RESIDENT / FELLOW RESEARCH DAY

Department of Ophthalmology and Visual Sciences

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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

Friday, May 11, 2018

UNIVERSITY OF IOWA HEALTH CARE

Department of Ophthalmology and Visual Sciences

RESIDENT/FELLOW RESEARCH DAY – 2018

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Aaron M. Ricca, MD
Brittni A. Scruggs, MD,PhD
Daniel C. Terveen, MD

FIRST-YEAR RESIDENTS

Matthew Benage, MD
Anthony T. Chung, MD
Austin R. Fox, MD
Benjamin J. Janson, MD
Heather A. Stiff, MD

TRANSITIONAL INTERNS

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Alexis K. Warren, MD
Caro line W. Wilson, MD

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GUEST FACULTY

Robert W. Nickells, PhD

Frederick A. Davis Professor
Department of Ophthalmology and Visual Sciences
University of Wisconsin-Madison

Rob Nickells was initially trained as a developmental biologist at the University of Calgary, in Calgary Alberta, Canada, where he received his PhD in 1987. After completing a post-doc in developmental biology at Caltech, he received training in visual sciences first at Indiana University and later at the Wilmer Eye Institute of the Johns Hopkins University School of Medicine. At Johns Hopkins he was involved in the early analysis of the mechanism of cell death in glaucoma in the laboratories of Drs. Donald Zack and Harry Quigley. Since 1994, Dr. Nickells has continued these studies as a faculty member of the Department of Ophthalmology and Visual Sciences at the University of Wisconsin-Madison. Using mouse models of acute and chronic ganglion cell death, his laboratory has helped identify several points of the cell death pathway that may serve as vital targets for intervention therapies.

Dr. Nickells has received several accolades for his work in the field of glaucoma, including sharing the Lewis Rudin Prize for glaucoma research in 1995 from the New York Academy of Medicine, the Ruth Salta Junior Investigator Achievement Award for glaucoma research in 1996 and 1998, the Douglas Johnson Memorial Award from the American Health Assistance Foundation in 2008, the Bright Focus Foundation Thomas R. Lee Award for Glaucoma Research in 2018, and from Research to Prevent Blindness, a Career Development Award in 1995, the Robert E. McCormick Scholar Award in 2002, the Lew Wasserman Research Award in 2008, and a Senior Scientist Award in 2014.

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The University of Iowa
Department of Ophthalmology and Visual Sciences
Resident and Fellow Research Program would like to thank
Research to Prevent Blindness
for their continued support of Resident Research

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8:00 Breakfast - Blodi-1 and Blodi-2 Conference Rooms

8:30 Welcome: **Ian Han, MD; Michael Wagoner, MD, PhD**

8:36 – 9:50 **Scientific Papers, Session I**
Braley Auditorium
Moderator: Michael Wagoner MD, PhD

10:00 – 10:25 **Morning Break**
Blodi-1 and Blodi-2 Conference Rooms

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10:25 – 11:30 **Scientific Papers, Session II**
Braley Auditorium
Moderator: Pavlina S. Kemp, MD

10:25 Introduction: Pavlina S. Kemp, MD, Moderator

10:30 **Spenser Morton, MD**, sponsor: Michael Wagoner, MD, PhD .....page 8
Prevalence and severity of evaporative dry eye syndrome after cataract surgery

10:42 **Daniel Terveen, MD**, sponsor: Thomas Oetting, MD, MS .....page 9
Accuracy of partial coherence interferometry in patients with large inter-eye axial length difference

10:54 **Daniel Feiler, MD**, sponsors: James Folk, MD; Ian Han, MD .....page 10
Automated Posterior Vitreous Inflammation Measurement using Optical Coherence Tomography

11:06 **Ze Zhang, MD**, sponsor: John H. Fingert, MD, PhD .....page 11
Association between genotype and phenotype in exfoliation syndrome

11:18 **Sun "Sunny" Young Lee, MD, PhD,** sponsors: Edwin M. Stone, MD; Ian C. Han, MD .....page 13
Longitudinal macular changes in gyrate atrophy: correlation of cystoid macular edema with serum ornithine levels

11:30 – 12:30 **Keynote Address**
Braley Auditorium

11:30 **John Fingert, MD, PhD,** Introduction of Robert W. Nickells, PhD, Keynote speaker

11:35 **Robert Nickells, MD, PhD,** "Treating ganglion cells in glaucoma: A long and winding road"

12:30 – 1:25 **Buffet Luncheon**
Melrose Conference Center, 5th Floor, PFP

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1:25 – 2:30 **Scientific Papers, Session III**
Braley Auditorium
Moderator: John Fingert, MD, PhD

1:25 Introduction: John Fingert, MD, PhD, Moderator

1:30 **Christy Cunningham, MD**, sponsors: Ian Han, MD; Edwin Stone, MD, PhD .....page 14
Scleral pits are a sign of disease severity in choroideremia

1:42 **Bryce Radmall, MD**, sponsors: Keith Carter, MD; Erin Shriver, MD.....page 15
Treatment of recurrent ptosis after Muller's muscle-conjunctival resection with repeat Muller's muscle-conjunctival resection

1:54 **Sam Abbassi, MD, MS**, sponsors: Ian Han, MD; Edwin Stone, MD, PhD .....page 16
Predominance of hyperopia in patients with molecularly confirmed Best disease

2:06 **Tara McGehee, MD,** sponsor: Mark A. Greiner, MD .....page 17
Outcomes of resident performed Descemet membrane endothelial keratoplasty (DMEK)

2:18 **Elaine Binkley, MD,** sponsor: H. Culver Boldt, MD .....page 18
Gene expression profiling and outcomes in patients with uveal elanoma

2:30 **Ian Han, MD,** Closing Remarks

RESIDENT/FELLOW RESEARCH DAY - 2018

Morning Session – Paper 1

The impact of recipient diabetes mellitus status on Descemet membrane endothelial keratoplasty outcomes

Ben Janson, MD

Primary Supervisor: Mark Greiner, MD

Background and Purpose: Diabetes mellitus is an increasingly prevalent disease that is known to cause damage to numerous organs of the body. Recent studies have shown deleterious effects of diabetes on the corneal endothelium including reduced tissue preparation success, morphologic derangements, decreased mitochondrial function, increased endothelial cell loss after cataract surgery, and increased rates of penetrating keratoplasty graft failure. However, the influence of the recipient's diabetes status on keratoplasty outcomes is poorly understood. With a growing diabetic population and increased utilization of keratoplasty, understanding this interaction is important to optimizing patient visual outcomes and quality of care. The purpose of this study is to evaluate Descemet membrane endothelial keratoplasty (DMEK) outcomes using nondiabetic grafts in diabetic and nondiabetic recipients.

