aspheric periphery that increased proportionately to the amount of central myopic power was added to the design. The target amount of spherical aberration was determined from a pre-existing database correlating the increased amount of spherical aberration after photorefractive keratectomy or laser epithelial keratomileusis. Ten volunteers (20 eyes) underwent ray tracing and Hartmann-Shack aberrometry. The volunteers were fit with contact lenses and the ray tracing and Hartmann-Shack aberrometry scans were repeated to demonstrate the increase in spherical aberration with the contact lenses.

**Results**: The contact lenses reliably induce spherical aberration as measured by ray-tracing and Hartmann-Shack aberrometry.

**Conclusion**: We have created contact lenses that can predictably increase spherical aberration in similar levels and zones to eyes that have undergone myopic photorefractive keratectomy or laser epithelial keratomileusis. These lenses may serve as a model to investigate the effect of spherical aberration on subjective visual function.

## Identification of Cystoid Macular Edema in Patients Following Cataract Extraction Utilizing Optical Coherence Tomography

Andrew Doan, M.D., Ph.D.
Drs. Randy Kardon andThomas Oetting, sponsors

**Purpose**: The purpose of our study is to use optical coherence tomography (OCT) of the retina as a means to morphologically identify cystoid macula edema (CME) in the early post-operative period following cataract surgery. If CME is found, then OCT will be used to assess the efficacy of treatment with topical anti-inflammatory agents. Currently, the clinical identification of CME can be difficult to make until enough fluid has acummulated in the retina to significantly decrease best corrected visual acuity or be seen clinically on fundus examination. The most sensitive test for CME has been fluorescein angiography. Fluorescein angiography is not routinely used because of the injection required, the cost of the test, and the reluctance to repeat the test over time. Our hypothesis is that OCT will be a more sensitive test for detection of CME than just clinical observation and measurement of visual acuity. We also hypothesize that a decrease in critical flicker fusion frequency will help differentiate CME as the cause of suboptimal post-operative visual acuity from an optical cause (such as refractive error or corneal edema), which does not affect the critical flicker fusion frequency. In addition, it is hypothesized that the morphological quantification of CME using OCT will be useful in evaluating the course of CME over time and in response to treatment. The first goal of the study is to determine the frequency of CME using OCT of the macula at the pre-operative cataract and post operative visits (post op day 1, one week, one month, 3 months, and 6 months). The second goal of the study is to see how the extent of CME quantified by the area of fluid measured by OCT at the scan subtending the fovea correlates with other measures of visual function such as best corrected visual acuity and critical flicker fusion frequency at each visit.

**Methods**: Patients undergoing cataract surgery will be asked to participate. At the pre-operative visit, the best corrected visual acuity, critical flicker fusion, and OCT will be performed in each eye. The same tests will be performed at each post-operative visit (day of surgery or next morning, one week, one month, 3 months, 6 months). The incidence of CME will be determined based on OCT measurements and the amount over time will be quantified by repeating the measurements at each visit.

**Results and Conclusion**: Pending

## Accuracy of the IOLMaster in Obtaining Cataract Preoperative Measurements Compared to Traditional A-Scan Biometry and Keratometry

Russell B. Warner MD
Dr. A. Tim Johnson, sponsor

**Purpose**: To evaluate, in a tertiary care setting, the accuracy of measurements using the IOLMaster (Zeiss Humphrey, Dublin, Calif.) for intraocular lens calculations prior to cataract surgery compared to measurements using traditional contact A-scan biometry and keratometry.

**Methods**: A retrospective chart review of 87 cataract surgeries performed at a tertiary care center with resident participation. All patients prior to cataract surgery had measurements performed using both the IOLMaster and traditional contact A-scan biometry and keratometry. Predicted refractions from each were compared to postoperative manifest refractions. Patients with best-corrected final visual acuities less than 20/40 were separated into a separate subgroup. Three further subgroups were formed, one group of eyes with more than 3.00 diopters of myopia preoperative (19 eyes), and another with more than 2.50 diopters of hyperopia preoperative (12 eyes). The spread of errors between the two methods was compared using an F-test.

