RESIDENT/FELLOW
RESEARCH DAY

May 15, 2009

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

RESIDENT/FELLOW RESEARCH DAY - 2009

DEPARTMENT OF OPHTHALMOLOGY

PROFESSOR AND HEAD

Keith D. Carter, M.D.

PROFESSORS

Wallace L. M. Alward, M.D.
H. Culver Boldt, M.D.
Keith D. Carter, M.D.
Thomas L. Casavant, Ph.D.
James C. Folk, M.D.
Kenneth M. Goins, M.D.
Gregory S. Hageman, Ph.D.
A. Tim Johnson, M.D., Ph.D.
Chris A. Johnson, Ph.D.
Randy H. Kardon, M.D., Ph.D.
Patricia A. Kirby, M.D.
Stephen A. Kuusisto, M.F.A.
Young H. Kwon, M.D., Ph.D.
Jeffrey A. Nerad, M.D.
Thomas A. Oetting, M.D.
Stephen R. Russell, M.D.
Val C. Sheffield, M.D., Ph.D.
Milan Sonka, Ph.D.
Edwin M. Stone, M.D., Ph.D.
Michael D. Wagoner, M.D., Ph.D.
Michael Wall, M.D.
Thomas A. Weingeist, Ph.D., M.D.
Mark E. Wilkinson, O.D.

ASSOCIATE PROFESSORS

Michael D. Abràmoff, M.D., Ph.D.
Terry A. Braun, Ph.D.
Arlene V. Drack, M.D.
Karen M. Gehrs, M.D.
Robert F. Mullins, Ph.D.
Richard J. Olson, M.D.
Todd E. Scheetz, Ph.D.
Christine W. Sindt, O.D.

ASSISTANT PROFESSORS

Michael G. Anderson, Ph.D.
John H. Fingert, M.D., Ph.D.
Emily C. Greenlee, M.D.
Brian R. Kirschling, O.D.
Anna S. Kitzmann, M.D.
Markus H. Kuehn, Ph.D.
Reid A. Longmuir, M.D.
Susannah Q. Longmuir, M.D.
Vinit B. Mahajan, M.D., Ph.D.
Steven F. Stasheff, MD, PhD
Nasreen A. Syed, M.D.

ORTHOPTISTS

Pam J. Kutschke, C.O.
Melissa A. Madsen, C.O.
Wanda L. Pfeifer, OC(C), C.O.M.T.

FACULTY RESEARCH ADVISOR

Michael D. Wagoner, M.D., Ph.D.

RESIDENT/FELLOW RESEARCH DAY - 2009

PROFESSORS EMERITUS

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

VISITING PROFESSOR

William J. Kimberling, Ph.D.

ADJUNCT FACULTY

ADJUNCT PROFESSOR

Andrew G. Lee, M.D
Neil N. Silbermann, M.D., Clinical

ADJUNCT ASSOCIATE PROFESSOR

Constance Grignon, M.D., Clinical
Peter Soliz, Ph.D

ADJUNCT CLINICAL ASSISTANT PROFESSOR

Christopher F. Blodi, M.D.
Elizabeth Ann Brown, M.D
Christopher L. Haupert, M.D
Stephen H. Wolken, M.D.
Linda J. Lehman, M.D.

ADJUNCT CLINICAL INSTRUCTOR

David S. Dwyer, M.D.
John F. Stamler, M.D., Ph.D.
Lyse S. Strnad, M.D.

ASSISTANT TO THE CHAIR

Larry W. McGranahan, C.H.E.

MANAGER, RESEARCH AND DEVELOPMENT

Paul R. Montague, C.R.A.

RESIDENT/FELLOW RESEARCH DAY - 2009

FELLOWS

CORNEA

Maneesh K. Mehan, M.D.

GLAUCOMA

Mansi Parikh, M.D.

NEURO-OPHTHALMOLOGY

Mansoor S. Mughal, M.D.
Fabiana C. Policeni M.D.

OCULAR PATHOLOGY

Juan P. Fernandez de Castro, M.D.

OCULOPLASTIC SURGERY

Jill S. Melicher, M.D.

PEDIATRIC OPHTHALMOLOGY

Alejandro Leon, M.D.

VITREORETINAL DISEASE

Kori A. Elkins, M.D.
Jordan M. Graff, M.D.
Narendra Patel, M.D.
Rizwan Somani, M.D.

DORIS DUKE RESEARCH FELLOW

Audrey C. Ko

RESIDENT/FELLOW RESEARCH DAY - 2009

RESIDENTS

THIRD-YEAR RESIDENTS

Arpitha Muthialu Charlu, M.D.
Parley D. Fillmore M.D., Ph.D.
Matthew P. Rauen, M.D.
Parisa Taravati, M.D.
E. Bo Yang, M.D.

SECOND-YEAR RESIDENTS

Alex W. Cohen, M.D., Ph.D.
Nandini G. Gandhi, M.D.
A. Brock Roller, M.D.
Lucas J.A. Wendel, M.D.

FIRST-YEAR RESIDENTS

Emily S. Birkholz, M.D.
Jason P. Brinton, M.D.
Leslie T.L. Pham, M.D.
Brian K. Privett, M.D.
Gina M. Rogers, M.D.
Janet Y.M. Tsui, M.D.

ORTHOPTICS – TRAINING

Tara Bragg, First Year
Amy L. Ellis, Second Year
Amy J. Gilbertson, Second Year
Eva Lutz, First Year

OTHER PRESENTERS

Alina V. Dumitrescu, M.D., Postdoctoral Research Scholar
George R. Wandling, Medical Student

The University of Iowa
Department of Ophthalmology and Visual Sciences
Resident and Fellow Research Program
would like to recognize our patrons

Alcon Laboratories, Inc.
and
The William C. and Dorotha Gaedke Charitable Trust

for their continued support of
resident and fellow research

Research at The University of Iowa Department of Ophthalmology and Visual Sciences is supported in part by an unrestricted grant from
Research to Prevent Blindness

RESIDENT/FELLOW
RESEARCH DAY

May 15, 2009

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

OPHTHALMOLOGY RESIDENT/FELLOW RESEARCH DAY
SCHEDULE OF EVENTS

Friday, May 15, 2009

7:45 **Refreshments**

8:00 **Introduction and Welcome**

8:15 **Emily Birkholz**, Michael D. Wagoner, sponsor ..... 1.
Excisional Biopsy and Adjunctive Treatment of Ocular Surface Neoplasia

8:30 **Jason Brinton,** James C. Folk, sponsor ..... 2.
Antiretinal Antibodies in Posterior Uveitis

8:45 **Leslie Pham,** Michael D. Wagoner, sponsor ..... 3.
Superficial Keratectomy for Anterior Corneal Disorders

9:00 **Brian Privett,** Emily C. Greenlee, sponsor ..... 4.
Use of the EYESi Surgical Simulator as a Valid Model for Capsulorhexis Training

9:15 **Gina Rogers,** Thomas A. Oetting, sponsor ..... 5.
The Impact of a Structured Surgical Curriculum on Ophthalmic Resident Cataract Surgery Complication Rate

9:30 **Janet Tsui,** Michael D. Wagoner, sponsor ..... 6.
Descemet's Stripping Automated Endothelial Keratoplasty: Sequential vs. Staged Cataract Extraction

9:45 - 10:15 **Break**

10:15 **Nandini Gandhi,** Kenneth M. Goins, sponsor ..... 7.
Comparison of the 60 kHz femtosecond laser versus manual microkeratome in the dissection of donor tissue for endothelial keratoplasty

10:30 **A. Brock Roller,** James C. Folk, sponsor ..... 8.
Progression of Age Related Macular Degeneration after Vitrectomy

10:45 **Matt Rauen,** Kenneth M. Goins, sponsor ..... 9.
Descemet's Stripping Automated Endothelial Keratoplasty for the Management of Iridocorneal Endothelial Syndrome

11:00 **Alina Dumitrescu,** Young H. Kwon, sponsor ..... 10.
Sustained-release Timolol Maleate Microspheres: A New Treatment Approach for Glaucoma

11:15 **George Wandling,** Michael D. Wagoner, sponsor ..... 11.
Glaucoma Escalation after Deep Lamellar Endothelial Keratoplasty

11:30 **Amy Ellis,** Randy H. Kardon, sponsor ..... 12.
Differential Diagnosis of Vertical Deviations

OPHTHALMOLOGY RESIDENT/FELLOW RESEARCH DAY
SCHEDULE OF EVENTS

Friday, May 15, 2009

12:15 - 1:15 **Buffet Lunch**

2:45 - 3:15 **Break**

OPHTHALMOLOGY RESIDENT/FELLOW RESEARCH DAY
SCHEDULE OF EVENTS

Friday, May 15, 2009

4:15 **ADJOURN**

Faculty Vote on Presentations

Excused from Presentation: Manuscript requirement completed

Arpitha Muthialu Charlu ..... 25.
Sponsor: Jeffrey A. Nerad
Title: Endotine Forehead Device Effect on Brow Lift Over Time

Alex W. Cohen ..... 26.
Sponsor: Michael D. Wagoner
Title: Penetrating Keratoplasty vs. Deep Anterior Lamellar Keratoplasty for Keratoconus

Parley D. Fillmore ..... 27.
Sponsor: Kenneth M. Goins
Title: Visual Acuity, Refractive Error, and Endothelial Cell Density Six and Twelve Months after Deep Lamellar Endothelial Keratoplasty

Parisa Taravati ..... 28.
Sponsor: Kenneth M. Goins
Title: Outcomes after Descemet's Stripping Automated Endothelial Keratoplasty

Lucas J. Wendel ..... 29.
Sponsor: Michael D. Wagoner
Title: DSAEK: Fold vs. Pull-Through Insertion Technique

E. Bo Yang ..... 30.
Sponsor: Michael D. Abràmoff
Title: Comparison of Resident and Fellow Optic Disc Cup and Rim Segmentation from Stereo Photographs using Computer-Aided Planimetry

Excisional Biopsy and Adjunctive Treatment of Ocular Surface Neoplasia

Emily S. Birkholz, M.D.
Sponsor: Michael D. Wagoner, M.D., Ph.D.