Methods: A retrospective case series was performed on all eyes that underwent DMEK between October 2012 and February 2017. Eyes with less than three months follow-up were excluded. Each case was evaluated for repeat grafting, case time, indication, presence of an orienting "S stamp" on the graft, preoperative and postoperative visual acuities, presence of diabetic retinopathy, and insulin use. The need for a rebubble procedure as well as the occurrence and timing of graft failure and graft rejection were recorded. All donor tissues were from nondiabetic donors. Recipient diabetes status was subdivided into non-insulin dependent (NIDDM) and insulin dependent (IDDM) diabetes mellitus.

Results: Of 385 eyes analyzed (280 subjects, mean follow-up 591 days), 71 (18.4%) were diabetic recipient eyes. In comparison of the graft failure rate (n=22), there was no difference based on the presence or absence of diabetes (p=0.604). Over one year the mean visual acuity improved by four lines for diabetic recipients (20/70 to 20/30) and nearly five lines for nondiabetic recipients (20/70 to 20/25-2). Diabetic recipients had a higher mean logMAR acuity (p=0.058, mean difference of 0.063) averaged over all post-DMEK time intervals tracked. Rebubble procedures were more common in diabetic (15/71) versus nondiabetic (43/314) recipients (p=0.078, hazard ratio of 1.69 [95% CI: 0.94, 3.04]).
In comparison of primary grafts and repeat grafts, there was a significant difference in the graft failure rate (p=0.002) and visual acuity change (p=0.003), necessitating subgroup analysis controlling for repeat graft status. With repeat grafts excluded, diabetic recipients had a trend for increased rebubble procedures (p=0.111, hazard ratio 1.68 [95% CI: 0.89, 3.19]) and a statistically significant higher mean logMAR acuity (p=0.027, mean difference of 0.067).
Of primary grafts, the rates of rebubble were highest for IDDM (28.6%) compared to NIDDM (16.7%) and nondiabetic recipients (12.9%). The difference between IDDM recipients compared to nondiabetic recipients requiring a rebubble procedure reached statistical significance (p=0.037, hazard ratio 2.39 [95% CI: 1.04, 5.50]).

Conclusion: In patients with primary DMEK grafts, the rates of rebubble procedures were highest among IDDM recipients and this difference was statistically significant compared to nondiabetic recipients. In all groups and subgroup analyses, recipient diabetes showed trends or statically significant differences with higher mean logMAR acuity over one-year follow-up. Other outcomes, including graft failure rates, were equivalent in this series.

Morning Session – Paper 2

Long term evaluation of interferon alpha-2B as adjunctive therapy for conjunctival melanoma

Matthew Benage, MD

Primary Supervisor: Mark Greiner, MD

Background and Purpose: Conjunctival melanoma (CM) is a rare but potentially deadly ocular surface tumor. The current standard of care is wide local excision followed by double freeze-thaw cryotherapy to margins. However, recurrences are common due to incomplete excision and multifocal disease. Topical chemotherapeutic agents have been described as adjuvant therapies to enhance remission of disease, including mitomycin C (MMC) and interferon alpha-2b (IFN). There is significant literature regarding the use of MMC; however, there is motivation to find a less toxic chemotherapeutic agent for the adjunctive management of CM. Recent interest in IFN has arisen in the treatment of CM due to its more favorable side effect profile and efficacy against conjunctival squamous cell carcinoma. In this study, we report the use of adjunctive IFN in cases of biopsy proven conjunctival melanoma following biopsy and cryotherapy.

Methods: In this retrospective observational study, we conducted a chart review to identify all biopsy proven conjunctival melanoma cases treated between 1997 and 2017 at the University of Iowa Hospitals and Clinics (UIHC). All cases were included regardless of whether the initial surgical excision was performed at UIHC or performed by a referring physician. Of these, we identified cases in which topical interferon drops (1 million units four times daily for 3-6 months) were prescribed after the initial excision due to positive surgical margins. We noted the origin of CM (nevus, primary acquired melanosis [PAM], or de novo); presence and location of margins that were positive for residual melanoma; duration of IFN treatment; recurrence rate; time to development; and outcome at last follow-up.

Results: Of 26 cases of CM included for analysis, topical IFN was used in 5 cases (19.2%) as an adjuvant treatment to excisional biopsy. The indication for adjunctive use of topical IFN was positive surgical margins following excisional biopsy. The preceding lesion was PAM with atypia in 4 cases, and compound nevus in 1 case. In 3 cases, there were positive margins on the biopsy specimen for invasive melanoma. In all 3 of these cases, there was recurrence of CM after use of topical IFN that resulted in metastatic disease and death in 1 case, enucleation in 1 case, and repeat excisional biopsy with ultimate remission of melanoma in 1 case. In 2 cases, the surgical margins were positive for PAM with atypia with complete excision of CM. Both of these cases resulted in remission of melanoma with no recurrence at last follow-up (54 and 33 months, respectively).

Conclusions: Our results suggest that adjunctive use of topical interferon after excisional biopsy of conjunctival melanoma may be useful in preventing recurrence of disease in cases of surgical margins positive for PAM with atypia. However, our results also demonstrate that use of adjunctive topical interferon in cases where surgical margins are positive for invasive melanoma does not always lead to remission of disease and caution should be applied when considering interferon use in this context.

Morning Session – Paper 3

The Effect of Transcranial Direct-Current Stimulation on Microsurgical Simulation Performance

Anthony Chung, MD

Supervisors: Erin Shriver MD, FACS; Elliott Sohn, MD

Background and Purpose: Transcranial direct current stimulation (tDCS) is a rising area of research in the field of medicine. tDCS has been shown to improve skill acquisition, retention, and performance of various tasks when applied to the primary motor cortex, such as finger pinch and sequence tasks, dynamic lower extremity balancing tasks, and Olympic ski jumping. Evidence suggests short term effects of tDCS include lowering of neuronal membrane potentials, release of calcium from neurons and glial cells, and synergistic firing of action potentials via recruitment of neurons. In turn, brain derived neurotrophic factors are released to consolidate and strengthen newly formed synapses. The purpose of this proposed study is to evaluate the effect tDCS has on microsurgical skill acquisition as measured on Eyesi, a cataract surgical simulator.