**Results**: Of the 87 surgeries reviewed preoperative refractions ranged from –12.00 to +5.25 diopters with a mean of –1.18. 73 eyes had postoperative visions of better than 20/40. The error of each method was defined as the difference between the postoperative refraction and the predicted refraction. The mean error with the IOLMaster was -0.22 diopters with a mean standard deviation (SD) of 0.81 versus +0.17 diopters (SD 0.71) using traditional contact biometry and keratometry. The spread of error showed an F value equal to 1.28 with a P-value of 0.12. 57% of the predicted outcomes were within 0.50 diopters of the postoperative refractive error using the IOLMaster versus 56% using traditional contact biometry and keratometry. In the myopic subgroup the error was -0.11 diopters (SD 0.53) with the IOL Master versus +0.34 diopters (SD 0.68). 79% of the predicted outcomes were within 0.50 diopters of the postoperative refractive error using the IOLMaster versus 53% using traditional contact biometry and keratometry. In the hyperopic subgroup the difference was -0.29 diopters (SD 0.55) with the IOLMaster versus +0.14 diopters (SD 0.67). 62% of the predicted outcomes were within 0.50 diopters of the postoperative refractive error using the IOLMaster versus 69% using traditional contact biometry and keratometry. Conclusion: To accurately predict refractions using the IOLMaster and traditional A-scan biometry and keratometry an adjustment can be made to correct for the mean error of each method. The variance or spread of error was statistically equal between the two methods. In our tertiary care setting the IOLMaster and traditional A-scan biometry with keratometry are equally accurate in obtaining measurements for cataract surgery.

## Role of Intraocular Lens Implantation in Pediatric Patients With Juvenile Rheumatoid Arthritis

Michael A. Grassi, MD.
Drs. Wallace LM Alward and Ronald V. Keech, sponsors

**Introduction**: While intraocular lens implantation has enjoyed success in other forms of uveitis, its role in patients with juvenile rheumatoid arthritis remains controversial. Recent reports suggest that in selected adults with juvenile rheumatoid arthritis the results of intraocular lens implantation can be excellent. However, in the pediatric population the procedure is associated with more postoperative complications and significant reservations remain regarding its implementation.

**Methods**: The authors treated four children (five eyes) with juvenile rheumatoid arthritis associated cataract. All patients underwent cataract extraction with posterior chamber intraocular lens implantation. In two patients concurrent trabeculectomy was performed. The cataract was sufficient to limit visual acuity to 20/125 or less. The visual outcome and postoperative course were analyzed in those patients for whom a minimum follow-up of one year was available.

**Results**: Surgery was performed in four children. Follow-up ranged from fifteen months to 8.5 years. Final best-corrected visual acuity was better than 20/30 in all eyes except one which was limited by preoperative amblyopia. Notable early complications were limited to cystoid macular edema in one patient. Late complications included posterior capsular opacification in all of the treated eyes which was successfully managed with laser capsulotomy.

**Discussion**: The results of this study suggest that intraocular lens implantation in patients with juvenile rheumatoid arthritis associated uveitis can have very acceptable results. An aggressive perioperative regimen to control inflammation is critical to maximize visual outcome especially in the pediatric population. Long-term care of these patients is necessary to minimize the late complications of chronic uveitis.

## Identification of a Novel mtDNA Mutation in a Family With an Anterior Ischemic Optic Neuropathy Phenotype

James G. Howard
Drs. Sohan Singh Hayreh and Edwin M. Stone, sponsors

**Purpose**: Six members of a pedigree were each diagnosed with anterior ischemic optic neuropathy (AION) in their 40's or 50's. These patients were screened for mitochondrial mutations to determine if they were actually affected with a late-onset form of Leber's hereditary optic neuropathy (LHON) rather than true AION.

**Methods**: The mitochondrial DNA of the proband was sequenced and then compared against the revised Cambridge reference sequence. When a novel mutation that changed an amino acid was identified in the ND1 gene of the proband, other family members, 41 AION patients, and 1488 LHON probands were screened for this mutation.