Purpose: To analyze the outcomes of surgical treatment of ocular surface squamous neoplasia (OSSN), with and without the use of adjuvant intraoperative and postoperative therapy.

Methods: The clinical records of all patients with a positive biopsy for OSSN of the cornea or conjunctiva, conjunctival or corneal intraepithelial neoplasia, carcinoma in situ, and/or squamous dysplasia treated at the UIHC Department of Ophthalmology between January 1, 1980 and December 31, 2008 were reviewed.

Results: Sixty-seven eyes met the inclusion criteria. The mean patient age was 68.9 years (range, 36.6 to 88.4). The mean follow-up was 35.8 months (range, 0 to 192). The majority of patients were male (84%), had involvement of the left eye (68%), and predominance of limbal location (79%). Five eyes had either intraocular extension (2 eyes) or orbital extension (4 eyes) at the time of initial presentation and required either enucleation or exenteration, respectively. Sixty-two eyes had localized conjunctival neoplasia and were treated with simple excisional biopsy. Seventeen (27 %) eyes had adjuvant intraoperative therapy and thirty-two (52%) eyes had postoperative adjuvant therapy. In the patients with localized disease, recurrence occurred in twenty-two (35%) eyes. Recurrence rates in eyes treated with and without intraoperative adjuvant therapy were 29% and 38%, respectively. Recurrence rates with and without post-operative adjuvant treatment were 22% and 50%, respectively. Of the sixteen eyes treated with post-operative mitomycin C, only one had a recurrence (6%, p= 0.02). Nine eyes (27%) with positive margins had a recurrence compared to thirteen eyes (45%) without positive margins (p= 0.19). Of the thirty-one eyes with lesions smaller than 50 mm^2, twelve (39%) had a recurrence, compared to five (25%) of the twenty eyes with lesions larger than 50 mm^2. At the most recent examination, fifty-nine (95%) eyes were tumor-free. Fifty-three patients (86%) had best corrected visual acuity (BCVA) unchanged or improved after treatment for localized disease and only eight eyes (13%) had BCVA decrease from OSSN or treatment for OSSN. Of the twenty-two eyes with a recurrence, six (27%) had BCVA decrease from OSSN or treatment for OSSN, compared to two (5%) of the forty eyes without recurrent disease (p= 0.02).

Conclusions : Patients with OSSN treated with excisional biopsy alone frequently have recurrent disease and patients with recurrence may have poorer visual outcomes. Adjuvant intraoperative and/or post-operative therapy can reduce recurrence rates, with post-operative mitomycin-C having the most dramatic reduction in recurrence. Positive margins and larger lesions were not shown to be a risk factor for recurrent disease. Ophthalmologists should be cognizant of the risk of intraocular and orbital extension, as well as distant metastases after incomplete surgical excision.

Additional Author Acknowledgements: Kenneth M. Goins, M.D.; John E. Sutphin, M.D.

Antiretinal Antibodies in Posterior Uveitis

Jason P. Brinton, M.D.
Sponsor: James C. Folk, M.D.

Problem: Uveitis causes 10% of the new cases of blindness reported each year in the United States. A recent, large population-based study found that the incidence of uveitis was three times that of previous U.S. estimates. Inflammation involving the choroid and retina has a high potential for visual loss because of irreversible scarring, particularly in the macula.

With the exception of infectious causes, the pathogenesis of most posterior uveitis is unknown. Even the clinical classification of these diseases is controversial. Some clinicians divide them into categories (e.g. multifocal choroiditis, punctate inner choroidopathy, and the presumed ocular histoplasmosis syndrome) based on the location and appearance of scars, presence of inflammation and clinical course, whereas others maintain that these clinical scenarios represent subsets of a single, common inflammatory syndrome.

Purpose: This study examines levels of circulating antiretinal antibodies in patients with posterior uveitis and in normal controls. We also examined whether certain antibodies were associated with specific subsets of disease, severity, or clinical course of disease.

Design: Experimental/Laboratory Study

Methods: Serum was collected from 82 patients with inflammatory eye diseases and 32 controls. Human retina was collected from three donors without known ocular pathology within 6.5 to 17 hours post-mortem. Each whole retina was ground and vortexed in 400μL protease inhibitor cocktail in phosphate buffered saline. The solution was spun and the soluble fractions of retina protein were collected in the form of a supernatant. Soluble or insoluble retina protein was suspended in a buffer solution and transferred following electrophoresis from a gel to a nitrocellulose membrane. The ends of the strip of membrane were secured with the Blot-o-matic probing device, blocked for one hour, and incubated with human serum primary antibody. The strips were then probed with goat-anti-human IgG/A/M antibody. The membranes were then developed using the ECL Plus Western Blotting Detection System. Individual anti-retinal antibody profiles were compared between patients and patient group.

Results/Conclusion: Pending

All experiements were performed by Audrey Ko and Jason Brinton in the laboratory of Robert Mullins, PhD.

Additional Acknowledgements: Audrey Ko, MSIII; Edwin M. Stone, Ph.D., M.D.; Robert Mullins, Ph.D.

Superficial Keratectomy for Anterior Corneal Disorders

Leslie T.L. Pham, M.D.
Sponsor: Michael D. Wagoner, M.D., Ph.D.

Purpose: To evaluate the outcome of superficial keratectomy for the treatment of symptomatic superficial corneal opacities.

Design: Retrospective cohort series

Participants: Thirty eyes of 30 patients who underwent superficial keratectomy for superficial corneal disorders and for which 6 or more months of follow-up was available.

Methods: Review of all cases of superficial keratectomy performed on the Cornea Service at the University of Iowa Hospital and Clinics between January 1, 1998 and December 31, 2008.

Main Outcome Measure: Best corrected visual acuity

Secondary Outcome Measures: Keratometric and refractive astigmatism, wave front aberrations, recurrent erosions, subjective discomfort, recurrent disease

Results: There were 23 eyes with Salzmann's nodular degeneration and 7 eyes with epithelial-basement-membrane dystrophy. Best corrected visual acuity improved in 93% of cases due to elimination of central corneal opacities and/or reduction in irregular astigmatism. When present, recurrent erosions and/or chronic ocular discomfort improved in 80% and 92% of eyes, respectively. Five recurrences of the original disease occurred within this period, of which 2 were successfully treated with repeat surgery.

Conclusion: Superficial keratectomy appears to be a safe and effective method of treating superficial corneal disorders associated with impaired vision, recurrent erosions, or chronic discomfort. Although recurrences are common, the surgery can be repeated with similar results to the primary intervention.

Additional Author Acknowledgements: Kenneth M. Goins, M.D.; John E. Sutphin, M.D.

Use of the EYESi Surgical Simulator as a Valid Model for Capsulorhexis Training

Brian K. Privett, M.D.
Sponsor: Emily C. Greenlee, M.D.

Purpose: To investigate the construct validity of the EYESi Surgical Simulator's capsulorhexis module as valid training to improve capsulorhexis performance in the operating room.

Background: One of the more difficult tasks to learn and practice for cataract training is the creation of the curvilinear capsulorhexis. Traditionally residents have trained using animal models in a wet lab; commonly with pig eyes. Although pigs eyes anatomically closely resemble human eyes, the elasticity of the pig eye anterior capsule makes the creation of the capsulorhexis much different from that of a human eye. Advances in computer technology have lead to increasingly sophisticated virtual reality simulators for many different types of surgery. There are currently two commercially available ophthalmic simulators: EYESi (VRmagic, Mannheim, Germany) and PhacoVision (Melerit Medical, Linköping, Sweden). The EYESi simulator is the only one which allows for vitreoretinal surgery and cataract surgery. Construct validity has been shown for the vitreoretinal module of EYESi and anterior segment forceps and anti-tremor modules. Feudner *et al*. recently found that structured capsulorhexis training on the EYESi module significantly improved capsulorhexis performance on pig eyes in the wet lab; however, no construct validity study has ever been performed on this module.

Study Objectives: This will be the first study of the construct validity of the EYESi capsulorhexis module for capsulorhexis training. The goal of the study will be to compare experienced cataract surgeons to non-surgeons, all of whom have never used the simulator. The non-surgeon group will consist of 15-20 medical students and first year ophthalmology residents who have not been trained in capsulorhexis techniques. A brief orientation of simulator will be given to each participant as well as a brief presentation on creation of the capsulorhexis. The experienced surgeon group will consist of 15-20 faculty and local ophthalmologist who have never used the simulator. All participants will be given a practice round on the capsulorhexis module and will then complete three sessions. These sessions will be graded on various factors such as time, deviation from the circle, and tissue protection. If the capsulorhexis module is a similar construct to human capsulorhexis creation, we would expect that experienced surgeons would outperform non-surgeons.