Methods: Undergraduate and medical students from the University of Iowa are eligible to participate in this study. Participants will complete a questionnaire regarding handedness and history of fine motor activities. Participants will be randomized to either control or tDCS groups. tDCS will be provided using the Halo Neurostimulation System; a consumer product developed by Halo Neuroscience (San Francisco, CA). All participants will perform a baseline evaluation on the anti-tremor task on Eyesi that will be used to determine the level of difficulty of the training task. All participants will wear the Halo Neurostimulation System. Those in the control group will receive sham stimulation with a gradual increase in current over 30 seconds followed by gradual decrease in current over 30 seconds; where as those in the tDCS group will receive stimulation via the device that will be applied for 20 minutes in a single, continuous session. Participants will practice on the anti-tremor module on Eyesi throughout the stimulation period. Participants will then be instructed to train on Eyesi for 40 additional minutes after tDCS is completed. Participants will be provided a break after every two trials and will be allowed as many additional breaks as needed during the training period. After this training period, participants will complete another trial on Eyesi to be analyzed for intervention effect. Participants will then follow up for 2 additional training sessions following the same procedure over the next week. Participants will complete a trial to be analyzed for effect upon arrival. Participants will then receive either sham or tDCS stimulation for 20 minutes while training on Eyesi as day 1. Participants will continue to train on Eyesi for an additional 40 minutes and complete an additional training trial for analysis.

Results: The IRB submission has been approved and data collection is ready to begin.

Conclusions: The hypothesis of this study is that participants receiving true tDCS from the Halo Neurostimulation System will have better total scores and faster task completion times as measured on Eyesi compared to the control group receiving sham stimulation.

Morning Session – Paper 4

Curriculum for Improving Emergency Department Care of Orbital Compartment Syndrome

Austin Fox, MD

Primary Supervisors: Thomas Oetting, MD; Erin Shriver, MD

Background and Purpose: Timely diagnosis and treatment of orbital compartment syndrome (OCS) is critical for vision preservation. OCS is often managed by the ophthalmology service at academic centers, however, emergency department (ED) physicians diagnose and treat the majority of patients with OCS. An resident-initiated quality improvement project examining the care of University of Iowa Hospitals and Clinics (UIHC) ED patients with OCS between 2016-2017 revealed areas for improvement including: identification of OCS, timing of hospital transfer and ophthalmology consultation, measurement of IOP, and completion of a successful lateral canthotomy/cantholysis (LCC). To improve the quality of care for ED patients with OCS, a curriculum was established.

Methods: The Orbital Compartment Syndrome curriculum consisted of an pre-test focused on orbital anatomy, diagnosis, and management of OCS; a self-directed study including assigned reading and a video of LCC; an ophthalmology-led didactic session reviewing orbital anatomy, the clinical signs and management of OCS, the steps of LCC (including video), tonopen instructions, and a case-based critical analysis of the management and outcomes of patients who recently presented to the ED; and a post-test containing similar questions as the pre-test.

Results: A total of 33 Emergency Medicine and Surgery residents completed the 18-question pre-test. Twenty participants (61%) were able to identify the significant clinical signs of OCS. On a Likert scale, only 27% reported confidence in their ability to identify OCS and 21% expressed confidence in their ability to perform LCC. A 60 minute didactic session was conducted with the Emergency Medicine and Trauma Surgery residents and staff. Of the 22 participants who completed the post-test survey, the percentage reporting confidence in their ability to identify OCS and to perform LCC increased to 82% ($p<0.0001$) and 64% ($p=0.0021$), respectively.

Conclusions: The Orbital Compartment Syndrome curriculum improved the understanding of OCS and its management by Emergency and Surgery residents. In a multidisciplinary approach to improve outcomes, this curriculum will serve as a resource for educating emergency personnel about OCS at UIHC and other institutions, with the ultimate goal of reducing unnecessary vision loss. Future studies are underway to assess the clinical benefit of the Orbital Compartment Syndrome curriculum.

Morning Session – Paper 5

Vision Screening Outcomes in Children Less Than 3 Years of Age Compared to Children Older than 3 Years of Age

Heather Stiff, MD

Primary Supervisor: Scott Larson, MD

Background and Purpose: The USPSTF states that vision screening is recommended for children ages 3-5, but that current evidence is insufficient to assess the benefits and harms in those younger than age 3. In a response from AAPOS to this USPSTF recommendation, it was stated that early critical periods of neurodevelopment exist in infancy and early childhood, during which identification and treatment of amblyopia are most optimal. AAPOS therefore recommended that attempts to perform photoscreening should begin at the 12 month well child visit. A non-profit vision photoscreening program called Iowa Kidsight has been in existence since 2001 and has screened children as young as 6 months of age. This study aim was to compare the rates of amblyopia and treatment outcomes of children less than 3 years of age to those 3 years and older who failed photoscreening with Iowa Kidsight.

Methods: This was a retrospective chart review of children between 6 months and 5 years of age who failed photoscreening by Iowa KidSight and were subsequently seen at the University of Iowa from July 2001 to December 2014. Data related to amblyopia, treatment, and vision outcomes were recorded. These subjects were split into two groups; < 36 months of age and 36 months of age or older for comparison.

Results: Of 304 subjects, 21% were 0-2 years and 79% were 3 years or older at the time of screening. Amblyopia rates were statistically similar in the two groups with 19% in the younger group and 30% in the older group ($p=0.09$). Normal vision was attained on average at 35.27 months of age in the younger group and 68.58 months in the older group ($p <0.0001$). There were 8% of children in the younger group who did not attain normal vision and 40% in the older group ($p=0.028$).

Conclusions: Vision screening in children younger than 3 years of age identifies similar numbers of children with amblyopia compared with ages 3 and older. The younger group attained normal vision at a significantly younger age and were more likely to attain normal vision in follow-up. This study shows that earlier vision screening and referral leads to a better chance of attaining normal vision and at a younger age, thus providing evidence for vision screening in children under 3 years of age.