**Results**: Six affected members of this family first developed symptoms of AION in their forties or fifties, and all were related to one another through females. A novel mitochondrial mutation was identified in all six family members who had been diagnosed with AION. A guanine to adenine change was identified at position 4132 which would be expected to cause an ALA276THR change in the protein encoded by the ND1 gene. Four unaffected family members also harbored this mutation, but it was not identified in any of the 41 AION or the 1488 typical LHON probands in the study.

**Conclusions**: A novel mitochondrial DNA mutation (4132 G->A) is associated with late onset Leber's hereditary optic neuropathy. This mutation appears to be rare since it was not identified in a large group of LHON patients.

## Possible Radiographic Evidence of Pineal Gland Involvement in Active Birdshot Chorioretinitis

Matthew H. Wood, MD,
Dr. Edwin M. Stone, sponsor

**Purpose**: To examine for any relationship between birdshot chorioretinitis and abnormal radiographic characteristics of the pineal gland.

**Methods**: Magnetic Resonance Imaging (MRI) scans of the brain utilizing T1, T2, and gadolinium contrast media were obtained of two individuals with clinically active ocular disease. Clinical examination and the presence of a positive HLA-A29 confirmed diagnosis of birdshot chorioretinitis. An additional scan of the pineal gland of one of the subjects during disease quiescence is planned.

**Results**: During the initial period of active ocular inflammation both subjects' pineal glands were characterized by abnormal enhancement.

**Conclusions**: Given the small number of subjects no statistically significant conclusions may be made. The presence of radiographic abnormalities suggests a correlation between the pineal gland and birdshot chorioretinitis. Further study is needed.

## Long-Term Outcome of Mitomycin C Trabeculectomy in Patients with Normal Tension Glaucoma

Emily C. Greenlee, M.D.
Drs. Young H. Kwon and Wallace L. M. Alward, sponsors

**Purpose**: To present the long-term results after mitomycin C trabeculectomy in eyes with normal tension glaucoma.

**Design**: Retrospective, noncomparative, interventional case series.

Participants: The medical records of all normal tension glaucoma patients who underwent mitomycin C trabeculectomy at the University of Iowa Hospitals and Clinics between January 1988 to July 2002 were reviewed retrospectively. A total of 90 eyes of 65 patients were studied.

**Methods**: The success of mitomycin C trabeculectomy was evaluated by Kaplan-Meier survival analysis. Additional variables such as age, visual acuity, number of medications/ surgeries, intraocular pressures (IOP), spherical equivalent, family history, past medical history, and past ocular history were analyzed by Cox hazard regression analysis.

**Outcomes**: The success or failure of glaucoma surgery was evaluated by assessment of post-operative IOP, number of medications, and need for further surgery. Success of surgery was defined as a reduction of IOP by 30% with or without topical medications. Need for further surgery was considered a failure.

**Results**: The mean preoperative IOP was 14.6 +/- 2.6 mmHg. The mean number of preoperative medications was 2.1 +/- 1.1. The mean postoperative IOP was 9.8 +/- 3.4 mmHg. The mean number of postoperative medications was 0.7 +/- 1.1. The mean logMar visual acuity preoperatively was –0.13 +/- 0.26 and postoperatively –0.24 +/- 0.41. The mean average length of follow-up was 44 months (range 3 to 130 months). Kaplan-Meier survival analysis showed 61% survival at 24 months and 50% at 60 months. Lower IOP (Hazard ratio 0.86, p-value 0.015) and higher number of preoperative medications (Hazard ratio 1.38, p-value 0.027) were found to be significantly associated with surgical failure.

**Conclusions**: Mitomycin C trabeculectomy can successfully lower IOP in patients with normal tension glaucoma uncontrolled on topical glaucoma medications. The procedure has roughly a 61% surgical survival at 2 years and 50% at 5 years. Lower IOP and higher number of preoperative medications were found to be significantly associated with surgical failure.

