

307 The Impact of Low Vision on Function and Everyday Activities

Tuesday, May 09, 2017 8:30 AM–10:15 AM

Room 308 Paper Session

Program #/Board # Range: 2479–2484

Organizing Section: Low Vision Group

Program Number: 2479

Presentation Time: 8:30 AM–8:45 AM

Symmetry of inherited eye disease

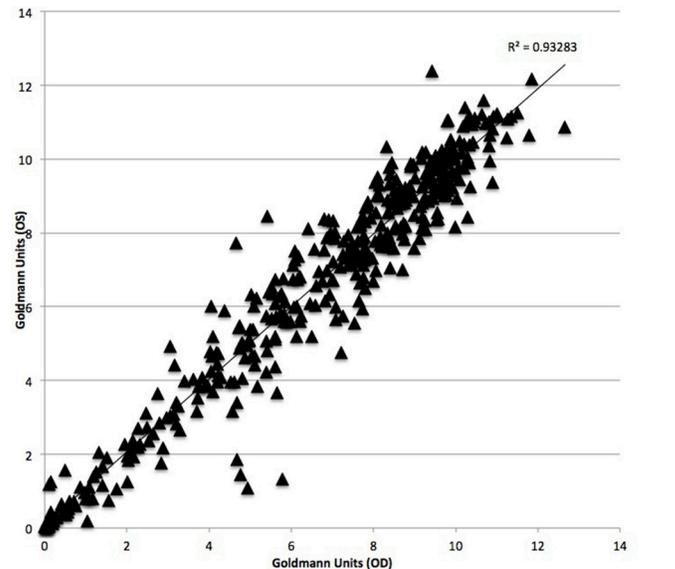
Todd E. Scheetz^{2,1}, Adam P. DeLuca^{2,1}, Nicole Tatro^{2,1}, Benjamin P. Faga^{2,1}, Douglas J. Oppedal^{2,1}, Meagan A. Luse^{2,1}, Richard G. Weleber³, Edwin M. Stone^{2,1}. ¹Ophthalmology, University of Iowa, Iowa City, IA; ²Wynn Institute for Vision Research, University of Iowa, Iowa City, IA; ³Casey Eye Institute, Oregon Health & Science University, Portland, OR.

Purpose: To investigate whether three inherited retinal diseases are symmetrical enough for untreated fellow-eyes to be used as controls in clinical trials of gene- and cell-based treatments.

Methods: We retrospectively evaluated Goldmann visual fields from patients over the age of 10 years with molecularly-confirmed MYO7A-associated Usher syndrome (n=7), ABCA4-associated Stargardt disease (n=172), and CHM-associated choroideremia (n=23). All patients provided informed consent in accordance with the tenets of the Declaration of Helsinki. TruthMarker (iOS) was used to digitally trace the isopters from scanned versions of each visual field, generating an XML file. Fields were excluded from the study if the perimetrist marked the field as unreliable, or if incomplete data were collected. Visual field volumes were calculated from the traced isopters. Visual field volumes were calculated from the traced isopters using the field-area method of Weleber et al., (1986) multiplied by the target luminance values given of Christoforidis (2011). The resulting paired data (OS and OD) from each visit were evaluated for concordance using Pearson's r.

Results: Fields from both eyes were digitally traced from 396 independent patient visits. The resulting data showed extremely high concordance of the visual field volumes between right and left eyes ($r^2=0.93$; $p<2.2 \times 10^{-16}$).

Conclusions: We have devised a method to capture quantitative functional measurements from historical, longitudinal visual field data. Our results demonstrate that the pattern of progression of these three diseases is highly symmetrical, supporting the use of fellow eyes as a control in gene- and cell-based treatment trials.



Correlation of visual field volumes between right and left eyes ($R^2 = 0.93$).

Commercial Relationships: Todd E. Scheetz, None; Adam P. DeLuca, None; Nicole Tatro, None; Benjamin P. Faga, None; Douglas J. Oppedal, None; Meagan A. Luse, None; Richard G. Weleber; Edwin M. Stone, None

Program Number: 2480

Presentation Time: 8:45 AM–9:00 AM

Characterizing the natural history of visual function in choroideremia using microperimetry and multimodal retinal imaging

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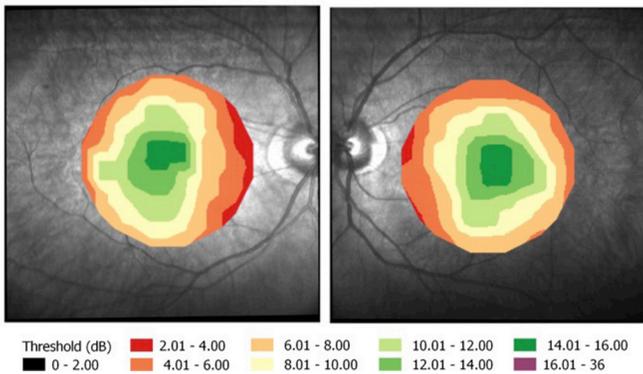
Purpose: Centripetal retinal degeneration in choroideremia (CHM) leads to early visual field restriction and late central vision loss. The latter marks an acute decline in quality of life but visual prognostication remains challenging. We investigate the natural history of visual function in CHM by correlating best-corrected visual acuity (BCVA) with microperimetry and multimodal retinal imaging. **Methods:** BCVA, 10-2 microperimetry (MAIA), OCT and fundus autofluorescence (AF) were performed in both eyes of 56 CHM patients. Microperimetry was repeated in 21 eyes, enabling Bland-Altman analysis of repeatability. BCVA and macular sensitivity were correlated with age and inter-eye symmetry was evaluated. Since loss of fixation stability from foveal degeneration could affect visual testing, the distance from the fovea (on OCT) to the nearest edge of AF (representing edge of degeneration) was assessed as a potential confounder on BCVA or macular sensitivity.