Additional Author Acknowledgements: Thomas A. Oetting, M.D.

The Impact of a Structured Surgical Curriculum on Ophthalmic Resident Cataract Surgery Complication Rate

Gina M. Rogers, M.D.
Sponsor: Thomas A. Oetting, M.D.

Background: Due to pressure from insurers, patient advocacy groups, and hospitals, resident education has undergone major changes recently. The Accreditation Council for Graduate Medical Education (ACGME), which governs ophthalmology residency programs, requires that we emphasize competency in our residents rather than numbers of cases or hours of lectures. Eventually the ACGME expects residency programs to prove that their program elicits change in residents and improves their competency.

Purpose: At the University of Iowa, we made significant changes in the early training of our residents a few years ago in an attempt to hasten the learning curve to make early resident surgery safer.

Methods: We analyzed quality data that has been collected at the Des Moines VAMC for the period that included academic years from 1998-2008. The quality data that was collected for this report included only cases of phacoemulsification where our residents were the primary surgeons. We excluded cases that were not phacoemulsification cases such as planned extracapsular procedures. We counted a posterior capsular tear (with or without vitreous loss) or vitreous loss (from any cause) as a sentinel complication.

Results: Here we show a statistically significant reduction in posterior capsular tears and vitreous loss in our residents operating at one of our associated VA hospitals during their 3rd year following the introduction of 4 changes in our 1st and 2nd year surgical curriculum: 1) structured wet lab and simulator training during the 1st year; 2) backing into cases of senior residents during the 1st year; 3) formative feedback during the 2nd year, and 4) deliberate practice of the capsulorhexis during the 2nd year.

Conclusions: The ACGME has asked residency programs to prove with outcome data that residents are competent and that our programs are improving[1]. Here, we show a significant decline in a sentinel complication rate over the past few years that correspond to significant new elements that we added to our cataract surgery curriculum. We feel that the decrease in the rate of these complications come from a hastening of the residents surgical learning curve that is at least in part due to the changes we have made in our surgical curriculum.

Additional Author Acknowledgements: Constance Grignon, M.D.; Emily C. Greenlee, M.D.; A. Tim Johnson, M.D. Ph.D.; Hilary A. Beaver, M.D.; Andrew G. Lee, M.D.; Keith D. Carter, M.D.

Descemet's Stripping Automated Endothelial Keratoplasty: Sequential vs. Staged Cataract Extraction

Janet Y.M. Tsui, M.D.
Sponsor: Michael D. Wagoner, M.D., Ph.D.

Purpose: To compare the outcomes of eyes with corneal edema treated with Descemet's stripping automated endothelial keratoplasty (DSAEK) and combined cataract extraction (CE) with posterior chamber intraocular lens (PC-IOL) with those treated with CE and PC-IOL before or after DSAEK.

Design: Retrospective, comparative, non-sequential cohort series

Participants: One hundred and forty five consecutive eyes undergoing primary DSAEK with combined CE and PC-IOL (79 eyes) or CE and PC-IOL before (60 eyes) or after (6 eyes) DSAEK and in which at least 6 months of follow-up was available.

Methods: The medical record of every case of DSAEK performed at the UIHC Department of Ophthalmology between December 1, 2003 and December 31, 2006 was reviewed.

Main Outcome Measures: Best spectacle corrected visual acuity (BSCVA), graft survival

Secondary Outcome Measures: Refractive accuracy, endothelial cell loss

Results: Postoperatively, the BSCVAs in logMAR units were 0.25 ± 0.36 in the combined group, 0.31 ± 0.36 in the CE before group, and 0.18 ± 0.12 in the CE after group. The final spherical equivalents were 0.07 ± 1.24, 0.50 ± 1.33, and -2.19 ± 4.38, respectively ($P < 0.05$). The percentages of endothelial cell loss after 1 year were 24%, 49%, and 57 %, respectively ($P < 0.05$). Primary graft failure occurred in 5 (6.3%) eyes in the combined group, 1 (1.7%) eyes in the CE before group, and none in the CE after group. Overall graft survival was 93.7 %, 95.0 %, and 83.3 %, respectively.

Conclusion: There were no significant differences in visual outcome and overall graft survival in eyes in which cataract surgery was performed before, during, or after DSAEK. There were significant differences between the groups with respect to refractive predictability (with combined surgery having the best results) and in endothelial attrition (with CE after DSAEK having the worst results).

Additional Author Acknowledgements: Kenneth M. Goins, M.D.; John E. Sutphin, M.D.; M. Bridgit Zimmerman, Ph.D., M.S.

Comparison of the 60 kHz femtosecond laser (IntraLase®) versus manual microkeratome in the dissection of donor tissue for endothelial keratoplasty (EK)

Nandini G. Gandhi, M.D.
Sponsor: Kenneth M. Goins, M.D.

Background: A large percentage of penetrating keratoplasties in the United States are performed for conditions in which corneal pathology is confined to the endothelium. The advent of endothelial keratoplasty has made it possible selectively to transplant the corneal endothelium, allowing for more optimal refractive outcomes and shorter recovery times. Endothelial keratoplasty donor tissue can be prepared using a manual microkeratome or a femtosecond laser. A comparison study of endothelial tissue cut using a manual microkeratome (Moria ALTK) and a 30 kHz femtosecond laser (Intralase) showed that the two were equally effective and safe in cutting endothelial tissue. However, the 30 kHz laser produces a rougher stromal surface than the Moria; this may enable good disc adherence but may also reduce optical quality. The 60 kHz femtosecond laser, with closer spot size separation and lower energy levels, may be able to create a smoother surface that has still has good disc adherence.

Purpose: To compare the tissue characteristics of endothelial keratoplasty tissue cut with the 60 kHz femtosecond laser (Intralase) and the manual microkeratome (Moria).

Methods: Eight corneas from eight donors were initially evaluated. Four endothelial lenticules were prepared using the Moria microkeratome and four were prepared using the 60 kHz femtosecond Intralase laser. The trephination diameter was 9.0mm with a depth of 400 microns. A spiral pattern was used with a firing rate of 60 kHz. The endothelial cell density was determined before each dissection, and was determined again 48 hours later. The cut surfaces of the endothelial lenticules were examined with scanning electron microscopy to evaluate the surface architecture.

Results: The mean age of the donors cut with the Moria was 59.5 years and with the Intralase was 67.3 years. The average death to preservation time for the Moria group was 5 hours and 7 minutes and for the Intralase group was 5 hours 27 minutes. There was no stastically significant difference between the preoperative endothelial cell counts of the Moria and Intralase groups ($p=0.80$) or between 48 hour post-operative endothelial cell counts ($p=0.72$). There was no significant difference in the change in ECD between the two groups ($p=0.13$). However, scanning electron microscopy demonstrated that the stromal surfaces of the Intralase-dissected lenticules were consistently more rough than the surfaces of the Moria-dissected lenticules.

Conclusion: Intralase-enabled dissection of the endothelial lenticule for endothelial keratoplasty has no detrimental effect on endothelial cell density, but produces a stromal surface that is qualitatively much rougher than the surface produced by the standard Moria microkeratome. In the next phase of this study the Intralase protocol will be altered to include a raster pattern and/or a double-pass ablation with an aim towards safely creating a smoother stromal surface.

Additional Author Credit: Robert M. Mullins, Ph.D.; Greg Schmidt

Progression of Age Related Macular Degeneration after Vitrectomy

A. Brock Roller, M.D., Ph.D.
Sponsor: James C. Folk, M.D.

Purpose: Recent studies have suggested that vitreous traction may play a role in neovascular age-related macular degeneration (AMD). Some investigators also believe that ischemia plays a role in AMD. Removal of the vitreous eliminates traction and improves oxygenation of the retina. We investigated the possibility that vitrectomy surgery reduces the progression of atrophic and/or neovascular AMD.

Methods: Retrospective case-control series. Included were subjects with AREDS category 3 AMD who underwent vitrectomy for an epiretinal membrane, macular hole or cataract complication. Subjects were excluded if they had a vitrectomy in both eyes, advanced (category 4) AMD, less than 2 years of follow-up, or a history of other significant retinal pathology. The fellow, non-vitrectomized eye was used as a case-control. Two vitreoretinal specialists evaluated fundus photographs of all eyes in a masked fashion. Primary endpoints for progression included onset or enlargement of geographic atrophy and development of choroidal neovascularization.

Results: Twenty-two patients who met the entry criteria were included. The average follow up interval was 5.6 years ± 3.6 years. Progression of AMD seen in 6/22 vitrectomized eyes compared to 12/22 non-vitrectomized eyes was statistically significant ($p=0.02$).

Conclusions: Our results suggest that vitrectomy does not worsen and may reduce progression of AMD, though our sample size is limited. Additional studies are needed to establish or refute this possibility.

Additional Author Credit: Vinit B. Mahajan,M.D., Ph.D.; Michael D. Abramoff, M.D., Ph.D.; Stephen R. Russell, M.D.; H. Culver Boldt, M.D.

Descemet's Stripping Automated Endothelial Keratoplasty for the Management of Iridocorneal Endothelial Syndrome

Matthew P. Rauen, M.D.
Sponsor: Kenneth M. Goins, M.D.