## A Novel GCAP1 Missense Mutation in a Family With Autosomal Dominant Cone-Rod Dystrophy

W.J. Dupps, MD
Dr. Edwin M. Stone , sponsor

**Purpose**: Guanylate cyclase activating protein 1 (GCAP1) is a calcium-dependent photoreceptor regulatory protein that has been localized to human cones and rods. Two GCAP1 mutations have previously been reported in association with autosomal dominant cone dystrophy (Y99C) and cone-rod dystrophy (P50L). In this study, a pedigree affected with autosomal dominant cone-rod dystrophy previously linked to a chromosome 6p21 locus was screened for disease-causing sequence variations in the GCAP1 gene.

**Methods**: Twenty-three members of a CRD pedigree underwent clinical examination and genetic analysis. Clinical testing included visual acuity, color testing, Goldmann perimetry, standardized full-field ERG, dark adaptometry and fundus photography. DNA prepared from peripheral blood of family members, 3 unaffected spouses and 200 normal subjects was screened for mutations in the coding sequence of the GCAP1 gene using automated DNA sequencing and SSCP analysis.

**Results**: Affected family members (12/23) experienced dyschromatopsia, photophobia and/or reduced visual acuity by the second decade of life. Characteristic features included a pigmentary maculopathy with central and paracentral scotomas, abnormal dark adaptation, and eventual progression to non-recordable cone responses on ERG (with attenuated rod responses). Linkage was demonstrated between the CRD phenotype and genetic markers from 6p21. Direct sequencing of the RDS gene revealed no disease-causing sequence variations. Sequencing of the GCAP1 gene in the proband detected a C to T missense mutation that would be expected to cause a Leu151Phe change in the GCAP1 protein. This change was present in all 12 affected family members, but absent from 11 unaffected family members, 3 unaffected spouses and 200 unrelated normal subjects.

**Conclusions**: A novel mutation (L151F) in the predicted calcium-binding EF4 hand domain of GCAP1 is associated with autosomal dominant cone-rod dystrophy. Current efforts are directed at designing paired-flash experiments to probe the rod recovery response in affected patients and normal volunteers to further define the electrophysiologic phenotype of this mutation.

## Size and Shape Characteristics of CNV Following Sequential Photodynamic Therapy With Verteporfin

Karin Sletten, MD
Drs. James C. Folk, H. Culver Boldt, Karen M. Gehrs, Edwin M. Stone, & Stephen R. Russell, sponsors

**Purpose**: To describe choroidal neovascularization (CNV) characteristics in a population receiving photodynamic therapy with verteporfin (PDT), with attention to the roundness of CNV lesions.

**Methods**: Charts of the first 100 patients receiving PDT were reviewed. Data collected were: age, gender, ocular history, visual acuity and characteristics of CNV including greatest linear diameter (GLD), vertical and horizontal dimensions. Exclusion criteria were: less than 1 year follow up, periocular steroid within 6 weeks of PDT and prior PDT at an outside institution. Shape characteristics of recurrent CNV were compared with recurrences following conventional laser treatment.

**Results**: 46 eyes of 42 patients with AMD met inclusion criteria. Average age was 75 years. Average GLD increased from baseline until the 18-month follow up visit. Eccentricity decreased (relative roundness increased) from an initial value of 0.69 to 0.85 at the 18-month follow up visit. Average number of treatments was 3.1 over 18 months.

**Conclusions**: A large percentage of CNV recurrences demonstrate enlargement after treatment with PDT, in many cases resembling the previous spot-size. Whether this effect may be due to the natural history of CNV will be discussed. Additionally noted in this series, prior conventional laser photocoagulation appears to be an important predictor of CNV worsening with PDT.

## Ultra Long-Term Outcomes of Penetrating Keratoplasty for Keratoconus

Sudeep Pramanik, MD,MBA
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**Purpose**: Keratoconus is a progressive, noninflammatory, bilateral degeneration of the central and paracentral corneal stroma that can lead to irregular myopic astigmatism. Penetrating keratoplasty is a well-accepted treatment for advanced keratoconus. Current studies have reported "long-term" graft survival data up to five years from the time of transplant. Also, scattered reports of late recurrence of keratoconus have been described, but the rate and predisposing factors are unclear.