Morning Session – Paper 6

Acanthamoeba Keratitis in the Midwest: A retrospective study and updated treatment guidelines

Brittni Scruggs, MD, PhD

Primary Supervisor: Mark Greiner, MD

Background and Purpose: Acanthamoeba is a ubiquitous protozoon that feeds on bacteria and yeast. Due to its ability to encyst in extreme environmental conditions, this organism is difficult to kill. Present in public water sources, it is known that patients develop acanthamoeba keratitis mainly from using, wearing, or cleaning contact lenses inappropriately. Acanthamoeba is commonly misdiagnosed as herpetic, bacterial, or fungal keratitis prior to being confirmed with culture or confocal microscopy. The combination of late diagnoses and the amoeba's resistance to killing makes these cases especially challenging for the treating ophthalmologist.

There are several agents available to treat of Acanthamoeba keratitis. However, the optimal timing, dose, and combination of agents has not been established. Systemic therapies are used occasionally as adjunctive therapy for recalcitrant cases. Steroid use remains controversial. Given that treatment regimens vary, we aimed to analyze all Iowa acanthamoeba cases over the last two decades to determine differences in outcomes when comparing treatment regimens, timing, and dosing. We aimed to identify causes of treatment failure in order to establish an algorithm for diagnosis and management of these cases. Furthermore, we gathered epidemiological data to identify potential sources of water contamination in Iowa.

Methods: To date, 104 patients with Acanthamoeba keratitis have been identified as being treated at UIHC Department of Ophthalmology between 1991 and 2017. We retrospectively analyzed the clinical records of these patients. Specifically, we compared patient demographics, risk factors, clinical course, medical and/or surgical treatments, and outcomes of these complicated cases. We used these data to design a protocol for both diagnosing and treating Acanthamoeba, in addition to preventing serious complications. IRB approval was obtained.
Results: A total of 104 patients were treated for Acanthamoeba keratitis in the period of analysis (mean age at diagnosis, 32.9 years). Of these, 84% were contact lens wearers with identifiable risk factors. All patients were known to have at least one identifiable risk factor for developing Acanthamoeba keratitis including overnight wear, fresh water swimming, showering in contacts, extended use of contacts, and using tap water to clean contacts. Nearly all patients (94%) were treated with chlorhexidine; additionally, 62% were treated with PHMB, 30% with brolene, and 15% with pentamidine. More than half (51.2%) required surgery (keratoplasty, enucleation, glaucoma surgery, cross-linking, etc.) and 25% of developed recurrence despite surgery. HSV co-infection was common (52%). The prevalence of Acanthamoeba keratitis increased over the study period and most patients lived in close proximity to a major Iowa river.

Conclusion: Acanthamoeba keratitis can resemble other infectious keratitis etiologies and is often misdiagnosed. Treatment with multiple anti-amoeba drugs is essential to disease resolution, and while surgery is frequently required to treat this infection it is not always successful. The prevalence of Acanthamoeba keratitis has increased over two decades at the University of Iowa and proximity to a major water source appears to be a risk factor for developing Acanthamoeba keratitis.

Morning Session – Paper 7

Intravitreal Fluocinolone Acetonide (ivFAc) may Decelerate Diabetic Retinal Neurodegeneration (DRN)

Stephanie Lynch, MD

Primary Supervisor: Michael Abràmoff, MD, PhD

Background and Purpose: There is no prevention or treatment for diabetic retinal neurodegeneration (DRN), which is a complication of diabetes that can occur independently of diabetic retinopathy (DR). We hypothesized that an intravitreal fluocinolone acetonide (ivFAc) implant may affect the rate of DRN when used in patients with diabetic macular edema (DME).

Methods: In this retrospective analysis, optical coherence tomography with neuroretinal analysis was obtained at 3-month intervals from 130 patients in the US Retrospective Chart Review in Patients Receiving ILUVIEN® study. We compared inner retinal thickness before (mean duration 903 days, range 35-4005 days) and after (mean 408 days, range 7 to 756 days) administration of ivFAc. The rate of DRN was defined as the change over time on OCTna using logistic regression. A DRN rate was calculated independently for 4 concentric macular regions centered on the fovea.

Results: In regions of the macula greater than 1 mm from the central fovea, there was a statistically significant decrease in rate of DRN in the post-ivFAc period. In the macula lying between 1 and 2 mm from the central fovea, pre-ivFAc neuroretinal loss was 2.7 μm/year, compared with a post-ivFAc loss rate of 0.4 μm/year ($p = 0.001$).

Conclusions: This retrospective study demonstrates that ivFAc decelerated the rate of inner retinal thinning in patients with active DME. Further studies are necessary to determine the effects of ivFAc on the rate of DRN in patients with diabetes who do not have DME.

Morning Session – Paper 8

Prevalence and Severity of Evaporative Dry Eye Syndrome after Cataract Surgery

Spenser Morton, MD

Primary Supervisor: Michael Wagoner, MD, PhD

Background and Purpose: It is a common anecdotal observation that many patients with a history of cataract surgery have evaporative dry eye syndrome secondary to eyelid meibomian gland dysfunction. While the association between LASIK surgery and dry eye symptoms in young LASIK patients has been definitively documented, the association between cataract surgery and similar changes in older patients has not been thoroughly investigated. It is not clear whether the increased prevalence of evaporative dry eye in pseudophakic patients is due to the coincidental occurrence of this relatively common condition in older patient populations or if the cataract surgery itself actually increases the likelihood of its development (when absent) or worsens its severity (when already present).