Purpose: Metaplastic corneal endothelium has been implicated in the pathogenesis of the iridocorneal endothelial (ICE) syndrome. This typically unilateral condition may manifest with vision threatening glaucoma and corneal edema. This clinicopathologic study evaluates the outcomes of patients with ICE syndrome who underwent Descemet-stripping automated endothelial keratoplasty (DSAEK).

Methods: In a retrospective chart analysis, five patients had DSAEK for the treatment of bullous keratopathy associated with ICE syndrome at the University of Iowa since December 2003. The preoperative diagnoses included Cogan-Reese syndrome (3/5) and Chandler's syndrome (2/5). Two eyes (40%) had DSAEK alone with pre-existing Seton placement, two eyes (40%) had DSAEK and phacoemulsification combined with seton placement, and one eye (20%) had DSAEK with phacoemulsification. All Descemet's membrane specimens acquired at the time of DSAEK were examined and characterized using histologic analysis. The follow-up period ranged from 3 to 36 months (mean, 20 months).

Results: The mean preoperative best corrected visual acuity (BCVA) was 20/400 (range 20/25 to 20/800, n = 5), which improved to 20/160 (range 20/20 to 20/400, n = 3) at 6 and 12 months. One of five patients (20%) had a dislocated DSAEK button after surgery, which necessitated a re-bubble procedure. The mean preoperative donor endothelial cell density (ECD) was 3090 ± 220 cells/mm^2 (n = 5). The postoperative ECD at 6 and 12 months was 1651 ± 186 and 1000 ± 932 cells/mm^2, which represents a 47 and 67% ECD loss (n = 3). Two eyes (40%) had allograft rejection between 12-24 months after DSAEK, with one necessitating a repeat DSAEK. Non-iatrogenic primary graft failure was observed in one eye (20%) at three months, which required a repeat DSAEK. After initial surgery, three eyes (60%) have remained clear during the postoperative follow-up period. Graft survival ranges from 3 to 36 months (mean 14.4 ± 13 months). No patients have experienced escalation of intraocular pressure during the postoperative course. The Descemet's membrane specimens obtained intraoperatively had variable thicknesses, rare endothelial cells, and lacked corneal guttae.

Conclusions: DSAEK for endothelial replacement in ICE syndrome is successful in the treatment of pain and vision loss from bullous keratopathy. However, ICE syndrome patients who require a re-bubble procedure after DSAEK and/or have more severe preoperative glaucoma are more likely to have a higher degree of ECD loss after surgery.

Additional Author Acknowledgement: Nasreen Syed, M.D.; John E. Sutphin, M.D.; Juan Fernandez de Castro, M.D.; Michael D. Wagoner, M.D., Ph.D.; Nasreen Syed, M.D.; W.L.M. Alward, M.D.; Young H. Kwon, M.D., Ph.D.

Sustained-release Timolol Maleate Microspheres: A New Treatment Approach for Glaucoma

Alina Dumitrescu, M.D., Ph.D.
Sponsor: Young H. Kwon, M.D., Ph.D.

Purpose: Poor compliance and ineffective delivery of topical drugs is a significant cause of failed medical treatment and disease progression in the glaucoma patient population. A drug delivery system that can be administered by the physician and provide a continuous supply of the medication would overcome the compliance issue and might preserve sight. Since glaucoma patients typically see their ophthalmologist once every 3-4 months delivery systems should be designed to be effective for this period. Here we investigate he efficiency and safety of a sustained release formulation of Timolol® which is administered by subconjunctival injection.

Materials and methods: Timolol maleate was complexed to poly(lactic-co-glycolic acid) (PLGA) microspheres. The average volume-weighted diameter is 15.9 ± 3.2 μm, and spheres contain Timolol at a drug to polymer ratio of 20% (40 mg drug/200 mg beads). These microspheres are re-suspended in saline immediately prior to injection and form homogenous slurry with minimal aggregation.

Following in vitro characterization spheres were delivered by subconjunctival injection to the eyes of two different mouse models of glaucoma. The IOP profile and the amount of Timolol in the aqueous humor were monitored up to 3 months. In addition, immunohistochemistry was carried out to detect a possible inflammatory response after injection. Currently, these experiments are repeated using NZW rabbits.

Results: In vitro studies demonstrated that the microspheres are capable of releasing Timolol for up to 107 days In mouse glaucoma models the IOP decreased after injection of Timolol- microspheres at a level comparable with traditional twice-daily drops. The concentration of the drug in the aqueous humor was maintained at levels known to be effective in humans for up to 90 days. A local inflammatory response was not detected. Studies in rabbits are ongoing, but have confirmed that subconjunctival injections of the microspheres are well tolerated.

Conclusions: Subconjunctival injection of microspheres has the potential to deliver active drugs to the aqueous humor for clinically relevant periods, without systemic or local side effects. This system removes patient compliance issues and has the potential to become the drug delivery system of choice for a subset of patients.

Additional Author Acknowledgement: Markus Kuehn, Ph.D.

Glaucoma Escalation after Deep Lamellar Endothelial Keratoplasty

George Wandling, **B.A., B.S.**
Sponsor: Michael D. Wagoner, M.D., Ph.D.

Purpose: To determine the prevalence and risk factors for escalation of glaucoma therapy after deep endothelial lamellar keratoplasty (DLEK).

Design: Retrospective case series

Participants: Seventy-six consecutive eyes of 73 patients undergoing primary DLEK and 11 eyes of 11 patients undergoing repeat DLEK after graft failure.

Methods: Retrospective review of every case of DLEK performed at the University of Iowa Hospitals and Clinics between December 1, 2003 and January 31, 2006.

Main Outcome Measures: Escalation of glaucoma therapy

Secondary Outcome Measures: Central corneal thickness (CCT), endothelial cell density (ECD), visual acuity, graft survival

Results: Escalation of glaucoma therapy occurred in 9 (11.8%) eyes following primary DLEK and in 5 (45.5%) eyes following secondary DLEK (P = 0.01). Following primary DLEK, 7 eyes required additional topical medical therapy and 2 eyes required surgical intervention. Following secondary DLEK, 4 eyes required additional topical medications and 1 eye required surgical intervention. Glaucoma escalation was not significantly associated with a worsened prognosis for graft survival, endothelial cell loss, or visual outcome after either primary or secondary DLEK.

Conclusions: Escalation of glaucoma therapy is more common after secondary DLEK than after primary DLEK. When present, it is not associated with an adverse outcome on visual acuity or graft survival.

Additional Author Acknowledgements: Mansi Parikh, M.D.; Kenneth M. Goins, M.D.; John E. Sutphin, M.D.; Young H. Kwon, M.D., Ph.D.; Emily C. Greenlee, M.D.; Wallace L.M. Alward, M.D.

Differential Diagnosis of Vertical Deviations

Amy Ellis
Sponsor: Richard J. Olson, M.D (Randy H. Kardon, M.D., Ph.D.)

Purpose: Skew deviation is usually a diagnosis made based on the exclusion of cranial nerve or extraocular muscle dysfunction. Instead, it is caused by an imbalanced input of information from the vestibuloocular system to the extraocular muscles. Currently there is no widely accepted clinical test available to positively support the diagnosis of skew. It has been suggested that measuring a patient's strabismus in supine position should show decreased deviation. Measuring the patient's vertical and torsional deviations in forward as well as supine body positions could become a practical method of helping clinicians diagnose skew deviation based on changes in these positions.

Methods: 25 patients with binocular vertical diplopia had vertical and torsional deviation measurements taken in primary, supine, and face forward body positions using the Maddox Wing. Patient diagnoses consisted of skew deviation, thyroid ophthalmopathy, myasthenia gravis, 4^{th} cranial nerve palsy, 3^{rd} cranial nerve palsy, and orbital floor fractures. Distance measurements were also taken in upright position in lateral gazes, vertical gazes, and head tilts. In addition, Bagolini lenses were used to measure torsion in upright primary position.

Results/Conclusion: Pending

Additional Author Credit: Pamela Kutschke, CO

Pediatric Ophthalmology Attire: Do Our Patients Prefer White Coats?

Amy Gilbertson
Sponsor: Richard J. Olson, M.D.

Purpose: To determine if patients in the Pediatric Ophthalmology and Adult Strabismus Service have a preference regarding physician and staff attire. It is a common perception that younger patients respond negatively to medical professionals in white coats, while older patients are thought to prefer more traditional attire.

Methods: Patients seen in the Pediatric Ophthalmology and Adult Strabismus clinic were invited to complete a three-question survey. One version of the survey was designed for patients thirteen years of age and older; the other was completed by parents of patients under thirteen years of age. Surveys were distributed and completed at the conclusion of the physician visit. Physician attire was recorded each day of the study to see if changes in attire (white coat vs. professional clothing without white coat vs. more casual attire without white coat) influenced survey responses.

Results/Conclusion: Pending

Additional Author Credit: Pamela Kutschke, CO, Melissa Madsen, CO, Wanda Pfeifer, OC(C), COMT

Can an Expert Be Wrong: Determining Diagnostic Agreement?

Narendra M. Patel, M.D.
Sponsor: Michael D. Abràmoff, M.D., Ph.D.