**Methods**: We will review retrospectively the records of all patients with keratoconus who underwent penetrating keratoplasty at UIHC more than 20 years ago to determine the rate of ultra long-term graft survival. Secondary outcome measures would include visual acuity, rejection episodes, complications, recurrence of keratoconus, secondary procedures, and need for repeat corneal transplant.

## Linkage of a Large Pattern Dystrophy Pedigree to Chromosome 6p21

John H. Fingert, MD, PhD
Dr. Edwin M. Stone, sponsor

**Purpose**: To map the gene causing pattern dystrophy in a large pedigree with linkage analysis and to evaluate candidate genes within the linkage interval.

**Methods**: Of 38 family members examined, 15 were found to have an abnormal retinal exam. The retinal findings in this family were variable, ranging from subtle RPE changes to atrophy of the central macula, but as a whole were most consistent with a diagnosis of pattern dystrophy. DNA was prepared from the blood of study subjects and typed with genetic markers distributed evenly across the genome. The genotypes were evaluated using the LINKAGE statistics package. The coding sequences of three candidate genes in the linked region (RDS, GCAP1, and GCAP2) were screened for mutations in the proband of the pedigree using both direct DNA sequencing and SSCP analysis.

**Results**: Significant linkage was obtained with several markers on chromosome 6p21 (D6S271 Zmax = 5.4 at theta = 0). Recombinations at markers D6S1650 and D6S1552 defined a linked interval that included genes RDS, GCAP1, and GCAP2. Direct sequencing of these candidate genes revealed no likely disease-causing mutations.

**Conclusions**: The gene causing the pattern dystrophy in this pedigree is located on chromosome 6p21. No mutations were detected in the RDS, GCAP1 and GCAP2 genes. The retinal degeneration in this family may still be due to a mutation in one of these genes, which is not detectable by PCR-based sequencing (e.g. a deletion or a rearrangement). Alternatively, there may be another retinal degeneration gene in close proximity to RDS, GCAP1 and GCAP2.

## Characteristics and Course of Patients With Deteriorated Monofixation Syndrome

Michael G. Hunt, MD
Dr. Ronald V. Keech, sponsor

**Background**: Monofixation syndrome is characterized by small angle strabismus with vergence fusional amplitudes and "peripheral fusion". Although it is considered a relatively stable condition, some patients with this syndrome deteriorate resulting in an increasing tropia and diplopia. Deteriorated monofixation syndrome is well known among clinicians, however, there are no studies describing the course and outcomes for these patients.

**Purpose**: To assess the clinical characteristics and course of patients with monofixation syndrome who deteriorate, including their response to treatment.

**Methods**: We identified all patients from our database with deteriorated monofixation syndrome. From this group we assessed patient clinical characteristics, clinical course, and response to therapy.

**Results**: We identified 29 patients who were deteriorated monofixators and were treated (28 with surgery, 1 with minus lens therapy) after deterioration. Nearly all (97%) of the patients had a history of esotropia and 20 of 29 (69%) had a history or amblyopia. Nine patients noted diplopia at the time of deterioration which persisted in four patients following treatment. In all, 14 of the 29 (48%) met the criteria for monofixation again after therapy (11/20 with no diplopia, 3 of 9 with diplopia) while 20 of 29 (16/20 with no diplopia, 4/9 with diplopia) had successful motor alignment, defined as a deviation of less than or equal to 8 prism diopters. Follow up ranged from one month to twenty-one years.

**Conclusion**: Though monofixation is considered a stable condition, some patients will deteriorate or "break down" over time as demonstrated by an increase in the ocular deviation and loss of fusion. In this study 31% of our patients noted the onset of diplopia. Following treatment, 48% of the patients regained monofixation. Patients with diplopia seemed to have poorer outcomes with surgery after deterioration; however, this was not statistically significant.

## Anecortave Acetate Monotherapy for the Treatment of Occult and Minimally Classic Choroidal Neovascularization in Age-Related Macular Degeneration

John W. Kitchens
Drs. Stephen R. Russell and Edwin M. Stone, sponsors

**Purpose**: Prospective case series evaluating the efficacy and safety of anecortave acetate in the treatment of choroidal neovascularization in patients with age-related macular degeneration ineligible for other investigational or approved treatments.