Methods: We conducted a prospective, non-randomized study to test the hypothesis that differences may exist between the operated and non-operated eyes of veterans with unilateral pseudophakia with respect to objective evidence of meibomian gland dysfunction and evaporative dry eye syndrome. The inclusion criteria included presentation at the Iowa City Veterans Affairs Medical Center Eye Clinic for routine follow-up of unilateral pseudophakia between March 1, 2017 and December 31, 2017 on a day when one of the investigators was present to review the case and offer study participation. Exclusion criteria included any history of intraocular surgery (other than uncomplicated cataract surgery), ocular surface or intraocular disorders requiring medical or laser therapy (other than dry eye syndrome), or eyelid surgery. Data that was collected from veterans who provided informed consent to participate in the study included LipiView imaging of the meibomian glands and measurement of the tear lipid layer thickness over a 20 second interval, and slit lamp evaluation of meibomian gland expressibility, tear film break-up time and fluorescein staining. The main outcome measure was a comparison of the degree of preservation of normal meibomian gland anatomy in the operated vs. the non-operated eye (as judged by 3 masked observers). Secondary outcome measures were differences between the operated and non-operated eye with respect to the maximum and minimum thickness of the lipid tear film layer (in microns), meibomian gland expressibility (graded on a scale of 0 to 15), tear film break up time (in seconds), and fluorescein staining (graded on a scale of 0 to 8).

Results: Eighteen of 19 veterans who met the inclusion criteria were enrolled in the study. The average age of the participants was 68.6 years (range, 43-88). The mean interval from cataract surgery to enrollment was 53.7 months (range, 7-310). The meibomian gland anatomy was graded as worse in the operated eye in 4 cases, worse in the non-operated eye in 5 cases, and similar in 9 cases (P = 1.0). Dry eye symptoms were present in 11 cases and absent in 7 cases. When present, dry eye symptoms were symmetric in every case. There were no significant differences between the operated and non-operated eyes with respect to maximum lipid layer thickness (mean = 81.5 vs. 87.9 microns; P = 0.25), minimum lipid layer thickness (mean = 67.8 vs. 71.0 microns; P = 0.69), meibomian gland expressibility (mean = 5.1 vs. 5.6; P = 0.58), tear film break up time of less than 5 seconds (n = 7 vs. 5; P = 0.73), or fluorescein score (mean = 0.7 vs. 0.6; P = 0.87).

Conclusion: Our findings do not support the hypothesis that cataract surgery is associated with an increased prevalence of meibomian gland dysfunction and evaporative dry eye syndrome.

Morning Session – Paper 9

Accuracy of Partial Coherence Interferometry in Patients with Large Inter-eye Axial Length Difference

Daniel Terveen, MD

Primary Supervisor: Thomas Oetting, MD, MS

Background and Purpose: Accurate pre-operative biometry is essential for intraocular lens (IOL) selection in cataract surgery, and is commonly obtained with partial coherence interferometry (PCI). A difference of > 0.3 mm in axial length (AL) between eyes on PCI measurement often triggers confirmatory measurements. To determine whether confirmatory measurements are necessary in patients with large inter-eye AL difference, we performed a retrospective chart review to compare the observed-expected post-operative spherical equivalent (SE) between patients with and without an AL difference of >0.3 mm.

Methods: Retrospective chart review of all patients undergoing cataract surgery at two institutions over a one-year period was performed. Exclusion criteria including IOLMaster SNR<100, pre-operative cylinder of >3D, toric IOL, history of refractive surgery, cataract surgery combined with any other surgery, any intra- or post-operative complication, or POM1 BCVA <20/20 were applied, and 131 eyes of 93 patients were included. Control patients without an AL difference > 0.3 mm were identified and matched for age, sex, and AL. The expected post-operative refraction for the implanted IOL using Holladay II, SRK-T, and Hoffer Q formulae was calculated. The observed post-operative refraction at the post-op month one (POM1) visit was recorded. A difference of observed-expected SE of > 0.5 diopters (D) was chosen to be significant. The Mann-Whitney U Test was used to compare the mean observed-expected SE for each formula. A two-tailed Fisher's exact test was used to evaluate the number of cases vs controls whose observed SE was at least either 0.5 D or 1.0 D away from the expected SE.

Results: Mann-Whitney U Testing found no significant difference between the observed-expected POM1 SE for any of the 3 formulae tested. The two-tailed Fisher's exact test found no significant difference in the number of cases vs controls with a post-operative SE at least 0.5 D or 1.0 D different from the expected post-operative SE outcome.

Conclusions: Good-quality PCI data is equally accurate in patients with AL difference > 0.3 mm, with no statistically significant difference in the observed-expected SE on POM1 refraction for patients with vs without a > 0.3 mm difference in AL using IOLMaster 500 pre-operative biometry measurements. Confirmatory AL measurements (e.g. with immersion A-scan biometry) in patients with large inter-eye AL difference may not be necessary.

Morning Session – Paper 10

Automated Posterior Vitreous Inflammation Measurement using Optical Coherence Tomography

Daniel Feiler, MD

Primary Supervisors: James Folk, MD; Ian Han, MD

Background and Purpose: The degree of vitreous inflammation is important for following disease severity and treatment response in uveitis, but clinical measurement is highly subjective, and no reliable imaging-based method of measurement currently exists. This study was to determine the feasibility of automated quantification of posterior vitreous inflammation on optical coherence tomography (OCT) and to assess its correlation with clinician-graded OCT and vitreous haze scores.

Methods: This was a retrospective, observational study of patients with active posterior uveitis or panuveitis. At each clinic visit, OCT volume scans (512x128) of the posterior vitreous were obtained by centering the scan on the fovea and placing the retina at the lowest part of the scan window (Cirrus 5000 HD-OCT, Carl Zeiss Meditec, Dublin, CA). Volume scans were sectioned into individual frames, and contrast was adjusted in a standardized fashion across all included scans to eliminate the fine, granular pattern felt to represent noise in lower signal scans. Larger, hyperreflective foci, felt to represent clumps of inflammatory cells, were quantified using the marching squares algorithm, which encapsulates each identified region in a unique path and approximates the diameter, allowing selective quantification of foci based on pixel size (DotCount, v1.2, LCLN, Cambridge, MA). An OCT grade was assigned based on the average number of hyperreflective foci per OCT frame. Pearson's correlation was then used to compare automated OCT grades to clinician-graded OCT scores based on OCT standards, as well as vitreous haze grade by clinical examination.

Results: Automated OCT grade correlated well with clinician-measured OCT grade (R = 0.79) in 21 patients, 31 eyes and poorly with clinical haze grade (R = 0.099) in 8 patients, 16 eyes.

Conclusions: OCT may be useful for visualizing posterior vitreous inflammation, which can be quantified using an automated algorithm with good correlation to clinician grading. The poor correlation with vitreous haze is likely due to the small sample size and relatively low grades of inflammation in the study population.