Background: The risk of blindness from diabetic retinopathy is 25 fold higher among individuals diagnosed with diabetes. By 2025, 75% (228 million individuals) of all diabetics will come from the developing world. With the recommendation of regular screening for all diabetics by the International Diabetes Federation, the need for low cost screening is an imperative. We, and others have developed and tested computer aided detection of diabetic retinopathy. We concluded that the algorithms are comparable to retinal specialists, however, also found large differences between experts, from different academic centers and countries.

Purpose: Our purpose is to determine the variability in the sensitivity and specificity for referable diabetic retinopathy among 3 different retina experts as compared to a single human observer.

Methods: 500 of 7689 exams (photographic sets) were randomly chosen and read independently by 5 masked retinal specialists. The results of these readings were compiled and data identifying pathology was codified and compared between observers. Agreement between specialists was determined for pathology identified as well as pathology noted by at least one observer that was not shared among two or more observers.

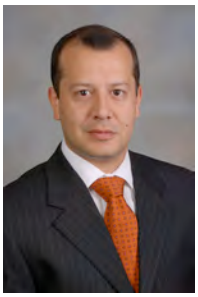
Results: The number of responses varied greatly between observers, ranging between 311 to 3245 across the dataset. Agreement of Responses: Observer A had the fewest responses (311) and had moderate agreement with each observer, whereas agreement for observers with >1500 responses declined. The variability seen among observers for responses ranged from 14% to 54% when evaluating agreement between at least 2 observers. Agreement of Nonresponses: Observer E had the greatest number of responses (3245) and good agreement between observers. This improved with observers with fewer responses. The variability seen among observers for nonresponses ranged from 0% to 97% when evaluating agreement between at least 2 observers. Accordingly, there was no agreement between all five observers for each nonresponse.

Conclusions: The variability among the independent readings by five masked retinal specialists presents challenges for the determination of a standardized reference dataset for diabetic retinopathy from which to base computer algorithms. These differences may be found due to differences in practice patterns, training, and independent observer thresholds for the presence of disease. The agreement noted between observers for nonresponses suggest good correlation when pathology was not seen. The variability of the responses, however, cannot be accounted for by sensitivity to identification of pathology alone.

Discussion: The lack of agreement between specialists for a standard dataset of photos with diabetic retinopathy suggests that other variables impact the expert in choosing or not choosing pathology. The "gain" set by each specialist may be different. In addition, parameters which constitute pathology would help to limit variability. Grading the experts response may aid in identifying the correlation between sensitivity and specificity among experts. Further work to characterize observer variability and determination of a standardized data set is being pursued through Retinopathy Online Challenges (http://roc.healthcare.uiowa.edu).

Additional Author Credit: Stephen R. Russell, M.D., James C. Folk, M.D., Jordan Graff, M.D., Frank D. Verbraak.

Cytokeratin Expression in Human Corneal Endothelium



Juan Fernandez de Castro, M.D.
Sponsor: Nasreen A. Syed, M.D.

Purpose: Aberrant expression of cytokeratins in corneal endothelial cells has been described in several corneal conditions including posterior polymorphous dystrophy (PPMD) and the iridocorneal endothelial (ICE) syndromes. The expression of cytokeratins has been used to distinguish these diseases from other conditions histopathologically. However, recent studies suggest that cytokeratin expression may be a more general manifestation of corneal endothelial dysfunction and that it may not be disease specific. The purpose of this study is to characterize the spectrum of cytokeratin expression in human corneal endothelium in Fuchs endothelial dystrophy (FED), pseudophakic bullous keratopathy (PBK), PPMD, epithelial downgrowth (ED) and ICE in order to determine if patterns of expression are disease specific.

Methods: Immunohistochemistry was performed on formalin-fixed, paraffin-embedded sections of twenty corneas with the diagnosis of FED, ten with PBK, four with ICE, six with PPMD, eight with ED and eight control corneas. Specimens were stained with monoclonal mouse antihuman antibodies CK 3/12, CK 5/6, CK 7, ZYM 5.2 (8 and 18), CK19, AE1/AE3 (CK 10,14,15,16,19 and CK 1,2,3,4,5,6,7,8), high molecular weight cytokeratin (HMWC) clone 34βE12 (CK 1, 5, 10 and 14) and vimentin, an intermediate filament found in mesenchymal cells. The sections were then analyzed using light microscopy and cells were graded as either positive or negative by two independent observers.

Results: CK 3/12 is consistently expressed in the endothelium of normal controls and all of the endothelial diseases. CK 5/6 is only positive in PPMD and ED. CK 7 appears widely expressed in all the diseases but not the controls. ZYM 5.2 is expressed only in a few cases of PPMD, PBK and FED. Vimentin is expressed uniformly in the control endothelial cells but is not present in some cases of ED and PPMD. The 34βE12 is only expressed in ED and PPMD after the cells lose their normal vimentin expression. AE1/AE3 and CK 19 are positive in all PBK but just some FED, suggesting a different mechanism of disease.

Conclusions: Cytokeratin expression, normally exclusive to epithelial cells, is present in normal endothelium and in various pathological states of the endothelium. HMWCs are expressed in ED and PPMD while low molecular weight cytokeratins are expressed in ICE, PBK and FED implying two distinct pathways resulting in endothelial dysfunction.

Patient Preference and Safety of Bilateral Intravitreal Injection of Anti-VEGF Therapy

Kori A. Elkins, M.D.
Sponsor: Vinit B. Mahajan, M.D., Ph.D.

Purpose: To determine patient preference and rate of endophthalmitis, cerebrovascular accident, and myocardial infarction following bilateral intravitreal injection of anti-VEGF agents.

Methods: Retrospective, noncomparative case series. A chart review was conducted of patients receiving bilateral, intravitreal anti-VEGF injections between August 2006 and October 2008 in the Department of Ophthalmology at the University of Iowa. The response to standardized questions regarding preferences and adverse events was collected.

Results: One hundred-one patients were identified receiving 348 total injections with a range of 1 to 13 bilateral injections and an average of 3.5. Subjects showed a strong preference for bilateral eye injections on the same visit rather than single eye injections on two different visits. Amongst those patients that previously had single eye injections, they reported a nearly equal level of discomfort with either regimen. There were no cases of endophthalmitis or myocardial infraction. One patient had a sensory stroke. There was one death.

Conclusions: In those patients with exudative age-related macular degeneration in both eyes, there is a strong preference for bilateral injections on a single visit. Although limited by the retrospective design and number of subjects, bilateral intravitreal injections appear safe.

Additional Author Acknowledgements: James C. Folk M.D. ; Stephen R. Russell M.D.; H. Culver Boldt M.D.; Karen M. Gehrs M.D.; Thomas A. Weingeist Ph.D., M.D.; Edwin Stone M.D., Ph.D.

Design and Testing of a Triplanar Sclerotomy for Sutureless 23-gauge Vitrectomy

Jordan Graff, M.D.
Sponsor: Vinit B. Mahajan, M.D., Ph.D.

Objective: To evaluate the intraoperative wound integrity of 23-gauge triplanar sclerotomies.

Methods: Consecutive case series of 102 sclerotomies from thirty-one eyes. Triplanar scleral wounds were created with a 23-gauge trocar. After an air-fluid exchange, unsutured scleral wounds were tested for permeability to vitreous, gas and fluid. Postoperative intraocular pressures were recorded at the first day, week and month.

Results: Triplanar sclerotomies were closed to vitreous, gas, and fluid in 98/102 (96%) wounds intrapoeratively. In the four open sclerotomies: gas escaped from two wounds, vitreous was detected in one, and Seidel testing was positive in one. There was no postoperative hypotony.

Conclusions: Triplanar 23-Gauge sclerotomies achieve a high rate of intraoperative wound closure.

Background: Sutureless 23-gauge wounds put patients at higher risk of endophthalmitis following vitrectomy. A new triplanar sclerotomy design was tested in vivo, and showed a high rate of intraoperative closure without sutures and no postoperative hypotony.

Precis: Creating a triplanar 23-gauge sclerotomy achieves high rate of intraoperative wound closure and may reduce the risk of endophthalmitis following vitrectomy.

Additional Author Credit: H. Culver Boldt, M.D., Michael D. Abramoff, M.D., Ph.D.[1], Stephen R. Russell, M.D., James C. Folk, M.D.

The Prevalence of Amblyopia and Its Relationship with the Child's Diagnosis and Age: The Iowa KidSight Vision Screening Experience

Alejandro Leon, M.D.
Sponsor: William E. Scott, M.D.

Purpose: Vision screening programs allow early detection of children with or at risk for amblyopia. We analyzed the effect of child's diagnosis and age on the prevalence of amblyopia in children screened by Iowa KidSight Vision Screening Program.

Methods: Database from Iowa KidSight Vision Screening Program was used to identify children referred to an eye specialist. The diagnosis from eye specialist, presence of amblyopia, and child's age were recorded and analyzed with logistic regression analysis.

Results: From May 1, 2000 to April 30, 2007, 2680 children were referred for an eye specialist evaluation. Follow-up information was available for 1981 children. Of these, 731 children were found to have amblyopia. After performing our statistical analysis we found significant interaction between diagnosis and age ($p=0.02$). We analyzed the effect of age on all diagnosis types and found only statistically significant increase of prevalence in amblyopia in the children with anisometropia ($p=0.002$) with increased age.

Conclusions: Among the different diagnosis groups, anisometropia was the only diagnosis group in which the prevalence of amblyopia increased significantly with age. Vision screening technologies have allowed earlier detection of this condition. Strategies for early treatment for anisometropic children could lead to prevention or early treatment of amblyopia. Continued efforts in early detection of this condition could lead to better outcomes.