**Methods**: Under an open label compassionate use protocol, 24 patients with occult or minimally classic choroidal neovascularization were treated with posterior juxtascleral administration of anecortave acetate (15 or 30 mg). Ocular examinations were performed within one week prior to treatment and at 2 weeks, 6 weeks, 3 months, 6 months, and 1 year after injection. ETDRS refraction and dilated fundus examination were performed at each visit. Fluorescein angiography was performed at the 6 month and 1 year visits. Re-treatment was performed at the discretion of the treating physician based upon evidence of improvement or clinical progression of the lesion. If re-treated, the examination cycle was repeated within the one year study interval. Three patients received photodynamic therapy prior to the study. Two patients received photodynamic therapy during the course of the study when the CNV lesion progressed to TAP eligibility.

**Results**: Visual acuity improved from baseline in 25% (6 of the 24) at one year. Sixty seven percent (16 of 24) lost less than 15 letters of vision. Only 4 patients (17%) experienced severe visual loss at one year. Clinical improvement (decreased subretinal fluid, decreased subretinal hemorrhage, or reduced hyperfluorescence) was evident in 12 of the 24 patients as judged by the examiner. Sixteen patients recieved re-treatment. Adverse events were limited to disconfort in the injection area (3 patients) which resolved after one to two weeks.

**Conclusions**: Anecortave acetate is safe and appears effective in the treatment of occult or minimally classic choroidal neovascularization.

## Lattice Degeneration of the Retina in an Extended Family

Denise L. Kayser, MD
Drs. James C. Folk, Stephen R. Russell, and Edwin M. Stone, sponsors

**Purpose**: To determine if lattice degeneration of the retina is a hereditary disease and if so, to establish genomic linkage.

**Methods**: After IRB approval and informed consent, family members were examined with indirect ophthalmoscopy and scleral depression. Blood was drawn and sent to Dr. Ed Stone's lab for processing and linkage analysis.

**Results**: A total of 40 family members were examined: seventeen were affected, thirteen were unaffected, three were clinically normal but were obligate carriers since they had affected children, two were probably (but not definitely) affected, and five were informative spouses of affected family members. So far, a genomic-wide search using forty markers has found no linkage. The site for Wagner's Disease and Erosive Vitreoretinopathy has been excluded.

**Conclusions**: Lattice degeneration of the retina is an inherited disease. Three obligate carriers did not appear to be affected on careful clinical examination. This indicates that, in some patients, lattice is non-penetrant using currently available examination techniques or perhaps is a disease that requires expression of more than one gene in order to become penetrant. This family should be of sufficient size to establish genetic linkage. Further studies using additional markers are underway.

## Reaction Time: A New Diagnostic Parameter of Automated Kinetic Perimetry

Steven L. Goldin, MD
Drs. Randy H. Kardon, Andrew G. Lee, and Michael Wall, sponsors

**Purpose**: To evaluate the effect of visual field eccentricity and duration of perimetric testing on reaction time within the boundary of an isopter. The perimetric testing will make use of a new automated kinetic perimeter that adjusts the size of the isopter based on the reaction times to a kinetic light stimulus, which is obtained during the course of kinetic visual field testing. The mean and standard deviation of the reaction time will be compared among the following groups: normals, patients with organic visual field loss, patients with non-organic visual loss, and patients who are mentally impaired. The goal will be to provide confidence intervals for reaction time in normal subjects in order to better understand how diseases affecting the visual system can be differentiated from disorders affecting patient judgement.

**Methods**: 10 normal subjects, 10 patients with optic neuropathy, and 10 patients with non-organic visual loss will be tested with 2 isopters, I2e and I4e, using a new automated kinetic perimeter (Interzeag). Patients with non-organic visual field loss will consist of patients with either functional vision loss or patients with dementia. For each isopter, the reaction time will be assessed at three starting locations, moving toward the center, within the isopter, equidistant from each other. The cycle will be repeated three times to provide 3 reaction times for each location tested for each isopter. In half of the subjects the smaller isopter will be tested first and in the other half, the larger isopter will be tested first. The mean reaction time will be compared across locations, and between isopters. The mean and standard deviations will be compared across patient groups. A correlation between time from beginning of visual field test and reaction time will also be tested.