Morning Session – Paper 11

Association between Genotype and Phenotype in Exfoliation Syndrome

Ze Zhang, MD

Primary Supervisor: John H. Fingert, MD, PhD

Background and Purpose: Exfoliation syndrome (XFS) is common cause of glaucoma and visual disability that has a strong genetic basis. Seven genetic risk factors for XFS have been discovered: AGPAT1, CACNA1A, LOXL1, POMP, RBMS3, SEMA6A, and TMEM136. However, little is known about the influence of these factors on clinical features of XFS. The purpose of this pilot study was to search for associations between risk factor genotypes and clinical characteristics of exfoliation syndrome (XFS) and exfoliation glaucoma (XFG).

Methods: The medical charts of 162 patients previously diagnosed with XFS or XFG in the Glaucoma Clinic at the University of Iowa were reviewed. Clinical diagnosis of XFS or XFG was made by direct visualization on slit lamp examination of typical pattern of exfoliation material on the anterior lens capsule or pupillary margin or in the angle. XFG was diagnosed as those showing XFS with intraocular pressure (IOP) greater than 22 mm Hg and a presence of typical glaucomatous cupping and visual field loss. Each subject was graded for several key clinical features of disease including: age at diagnosis, family history, asymmetric disease, maximum intraocular pressure (IOP), central corneal thickness (CCT), trabecular meshwork pigmentation, iris transillumination defects, zonular instability, and complications during cataract extraction. DNA was collected from XFS patients (n=162) and matched control subjects (currently n=10) and tested for high risk alleles at each of the seven XFS risk factor gene loci using a real-time PCR assay. The total number of risk alleles for each patient was recorded. The association between risk factor genotype and clinical features was examined using the Chi-square test and Fisher's exact test.

Results: The 162 unrelated exfoliation cases comprised of 156 with XFG. The mean age of diagnosis was 68.8 $\pm$ 10.5 years (range 32-94). The gender distribution was 116 (71.6%) females and 46 (28.4%) males. One-hundred-fifteen patients had bilateral disease, and 81 (50%) had a positive family history of glaucoma. Only 22 (13.6%) of the patients remained phakic in both eyes by the end of the last know follow-up. Of the 140 patients who had undergone cataract extraction in at least one eye, 130 (80.2%) had in-the-bag placement of their intraocular lenses. Forty-five (27.8%) of patients showed any signs of zonular pathology, including evidence of phacodonesis, lens subluxation, need for capsular tension ring, or signs of zonular dehiscence during cataract surgery. Bulls-eye pattern of exfoliation deposits on the anterior lens capsule was documented on 123 (75.9%) of the cases. Peri-pupillary transillumination defects were noted in 37 (22.8%) of the patients. One-hundred-eight (66.7%) patients had a maximum IOP 30 mm Hg or greater. Seventy-two patients had CCT of 535 um or greater. Clinical notes described 66 (40.7%) of the patients as having asymmetric disease. Gonioscopy showed angles that were open to ciliary body band or wider in 137 (84.6%) patients. Sixty-seven (41.4%) of the patients had a documented trabecular meshwork pigmentation of 3+ or more, though only 41 (25.3%) patients had a documented Sampolesi's line on gonioscopy. The average total number of risk alleles was 4.1$\pm$1.4 (range 2-8). Statistical analysis showed significant associations between thinner CCT and the number of risk alleles (uncorrected p=0.033) as well as higher maximum IOP and the number of risk alleles (uncorrected p=0.028).

Conclusions: This pilot study described the phenotypic range of XFS in patients from the Glaucoma Clinic at the University of Iowa. A typical XFS patient was a 70 year-old pseudophakic

female with a maximum IOP over 30 mm Hg. Our pilot study further suggests that the number of genetic risk alleles may be proportional to a patient's maximum IOP and/or CCT. Further studies to confirm these potential associations are with additional XFS patients and normal control subjects are warranted.

Morning Session – Paper 12

Longitudinal macular changes in gyrate atrophy: correlation of cystoid macular edema with serum ornithine levels over a 7-year trial of low protein diet

Sun Young Lee, MD, PhD

Primary Supervisors: Edwin M. Stone, MD, PhD; Ian C. Han, MD

Background and Purpose: The therapeutic benefit of a low protein diet in patients with gyrate atrophy is debated. Here, we describe longitudinal changes in the macula in a patient with gyrate atrophy during a trial of low protein diet over 7 years.
Methods: Clinical data was reviewed from a 7-year-old-girl with molecularly confirmed gyrate atrophy placed on a low protein diet in coordination with the pediatric nutrition team. Central macular thickness measured on serial spectral-domain optical coherence tomography (SD-OCT) imaging was correlated with serum ornithine levels over time (until age 14).
Results: Cystoid macular edema was observed on SD-OCT imaging prior to any clinically-apparent chorioretinal atrophy in the macula. Central macular thickness was found to have a positive correlation with serum ornithine levels ($R=0.73$), and this correlation was statistically significant ($P<0.05$).
Conclusion: Our data suggests a potential beneficial effect of a low protein diet on cystoid macular edema in gyrate atrophy.

Afternoon Session – Paper 13

Scleral pits are a sign of disease severity in choroideremia

Christy Cunningham, MD

Primary Supervisors: Ian Han, MD, Edwin Stone, MD, PhD

Background and Purpose: Choroideremia is an X-linked retinal dystrophy characterized by progressive chorioretinal atrophy. Recently, a novel observation of focal scleral excavations, termed "scleral pits," was reported in patients with choroideremia. These pits may have corresponding hyporeflective channels in the sclera on optical coherence tomography, termed "scleral tunnels." This study aims to characterize the frequency of scleral pits and correlate their presence with measures of disease severity.

Methods: This was a retrospective chart review of consecutive patients with molecularly confirmed choroideremia seen at the University of Iowa. Age, gender, visual acuity, and genotype were recorded for each patient. Clinical testing, including Goldmann visual fields, color fundus photographs, and optical coherence tomography were reviewed, and the presence of scleral pits on color fundus photographs determined by two independent graders. For patients with longitudinal data, the patient's vision and age at the earliest visit where a scleral pit was seen were also recorded.