Additional Author Acknowledgements: Susannah Q. Longmuir, M.D.; Richard J. Olson, M.D.; Wanda Pfeifer,OC(C), COMT; M. Bridget Zimmerman, Ph.D.

Descemet's Stripping Automated Endothelial Keratoplasty: Initial Severity vs. Surgical Outcome

Maneesh K. Mehan, M.D.
Sponsor: Michael D. Wagoner, M.D., Ph.D.

Purpose: To determine the correlation between initial severity of corneal endothelial decompensation and final outcome of primary Descemet's stripping automated endothelial keratoplasty (DSAEK).

Design: Retrospective case series

Participants: One hundred and thirty nine eyes of 123 consecutive patient undergoing primary DSAEK for either phakic corneal edema (79 eyes) or pseudophakic corneal edema associated with a posterior chamber intraocular lens (60 eyes) and for which 6 or more months of follow-up was available.

Methods: Retrospective review of every case of DSAEK performed at the University of Iowa Hospitals and Clinics between December 1, 2005 and January 31, 2007.

Main Outcome Measure: Best spectacle corrected visual acuity (BSCVA)

Secondary Outcome Measures: Central corneal thickness (CCT)

Results: Among 79 eyes with phakic corneal edema, preoperative BSCVA was 20/40 or better in 44 eyes, 20/50 to 20/70 in 25 eyes, and 20/80 or worse in 10 eyes. Postoperative visual acuity of 20/40 or better was obtained in 90.9 %, 84.0 %, and 90.0 % of eyes in these 3 groups, respectively. Visual acuity of 20/25 or better was obtained in 77.3 %, 12.0%, and 30.0 % of these eyes, respectively. Final BSCVA of 20/25 or better was significantly more likely to be obtained if the preoperative acuity was 20/40 or better ($P < 0.001$).Among 60 eyes with pseudophakic edema, preoperative BSCVA 20/40 or better in 20 eyes, 20/50 to 20/70 in 17 eyes, and 20/80 or worse in 23 eyes. Postoperative visual acuity of 20/40 or better was obtained in 85.0%, 88.2%, and 56.5% of eyes in these 3 groups, respectively. Visual acuity of 20/25 or better was obtained in 65.0 %, 35.3 %, and 17.4 % of these eyes, respectively. Final BSCVA of 20/40 or better was significantly more likely to be obtained if preoperative acuity was 20/70 or better ($P = 0.01$). Final BSCVA of 20/25 or better was significantly more likely to be obtained if the preoperative acuity was 20/40 or better ($P = 0.01$).

Conclusion: There was a statistically significant correlation between initial and final BSCVA in eyes undergoing DSAEK on univariate analysis. Multivariate regression analysis will be performed to exclude the contribution of ocular co-morbidity as a contributing factor to decreased preoperative and postoperative BSCVA in eyes with pseudophakic and phakic corneal edema.

Additional Author Acknowledgements: Kenneth M. Goins, M.D.; John E. Sutphin, M.D.

Macular-Optical Coherence Tomography can be used to Detect and Monitor Reduction in Total Retinal Thickness Caused by Hydroxychloroquine (Plaquenil) -Associated Visual Loss

Mansoor Mughal, M.D.
Sponsor: Randy H. Kardon, M.D., Ph.D.

Introduction: We discovered patients referred to our neuro-ophthalmology clinic with hydroxychloroquine-associated vision loss who had abnormal reduction of total retinal thickness in the macular OCT scan compared to age matched normal subjects. We reviewed all cases with hydroxychloroquine-associated visual loss seen in our clinic who also had macular OCT to delineate the occurrence of retinal thinning, correlate it with dosage and abnormalities of other tests of visual function as well as eventual outcome.

Methods: Nine patients with a diagnosis of hydroxychoroquine toxicity were identified who were tested by time domain OCT of the macular volume. Comparative testing included perimetry (kinetic and static), best-corrected visual acuity, digital fundus photography, and multifocal ERG (mfERG). Dose of hydroxychoroquine, relative to total body weight and lean body weight was calculated and compared to testing that was performed.

Results: Nine of 9 patients (100%) showed significant thinning of the total retinal thickness in sectors of the fast macula scan at the <1% level (red color on printout) compared to age matched (machine) normal eyes. The regional pattern of retinal thinning spared the superior-temporal retina in most cases. Visual acuity continued to worsen in almost all eyes with OCT retinal thinning after discontinuing Plaquenil®. Six of 9 patients were taking doses of hydroxychloroquine exceeding that recommended for lean body mass.

Conclusions: Total retinal thickness of the macula becomes abnormally thin in patients taking hydroxychloroquine when the dose exceeds recommendations based on *lean body mass*. The macula OCT may be a useful diagnostic indicator of early hydroxychoroquine retinal toxicity and could be easily used to detect and monitor retinal damage in patients at risk over time

Our Experience with Trabectome

Mansi Parikh, M.D.
Sponsor: Young H. Kwon, M.D., Ph.D.

Purpose: To describe clinical results after Trabectome.

Methods: Retrospective chart review of all Trabectome procedures performed at the University of Iowa between August 2007 and April 2009 by a single surgeon (YHK). Intraocular pressure and medication use before and after surgery was assessed.

Results: A total of 31 Trabectome procedures were performed. Twenty eyes underwent combined cataract extraction and Trabectome and eleven eyes underwent Trabectome alone. Average preoperative pressure was 23.3±9.5 mm Hg on 3.1±0.9 drops. At one month, the average drop in intraocular pressure was 7.9±9.8 mm Hg ($P<0.001$). Sixteen eyes had at least 6 months of follow up and 7 had at least 1 year follow up. At 6 months, the average intraocular pressure was 16.4±7.0 mm Hg and at 1 year was 12.6±4.3 mm Hg. Medication use at 1 year was 2±1.1. Two patients failed Trabectome and required trabeculectomy

Conclusions: Trabectome is a safe alternative to trabeculectomy. Most patients still require medications for intraocular pressure control after Trabectome

Efficient Molecular Testing for Genetically Heterogeneous Photoreceptor Degenerations

Audrey C. Ko
Sponsor: Edwin M. Stone, M.D., Ph.D.

Purpose: Retinitis Pigmentosa (RP) is a term used to describe a genetically heterogeneous group of retinal degenerations that are inherited in an x-linked, autosomal dominant, or autosomal recessive manner. These permanently blinding conditions affect 76,000 people in the United States. Autosomal Recessive RP (ARRP) is responsible for approximately 70% of all RP. At least 22 genes are associated with ARRP and many remain to be discovered. Genetic characterization of an inherited disease is critical to understanding the disease mechanism, determining prognosis and designing treatments. The high degree of genetic heterogeneity within ARRP has made genetic screening and gene discovery difficult, expensive, and time consuming. To make ARRP testing more efficient, we drastically narrowed the search for disease-causing mutations by coupling a focused allele-specific test with conventional DNA sequencing.

Methods: 401 patients and 313 controls were screened with a multiplex PCR assay (SNPlex, Applied Biosystems) designed to detect 101 known disease-causing mutations in 12 genes associated with ARRP. Identified mutations were confirmed with bidirectional DNA sequencing. Genes found to harbor one disease allele were then completely sequenced to find a second disease allele.

Results: Mutations were identified in 33/410 (8.2%) ARRP patients and 3/313 (0.9%) controls. A second disease allele was identified in 4/33 (12.1%) patients. Five novel mutations were detected with DNA sequencing.

Conclusions: We used a novel approach to create a cost and time-efficient genetic test for ARRP. This high-throughput assay has significantly increased our ability to detect previously reported disease-causing mutations and greatly increased the efficiency of detecting novel mutations. The current detection rate of 8.2% would identify disease-causing mutations in over 4,300 ARRP patients in the United States if all affected patients could be screened. The ability to detect both common and rare genotypes will aid in making genotype-phenotype correlations, studying disease mechanisms, and identifying patient subgroups eligible for specific treatments. Moreover, as patients continue to be screened through the assay, the patients with negative findings will create an enriched pool of patients for gene discovery. Finally, the flexibility of this multiplatform strategy will allow us to increase our detection rate as new genes and disease-causing mutations are discovered.

Additional Author Acknowledgements: Emily I. Schindler, William J. Kimberling, Ph.D.

The Value of MRI in the Diagnosis of Giant Cell Arteritis

Fabiana C. Policeni, M.D.
Sponsor: Randy H. Kardon, M.D., Ph.D.

Purpose: To demonstrate that head and neck MRI scanning with gadolinium contrast can be a valuable tool in the diagnosis of giant cell arteritis and may also have potential as an additional monitoring tool for assessing immunosuppressive treatment (i.e. prednisone) over time. This is based on recent reports of specific MRI findings of arterial wall enhancement in patients with giant cell arteritis.

Methods: We will perform a retrospective study to determine the sensitivity and specificity of MRI findings of segmental arterial wall enhancement in patients who have had a positive temporal artery biopsy and who also happened to have had MRI scans. We will compare patients with a positive biopsy with the control group that had a negative biopsy. Based on a preliminary chart review, we have found approximately 120 patients who had a biopsy for suspicion of giant cell arteritis (GCA) and who also had a MRI scan of the head and neck that will be retrospectively analyzed. We estimate 40 patients to be studied with biopsy proven giant cell arteritis and an MRI scan and 80 patients with a negative biopsy and an MRI scan. We propose to evaluate the MRI findings of their previous scans, looking for mural thickening and/or presence of mural enhancement with gadolinium.