## A Modification of the Cutler-Beard Procedure Utilizing Donor Achilles Tendon for Upper Eyelid Reconstruction

Erin L. Holloman, MD,
Dr. Keith D. Carter, sponsor

**Purpose**: Upper eyelid defects present challenges for ophthalmic reconstructive surgeons. The upper lid is a complex structure that must maintain its stability and motility for optimal function and cosmesis. Traditionally, large defects have been repaired by the two stage Cutler-Beard procedure. The first stage advancement flap only transplants soft tissue without tarsus. Without this tarsal stability, post procedure entropion and lid shrinkage have most frequently been described. Through the years, surgeons have tried many different substances to lend support to the new upper eyelid, some with complications. Currently, autogenous cartilage is most frequently used. We propose using donor Achilles tendon for increased stability of the upper lid when repairing large defects by the Cutler-Beard procedure.

**Methods:** A modified version of the Cutler-Beard procedure utilizing donor Achilles tendon as tarsal replacement was performed in four patients with large upper eyelid defects.

**Results**: Patients were examined in follow up and all cases were successful in recreating the upper eyelid. None developed infection or dehiscence. No secondary ptosis, retraction, or lid malposition have been found.

**Conclusions**: The replacement of upper eyelid tarsal stability with Achilles tendon as part of the Cutler-Beard procedure was successful in repairing four patients with large upper lid defects. The tendon graft is easily placed and incorporated into the normal lid anatomy. The tissue is readily available from most tissue banks. The modification produced excellent functional and cosmetic results without complications.

## Visual Outcome in Aggressively Patched Eyes in Cases of Unilateral Infantile Cataract or Unilateral PHPV

Susan Quick, MD
Dr. Ronald V. Keech, sponsor

**Purpose:** To determine if the normal eye of patients with unilateral infantile cataract or PHPV has more myopic progression compared to age-matched controls or has evidence of occlusion amblyopia after aggressive patching.

**Methods:** A retrospective chart review was done of patients with unilateral PHPV or congenital cataract. Exclusions included other sight-limiting eye diseases or surgeries, patients never able to give a visual acuity from a chart, inadequate follow-up, or patients with poor patching compliance. Percent of full-time versus part-time occlusion was tracked. Compliance was categorized as good (>75% of prescribed hours) or fair (50-75% of prescribed hours). Age at start of patching, duration of patching, duration of follow-up, final visual acuity of both eyes, and final refraction of the good eye were all tracked.

**Results:** 23 patients fit the study (13 female and 10 male). 15 patients had congenital cataract, 8 had PHPV. 65% documented good compliance with patching and 35% documented fair. 43% did a majority of full-time occlusion and 57% did a majority of part-time. Average age at the start of patching was 1.35 years. Duration of patching was an average of 4.9 years. Duration of follow-up was 12.6 years. Average spherical equivalent of the good eye at the end of follow-up was -0.67 D. Final visual acuity of the good eye ranged from 20/15-20/25. Final visual acuity of the bad eye ranged from 20/20-worse than 20/200.

Results - Bad Eye

| Final Visual Acuity | # | % |
|---|---|---|
| 20/20 | 4 | 17.4% |
| 20/25-20/50 | 9 | 39.1% |
| 20/60-20/160 | 2 | 8.7% |
| >20/200 | 8 | 34.8% |

Refractive Status by Age - Boys

| Age (#pt) | Study SE | Control SE |
|---|---|---|
| 5(1) | +0.75 | +1.62 |
| 6-7(2) | +1.38 | +0.74 |
| 8(1) | +2.63 | +0.24 |
| 15(1) | -2.50 | -2.07 |
| 18+(5) | -0.38 | -2.71 |

**Conclusions:** There was no evidence of occlusion amblyopia. There was no evidence of myopic progression in the aggressively patched eyes. In fact, the average of the differences between the study group and control group was plano for the females and +0.81 D in the males.