Results: Sixty eyes from 30 patients, including 9 disease-manifesting female carriers, were analyzed. Eight out of 21 affected males (38.1%) had scleral pits on fundus photographs, and in all but one patient, these pits were seen in both eyes (15 out of 42 eyes; 35.7%). Thirteen out of 19 affected males (68.4%) with available OCT imaging had scleral tunnels, and these were bilateral in all but 3 patients (23 out of 38 eyes, 60.5%). No scleral defects were visualized on fundus photography or OCT in any female carriers. Patients with a scleral defect (pit or tunnel) were older (45.3 versus 35.8 years old) than those without scleral defects. Eyes with scleral defects had worse mean visual acuity (logMAR 0.9; Snellen equivalent 20/146 versus logMAR 0.2; Snellen equivalent 20/28). Among eyes with scleral defects, 11/25 eyes (44.0%) had loss of the I2e isopter on GVF, versus 3/24 (12.5%) in those without scleral defects. Similarly, 14/25 eyes (56.0%) with scleral defects had <20 degree central island to the V4e, versus 5/24 eyes (20.1%) without scleral defects. Of those with an available refraction, the average spherical equivalent in eyes with a scleral defect was -2.73 compared to -0.82 in eyes without a scleral defect. Notably, in 2 patients, the formation and progression of scleral pits were observed with serial fundus photography, suggesting that these scleral excavations are not congenital but related to degeneration.

Conclusions: Scleral pits are relatively common in patients with choroideremia. These pits likely represent degeneration at areas of focal scleral weakness (e.g. the insertion of the long posterior ciliary arteries) and are seen in eyes with more severe disease. Further study is needed to evaluate possible genotype-phenotype correlations for this peculiar fundus finding.

Afternoon Session – Paper 14

Treatment of Recurrent Ptosis After Muller's Muscle-Conjunctival Resection with Repeat Muller's Muscle-Conjunctival Resection

Bryce Radmall, MD

Primary Supervisors: Keith Carter, MD; Erin Shriver, MD

Background and Purpose: There has been much debate and numerous studies in the field of oculoplastics regarding the best approach to ptosis repair (external vs internal). More recently, an internal approach with Mueller's muscle conjunctival resection (MMCR) has been favored if adequate response to phenylephrine testing and adequate levator function is demonstrated pre-operatively. This approach maintains a natural contour while successfully elevating the eyelid. Traditionally, recurrent ptosis after initial MMCR has been treated with a levator advancement through an external approach. To date, there has been no report in the literature of attempt to correct eyelid ptosis with a repeat MMCR after having undergone the same procedure previously. The aim of the study is to determine if repeat MMCR is a viable approach in the treatment of recurrent eyelid ptosis.

Methods: IRB approval was obtained and patients from two academic centers with duplicate CPT codes for ptosis repair were identified. A retrospective chart review of patients who underwent repeat MMCR from 1997 -2018 was then performed (N = 11). External photos were obtained pre-operatively, post-operatively after the first MMCR procedure, and at last follow up after the repeat MMCR. Computer imaging software (Image J) was used to perform digital image analysis to evaluate lid position in pre and post-operative photos. The primary outcome measure assessed was margin to reflex distance (MRD1) to calculate the objective change in lid height following ptosis repair.

Results: Digital image analysis is currently under review. We hypothesize that a second MMCR procedure after initial MMCR will produce adequate elevation of the eyelid given that the patient was responsive to phenylephrine testing pre-operatively.

Conclusions: Once complete, this study will help to objectively quantify the utility of a repeat MMCR procedure for recurrent ptosis after prior MMCR. Should our hypothesis prove correct, an internal approach to ptosis repair may be a viable alternative to an external levator advancement.

Afternoon Session – Paper 15

Predominance of hyperopia in patients with molecularly confirmed Best disease

Sam Abbassi, MD, MS

Primary Supervisors: Ian Han, MD; Edwin Stone, MD, PhD

Background and Purpose: Best disease is a hereditary maculopathy caused by mutations in *BEST1*. The most common phenotypic presentation is a subfoveal vitelliform lesion, which evolves over time. Recently, it was observed that patients with Best disease have a predilection for hyperopia. Our study aims to characterize the refractive error in molecularly confirmed Best disease and to correlate the change in vitelliform lesion size on optical coherence tomography (OCT) with the change in refractive error.

Methods: This was an IRB-approved retrospective chart review of 117 consecutive patients with molecularly confirmed Best disease. Visual acuity and manifest refraction were recorded on multiple visits and compared to age-matched patients with Stargardt disease. A subset of patients with multiple refractions and OCT data on the same day were reviewed to correlate changes to central macular thickness and total macular volume with changes to manifest refraction. Paired t-tests were used to determine statistically significant change in manifest refraction, central macular thickness, and total macular volume over time.

Results: For patients with Best disease, 73/106 (69%) were hyperopic. The average spherical equivalent for the right eye was +1.18 diopters (range -3.75 to +9.25). The average spherical equivalent for the left eye was +1.27 diopters (-3.00 to +8.00). The average spherical equivalent for both eyes was +1.21 diopters. For patients with Stargardt disease, 90/106 patients (85%) were myopic. The average spherical equivalent for the right eye was -1.44 diopters (-8.88 to +4.00). The average spherical equivalent for the left eye was -1.50 diopters (-6.38 to +5.00). The average spherical equivalent for both eyes was -1.47 diopters. There was a statistically significant difference in the mean spherical equivalent for the right eye, left eye, and both eyes between best disease and age-matched Stargardt patients ($p<0.001$ for all comparisons). Changes in manifest refraction in patients with Best disease did not seem to correlate with changes in central macular thickness on OCT.

Conclusions: In our population of patients with Best disease, there is a predominance of hyperopic refractive error relative to patients with Stargardt disease. This difference may be of diagnostic value in early stage disease, especially in the absence of molecular analysis. The degree of hyperopia in Best disease patients seems to be independent of the size of the vitelliform lesion as assessed by OCT. The *BEST1* gene product has been shown to play a role in ocular development and may be involved in the pathogenesis of hyperopia in the patients with Best disease. Further studies are needed to elucidate the underlying mechanism for hyperopia in Best disease patients.

Afternoon Session – Paper 16

Outcomes of Resident Performed Descemet Membrane Endothelial Keratoplasty (DMEK)

Tara W. McGehee, MD

Primary Supervisor: Mark A. Greiner, MD

Purpose: To report the outcomes of Descemet membrane endothelial keratoplasty (DMEK) performed by trainees versus experienced attending surgeons.