Results: The study is in progress. The results will be presented during Ophthalmology Resident and Fellow Research Day.

Conclusion: Our conclusion is that study should have more than sufficient power to detect a difference in the positive MRI findings between groups.

Additional authors acknowledged: J. Maley, P. Wheeler

Immunohistochemical Study of the Diamond-Dusted Tano Scratchers after Macular Surgery

Rizwan Somani,, M.D.
Sponsor: Vinit B. Mahajan, M.D., Ph.D.

Purpose: To identify the tissues removed following application of Tano diamond-dusted scrapers to the macula.

Methods: A Tano diamond-dusted scraper was applied to the macula of human donor eyes. The retina was fixed in 4% paraformaldehyde and processed for immunohistochemistry. Anti-laminin and DAPI stain were used to identify the internal limiting membrane and cell nuclei. A similar analysis was performed directly on the instrument tips following vitrectomy for macular hole.

Results: The macula showed distinct areas of limited and complete ILM tissue disruption. The tips of the Tano diamond-dusted tip scraper showed laminin-A positive tissue fragments and limited numbers of cells.

Conclusions: When applied to the macula, brushing the Tano diamond-dusted scraper disrupts the ILM of the retina. This technique may be sufficient to achieve macular hole closure at rates comparable to complete ILM peeling.

Additional Author Acknowledgements: Stephen R. Russell M.D.; James C. Folk M.D.; H. Culver Boldt M.D.; Karen M. Gehrs M.D.; Robert F. Mullins Ph.D.

Excused from presentation: Manuscript requirement completed

Endotine Forehead device effect on brow lift over time

Arpitha Muthialu Charlu, M.D.
Sponsor: Jeffrey A. Nerad, M.D.

Background: The Endotine Forehead 3.5 (Coapt Systems, Palo Alto, Calif.) has recently become more popular for use in endoscopic brow lifts for many reasons. The implantable bioabsorbable fixation device is designed to provide multipoint distributed tension for fixation during brow lift in a rapid manner. The multiple benefits include ease of use, the ability to adjust intraoperatively, fewer side effects with less pain, paresthesia, and alopecia as seen with the open coronal technique. Hesitation exists over the ultimate longevity of elevation, as compared with the coronal brow lift, largely considered to be the gold standard to which other methods are compared.

Purpose: The purpose of this study was to evaluate early results in a series of endoscopic brow lift cases using the Endotine Forehead device and to determine if there is any brow descent over a 6 month follow up period.

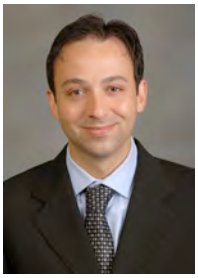
Methods: A retrospective review was done on 20 patients who underwent endoscopic brow lift using the Endotine Forehead device (original version polylactide homopolymer and 3.5 mm tines) between October 2005 and October 2007 at the University of Iowa under the supervision of two oculoplastic surgeons. Preoperative and postoperative standardized photographs were taken in the Frankfort horizontal plane. Two measurements, midpupil to superior brow and lateral canthus to superior brow, were compared from the preoperative period to the 1 week-1 month postoperative period and the 4-6 month postoperative period.

Results: Twenty patients were evaluated with at least 4-6 months of postoperative follow up. The mean age was 61 ± 22 years of age and all patients had visual functional deficits from brow ptosis. One week-1 month postoperatively, the mean percent increase compared to preoperatively for midpupil to superior brow was 28.5% and lateral canthus to superior brow was 18.8%. Four-six months postoperatively, the mean percent increase compared to preoperatively for midpupil to superior brow was 18.9% and lateral canthus to superior brow was 9.7%. The amount of brow descent from immediate postoperatively to 4-6 month postoperatively for midpupil to superior brow was 34% and lateral canthus to superior brow was 48%. There was one report of mild subcutaneous discomfort at the edge of the endotine platform and no reports of device extrusion, device removal, numbness, paresthesia, or alopecia.

Conclusions: The Endotine Forehead device provides significant brow elevation with minimal adverse events; however, there is significant brow descent (34-48% decrease) just over the 6-month postoperative period seen in our study patients. Further long-term studies are needed to determine the pattern of descent over time and if and when the end of the curve is a plateau. Based on the amount of descent over time, immediate postoperative goal brow height may need to be adjusted, or intraoperative changes, such as additional fixation methods, are needed to enhance the longevity of the brow lift effect.

Excused from presentation: Manuscript requirement completed

Penetrating Keratoplasty (PKP) versus Deep Anterior Lamellar Keratoplasty (DALK) For the Treatment of Keratoconus



Alex W. Cohen, M.D., Ph.D.
Sponsor: Michael D. Wagoner, M.D., Ph.D.

Purpose: The goal of this study was to compare the outcomes of penetrating keratoplasty (PKP) and deep anterior lamellar keratoplasty (DALK) in the treatment of keratoconus.

Design: Retrospective, nonrandomized comparative case series.

Participants: Forty-seven patients who underwent either PKP (36 eyes, 36 patients) or DALK (11 eyes, 11 patients) between January 1, 2000 and December 31, 2006 at the University of Iowa Hospitals and Clinics were included in the study.

Main Outcome Measures: Best-corrected visual acuity (BCVA), refractive results, keratometry, and complications

Results: Among 35 patients who were treated with PKP, the mean age was 37 years (range, 17 to 78) and the mean follow-up was 44 months (range, 13 to 74). Among 11 patients treated with DALK, the mean age was 44 years (range, 26 to 58) and the mean follow-up was 24 months (range, 6 to 41). There were no statistically significant differences between PKP and DALK with respect to final BCVA, spherical or cylindrical refraction, and keratometry. Final BCVA of 20/40 or better was obtained in 30 (83.3%) eyes after PKP and 9 (82%) eyes after DALK ($P = 1.0$). Final visual acuity of 20/25 or better was obtained in 27 (75.0%) eyes after PKP compared to 5 (45.5%) eyes after DALK ($P = 0.13$). Final visual acuity of 20/20 or better was obtained in 20 (55.6%) eyes after PKP compared to 3 (27.3%) eyes after DALK ($P = 0.16$). Complications that occurred after PKP included endothelial rejection episodes (14 eyes), wound dehiscence (7 eyes), endophthalmitis (1 eye), bacterial keratitis (1 eye), and interface scar (2 eyes). Complications that occurred after DALK included interface scar (4 eyes), and wound dehiscence (3 eyes).

Conclusion: Treatment of keratoconus with PKP or DALK is associated with similar visual outcomes and complication rates. While DALK offers the benefit of elimination of the risk of immune-mediated endothelial rejection, PKP provides a higher percentage of patients with final BCVA of 20/25 or better.

Additional Author Acknowledgements: Kenneth M. Goins, M.D.; John E. Sutphin, M.D.

Excused from presentation: Manuscript requirement completed

Visual Acuity, Refractive Error, and Endothelial Cell Density Six and Twelve Months after Deep Lamellar Endothelial Keratoplasty

Parley Fillmore, M.D., Ph.D.
Sponsor: Kenneth M. Goins, M.D.

Abstract: Purpose: To report the visual acuity, refractive outcome, and endothelial cell density (ECD) up to 1 year following deep lamellar endothelial keratoplasty (DLEK) in a large prospective series. Methods: Eighty-six DLEK procedures were performed and evaluated in a prospective, interventional case series. Subgroup analysis was performed to compare results from large incision (9 mm) DLEK [n=7], small incision (5-8 mm) DLEK [n=70], and penetrating keratoplasty (PKP) conversion [n=9]. Outcome measures included best corrected visual acuity (BCVA), manifest refraction, corneal topographic astigmatism, and ECD.

Results: The percentage of eyes that achieved a BCVA of 20/40 or better after DLEK was 55% at 6 months, increasing to 61% at one year. Topographic astigmatism and spherical equivalent were not significantly different than preoperative measurements up to one year following DLEK ($p > 0.05$). An endothelial cell loss of 40% at 6 months and 48% by one year was observed. The mean ECD after DLEK was 1831 ± 472 cells/mm2 at 6 months and 1569 ± 601 cells/mm^2 at 12 months. When evaluated by incision size, the ECD was better at 2066 ± 558 cells/mm^2 with a 9mm incision compared to only 1516 ± 585 cells/mm^2 with a smaller incision at one year, although this did not reach significance ($p = 0.075$). The endothelial cell loss after PKP-conversion was similar to the large incision group ($p > 0.05$).

Conclusions: DLEK provides good visual acuity (≥20/40) for the majority of patients at 1 year with stable refractive error compared to baseline. Refractive stability was observed with both large and small incision DLEK, however worrisome endothelial cell loss was observed, especially with a small incision technique.

Additional Author Credit: John E Sutphin, M.D.

Excused from presentation: Manuscript requirement completed

Outcomes after Descemet's Stripping Automated Endothelial Keratoplasty

Parisa Taravati, M.D.
Sponsor: Kenneth M. Goins, M.D.

Purpose: To determine the best-corrected visual acuity (BCVA) and corneal endothelial cell density (ECD) 1, 3, 6 and 12 months following Descemet's stripping endothelial keratoplasty (DSEK). The incidence of postoperative pupillary block, lenticule dislocation, and secondary procedures was also examined.