Methods: In this retrospective case series, we evaluated clinical outcomes of 262 eyes from 202 patients who underwent DMEK surgery at the University of Iowa between October 1, 2014 and February 7, 2017. Main outcome measures were operative time, best-corrected visual acuity (BCVA), endothelial cell density (ECD), and postoperative complications.

Results: The operative time was lower for cases performed by fellows (50 minutes) than by residents (58 minutes) or attending surgeons (56 minutes) (p=0.005). The rebubble rate was lower for cases performed by residents (2.0%) than by fellow (25.7%) or attending surgeons (26.9%) (p=0.007). There was no significant difference between groups in graft rejection, primary graft failure, best-corrected visual acuity measured at 1, 6, or 12 months post-operatively, or endothelial cell density measured at 6 or 12 months post-operatively.

Conclusion: Resident performed DMEK surgery is safe and does not result in longer operative time or increased postoperative complications in a supervised training environment.

Afternoon Session – Paper 17

Gene expression profiling and outcomes in patients with uveal melanoma

Elaine Binkley, MD

Primary Supervisor: H. Culver Boldt MD

Background and purpose: Despite excellent local tumor control, patients with uveal melanoma have a 50% risk of developing metastatic disease. Predicting which patients are at the highest risk of developing metastatic disease is of critical importance for counseling patients, designing metastatic surveillance protocols, and establishing therapeutic targets. Different strategies including examining clinical features, histopathology, and tumor molecular analyses have been used in an effort to provide prognostic information for patients. Gene expression profiling (GEP) is a technique that became available in 2009 and came into more widespread commercial use in 2012. Tumor expression of mRNA for specific genes is analyzed to categorize tumors into class 1A and 1B with low and intermediate risk of metastasis, and class 2 with high risk of metastasis. While this modality is valuable for providing prognostic information for patients, more long-term, well powered studies need to be performed in order to fully understand how to use these data to provide prognostic information to patients. This study aims to analyze the outcomes of patients with uveal melanoma treated at the University of Iowa Hospitals & Clinics who were evaluated with gene expression profiling at the time of plaque brachytherapy from 2012 to 2017.

Methods: IRB approval was obtained (IRB# 201708718). Eighty-seven patients were identified who had undergone fine needle aspiration biopsy for gene expression profiling at the time of I-125 plaque brachytherapy from 2012 to 2017. The patient age at diagnosis, eye involved, tumor measurements, gene expression profiling results, date of last follow up, and presence or absence of metastasis at last follow up was recorded for each patient.

Results: The average age at diagnosis of uveal melanoma was 60 years. There were 44 left eyes and 43 right eyes. The average longest basal tumor diameter was 12.5 mm (range 7-17 mm) and the average tumor height was 4 mm (range 1.7-10.9 mm). The median follow up was 26 months (range 0-59 months). There were 71 choroidal tumors, 14 cilio-choroidal tumors, and two ciliary body tumors. Twenty-eight tumors were class 1A, 25 tumors were class 1B, 31 were class 2, and three tumors failed to have gene amplification. At last follow up, 81 patients were alive and six patients were deceased. Six patients developed metastatic disease. Of the patients who developed metastatic disease, the average largest basal tumor diameter was 13.8 mm (range 9-16.5 mm) and the average tumor height was 4.8 mm (range 2.7-7 mm). Six tumors were choroidal, and one tumor was cilio-choroidal. Three patients with metastases were deceased and three patients were alive at last follow up. All six patients with metastatic disease had class 2 tumors by gene expression profiling.

Conclusions: While gene expression profiling is a useful tool for providing prognostic information to patients with uveal melanoma, more long term follow up data need to be obtained in order to fully understand how this information can best be combined with clinical features to determine metastatic risk and counsel patients. While there is a relatively small sample size in this study, and all of the patients who developed metastatic disease did have high-risk class 2 tumors, there were a number of patients with class 2 tumors who did not develop metastatic disease. This may be due to the short follow up interval for some patients, but also suggests that other variables may play a role in the risk for metastasis. In the future, we plan to combine these data with data from another institution to expand the sample size and to continue to follow these patients longitudinally for the development of metastatic disease in order to better understand the role that gene expression profiling plays in uveal melanoma prognosis.

RESIDENT/FELLOW RESEARCH DAY - 2018

Residents and Fellows who have completed research projects (submitted and/or published)

Thomas J. "T.J." Clark, MD (PGY4)
Clark TJE, Klejch WJ, Wang K, Allen RC, Nerad JA, Carter KD, Shriver EM. Hering's Law in Congenital Ptosis: Evaluation of the Contralateral Response to Unilateral Congenital Ptosis Repair. *Ophthal Plast Reconstr Surg.* 2017 Jul 18. [Epub ahead of print].

Lindsay M. DeAndrade, MD (PGY4)
McConnell LK, Syed NA, Zimmerman MB, Carter KD, Nerad JA, Allen RC, Shriver EM. An Analysis of Conjunctival Map Biopsies in Sebaceous Carcinoma. Ophthal Plast Reconstr Surg. 2017 Jan/Feb;33(1):17-21.

Matthew Miller, MD (PGY4)
Miller MA, Lenci LT, Reddy CV, Russell SR. Postoperative hemorrhagic occlusive retinal vasculitis associated with intracameral vancomycin prophylaxis during cataract surgery. *J Cataract Refract Surg*. 2016;42(11):1676-1680.

Lorraine A. Provencher, MD (PGY4)
Provencher LM, Fairbanks AM, Abramoff MD, Syed NA. Urinary β2-microglobulin and disease activity in patients with tubulointerstitial nephritis and uveitis syndrome. *Journal of Ophthalmic Inflammation and Infection.* (Submitted, April 2018).

Sun Young "Sunny" Lee, MD, PhD (Retina)
Lee SY, Cheng JL, Gehrs KM, Folk JC, Sohn EH, Russell SR, Guo Z, Abramoff MD, Han IC. Choroidal Features of Acute Macular Neuroretinopathy vis Optical Coherence Tomography Angiography and Correlation with Serial Multimodal Imaging. JAMA Ophthalm. 2017 Nov1;135(11):1177-1183.