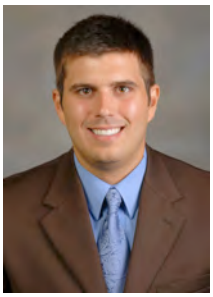
Methods: A retrospective review was done of 97 eyes (89 patients) that underwent DSEK between August 2005 and November 2006 at the University of Iowa. Baseline data included age, BCVA, and diagnosis. Outcome measures were recorded at 1, 3, 6, and 12 months postoperatively. ECD was measured predominantly using non-contact specular microscopy, when permitted by corneal clarity.

Results: The mean age at surgery was 71 ± 11 years. Preoperatively, the mean best-corrected visual acuity was 0.7 logMAR ± 0.6 logMAR, and the mean donor ECD was 3007 ± 299 cells/mm^2. Of the 97 eyes, 64 had Fuchs' endothelial dystrophy, 24 had pseudophakic bullous keratopathy, 1 had bullous keratopathy, 6 had failed penetrating keratoplasty grafts, 1 had a failed DSEK graft, and 1 had Fuchs' endothelial dystrophy with anterior stromal fibrosis. Fifty-four eyes underwent DSEK only, 37 underwent combined phacoemulsification and DSEK, 3 underwent DSEK and anterior vitrectomy, 1 underwent DSEK and synechiolysis, 1 underwent DSEK and superficial keratectomy, and 1 underwent DSEK and Ahmed shunt revision. The incidence of postoperative pupillary block was 20%. One patient developed aqueous misdirection requiring pars plana vitrectomy and peripheral iridectomy. The incidence of lenticule dislocation was 25%, all requiring lenticule repositioning and air tamponade. The incidence of iatrogenic graft failure was 3% and allograft rejection 1%, all requiring repeat DSEK. Mean postoperative BCVA was 0.5 logMAR ± 0.5 logMAR (n=93) at 1 month, 0.3 logMAR ± 0.3 logMAR (n=82) at 3 months, 0.3 logMAR ± 0.3 logMAR (n=76) at 6 months, and 0.3 logMAR ± 0.4 logMAR (n=53) at 12 months. The mean postoperative ECD was 1973 ± 648 cells/mm^2 (n=29) at 1 month, 2083 ± 601 (n=41) cells/mm^2 at 3 months, 1939 ± 539 cells/mm^2 (n=20) at 6 months, and 1575 cells/mm^2 ± 624 cells/mm^2 (n=29) at 12 months.

Conclusions: DSEK provides rapid visual rehabilitation and excellent BCVA in patients with endothelial dysfunction. Despite leaving just enough air in the anterior segment to cover the disc edges, there was a high rate of postoperative pupillary block and lenticule dislocation in this series. These findings confirm the necessity of multiple postoperative examinations immediately after DSEK in order to diagnose and treat complications.

Additional Author Acknowledgements: John E. Sutphin, M.D.

Excused from presentation: Manuscript requirement completed



DSAEK: Fold vs. Pull-Through Insertion Technique

Lucas J. Wendel, M.D.
Sponsor: Michael D. Wagoner, M.D., Ph.D.

Purpose: To compare the suture pull-through and forceps delivery techniques used in Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK).

Methods: A retrospective chart review of 56 eyes from 55 patients who underwent DSAEK between December of 2005 and September of 2007 at the University of Iowa was performed. All eyes included in the study had at least 12 months of post-operative followup. Outcome measures included best spectacle-corrected visual acuity (BSCVA), central corneal thickness, and endothelial cell density (ECD). These were compared at 12 months post-operatively. Because not all patients had all outcome measures recorded at their 12 month post-operative visit, most recent outcome measures, which could range from 6 months to 24 months post-operatively, were compared as well. Preoperative BSCVA, amount of followup, and donor characteristics were also compared between the two groups.

Results: There was no significant difference between the groups in terms of preoperative BSCVA or length of follow-up. Differences in all donor characteristics, including age, death-to-preservation time, preservation-to surgery time, ECD, lenticule thickness, and lenticule diameter, failed to reach statistical significance. At 12 months from surgery, mean BSCVA in the forceps delivered group was 0.27 logMAR (range 0.0-1.0 logMAR) and 0.31 logMAR (range 0.0-1.1 logMAR) in the suture pull-through group. Mean central corneal thickness was 627 $\pm$ 53 μm in the forceps delivered group and 628 $\pm$ 47 μm in the suture pull-through group. Percentage ECD loss was 52 $\pm$ 22% in the forceps delivered group and 54 $\pm$ 29% in the suture pull-through group. None of these outcomes showed a statistically significant difference. Most recent BSCVA was 0.26 logMAR (range 0.0-0.7 logMAR) in the forceps delivered group and 0.32 logMAR (0.0-1.1 logMAR) for the suture-pull through group. Mean central corneal thickness at last follow-up visit was 634 $\pm$ 47 μm and 641 $\pm$ 67 μm in the forceps delivered and suture pull-through groups, respectively. Percentage ECD loss was 51 $\pm$ 21% in the forceps delivered group and 44 $\pm$ 22% in the suture pull-through group. None of these outcomes showed a statistically significant difference.

Conclusions: The suture pull-through and forceps delivery method of performing DSAEK offer comparable outcomes in regards to best-corrected visual acuity, pachymetry, and endothelial cell loss after 12 months of follow-up.

Additional Author Credit: Kenneth M. Goins, M.D., John E. Sutphin, M.D.

Excused from presentation: Manuscript requirement completed

Comparison of Resident and Fellow Optic Disc Cup and Rim Segmentation from Stereo Photographs using Computer-Aided Planimetry

E. Bo Yang, M.D.
Sponsor: Michael Abràmoff, M.D., Ph.D.

Purpose: Optic disc segmentation into cup and rim for diagnosis of glaucoma is subjective and requires pattern recognition and experience. Learning may be more effective if the residents' or glaucoma fellows' assessment can be compared objectively, accurately, and instantaneously to a reference standard. Longitudinal assessment of the trainee's progress would also be informative. We have developed an online tool (Truthseeker, http://webscreen.ophth.uiowa.edu/disc) to objectively compare residents' and fellows' computer-aided planimetry with an expert's evaluation of cup and rim on digitized stereo optic disc images. Here, we evaluate and compare the performance of residents or fellows according to training level using this tool.

Methods: Six ophthalmology residents and 3 fellows performed online planimetry by delineating disc and cup margin on 57 pairs of stereo photographs from 57 eyes from 57 patients with suspected or open-angle glaucoma with varying severity (example in Figure). A reference standard (rs), was previously created for this dataset by having 3 glaucoma faculty evaluate these images. The fellows' and residents' planimetry were compared to the reference standard in two ways: linear cup-to-disc ratio $\left(lcdr = \sqrt{N_c / (N_r + N_c)}\right)$ and accuracy (number of pixels assigned correctly/total number of pixels).

Results: The correlation of 3 first year residents with the reference standard was 0.58 (95% CI, 0.38-0.73), 0.72 (0.57-0.83), and 0.77 (0.64-0.86); of second year residents 0.45 (0.22-0.64), 0.66 (0.48-0.79), and 0.75 (0.61-0.85); and of the 3 glaucoma fellows 0.73 (0.58-0.83), 0.81 (0.70-0.88), and 0.86 (0.74-0.93), respectively. The accuracy of correctly assigning each pixel to the right structure (rim, cup, or background) for the first year residents was 0.90, 0.91, 0.93; of the second years 0.92, 0.92, 0.94; and of the fellows 0.95, 0.95, and 0.96, respectively.

Conclusion: The Truthseeker can be used as a testing tool to evaluate trainee performance on the evaluation of optic disc assessment. In this preliminary study, the glaucoma fellows as a group performed better than residents on stereoscopic optic disc images. The glaucoma fellows also produced more consistent results; whereas, the residents produced more varying results. We are currently extending this study to include a larger number of residents at multiple ophthalmology residency programs.

Additional Author Acknowledgement: W.L.M. Alward, M.D., and Young H. Kwon, M.D., Yian Jin Jones, M.D.

RESIDENT/FELLOW RESEARCH DAY – 2009

Friday, May 15, 2009

Participant Financial Disclosure

Research Day as well as research by Residents and Fellows of the University of Iowa Department of Ophthalmology and Visual Science is supported in part by an unrestricted grant from Research to Prevent Blindness, Inc., New York, NY

No author reported any commercial or financial interests associated with the presentation.

Financial Relationship Disclosure

For purposes of this disclosure, a known financial relationship is defined as any financial gain or expectancy of financial gain brought to the Contributor or the Contributor's immediate family (spouse, domestic partner, parent, child or spouse of child, or sibling or spouse of sibling of the Contributor) by:

- Direct or indirect compensation;
- Ownership of stock in the producing company;
- Stock options and/or warrants in the producing company, even if they have not been exercised or they are not currently exercisable;
- Financial support or funding to the investigator, including research support from government agencies (e.g. NIH), device manufacturers, and/or pharmaceutical companies; or
- Involvement with any for-profit corporation that is likely to become involved in activities impacting The University of Iowa Department of Ophthalmology & Visual Sciences where the Contributor or the Contributor's family is a director or recipient of a grant from said entity, including consultant fees, honoraria, and funded travel.