Results: A Kaplan-Meier plot of the proportion of right or left eyes retaining 20/20 BCVA showed identical survival pattern (median survival 39yr). Macular sensitivity declined logarithmically with age ($r=0.60$, $p<0.05$) with a half-life of 14.72yr (95% CI 11.85 to 19.42). Zonal analysis showed faster decline nasal than temporal to the fovea. Inter-eye symmetry was more consistent for macular sensitivity ($r=0.95$, $p<0.001$) than BCVA ($r=0.42$, $p=0.0006$). The former had a coefficient of repeatability of 1.45dB (95% LOA +1.24 to -1.62). As the degeneration encroaches upon the fovea, linear reduction of

both BCVA and macular sensitivity was seen such that near normal functions were measured when the fovea was +2500 μ m away from the edge of AF whereas minimal detectable levels were reached by -800 μ m.

Conclusions: In around half of CHM eyes, BCVA falls below 20/20 by age 39 accompanied by logarithmic decline in macular sensitivity. Both visual functions showed a high degree of inter-eye symmetry, particularly in early stages, indicating that the fellow eye can provide a suitable control for assessing interventions to one eye. A critical period of BCVA and macular sensitivity drop when the fovea is +2500 to -800 μ m from the edge of degeneration corresponds to patient perception of progression from 'split' to 'eccentric' fixation. The findings will help to tailor visual prognosis and interpret outcomes of novel treatments such as gene therapy.

Figure 1: Composite map of MAIA microperimetry thresholds within the central 10 degrees of the macula in a cohort of 56 patients with choroideremia. Values in the key represent the mean threshold in each region.



Commercial Relationships: Kanmin Xue, None; Jasleen K. Jolly, None; Thomas Edwards, None; Markus Gropppe, None; Robert E. MacLaren, NightstarX (I)

Program Number: 2481

Presentation Time: 9:00 AM–9:15 AM

Effective dynamic range and retest-reliability of two-color dark-adapted fundus-controlled perimetry in patients with macular diseases

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Purpose: Differential rod versus cone dysfunction has been observed in various retinal diseases including age-related macular degeneration making it an interesting biomarker. Traditionally rod function is tested through two-color dark-adapted perimetry (Jacobson et al. 1986).

The recently introduced S-MAIA microperimeter (Scotopic-Macular-Integrity-Assessment, CenterVue, Italy) device allows for two-color dark-adapted fundus-controlled perimetry (FCP). We investigated the effective-dynamic-range (EDR), retest-reliability and number of discriminable steps (DS) of the S-MAIA.

Methods: 52 eyes of 52 subjects (mean age 62.0 \pm 16.9 years, range 19.1–90.1 years) with various macular diseases were examined by duplicate mesopic (achromatic stimuli, 400–800 nm), dark-adapted cyan (505 nm) and red (627 nm) FCP using a grid of 61 stimuli covering 18° of the central retina. The EDR and the number of DS were analyzed as proposed by Wall and associates 2010. Coefficients-of-repeatability (CoR) were used as measure for point-wise-sensitivity (PWS) retest-reliability. The effects of fixation

stability, sensitivity and age on retest-reliability were examined using mixed-effects models.

Results: The EDR was 10–30 dB with 5 DS for mesopic and 4–17 dB with 4 DS for dark-adapted cyan and red testing. PWS retest-reliability was good among all three types of retinal sensitivity assessments (CoR: \pm 5.79, \pm 4.72, and \pm 4.77 dB, respectively) and was independent from eccentricity, fixation stability and age. PWS had no effect on retest-reliability in dark-adapted cyan and red testing and a minor effect in mesopic testing.

Conclusions: Combined mesopic and two-color dark-adapted FCP allows for reliable topographic testing of cone and rod function in patients with various macular diseases with and without foveal fixation. Retest-reliability is homogeneous across eccentricities and various degrees of scotoma depth including zones at risk for disease progression. The reliability estimates inform future clinical trial designs that incorporate combined mesopic and two-color dark-adapted FCP as a functional outcome measure.

Commercial Relationships: Maximilian Pfau, Heidelberg Engineering (F), CenterVue (F), Optos (F), Carl Zeiss MediTec (F); Moritz Lindner, Heidelberg Engineering (F), CenterVue (F), Optos (F), Carl Zeiss MediTec (F); Philipp Mueller, Heidelberg Engineering (F), CenterVue (F), Optos (F), Carl Zeiss MediTec (F); Johannes Birtel, Heidelberg Engineering (F), CenterVue (F), Optos (F), Carl Zeiss MediTec (F); Robert P. Finger, Heidelberg Engineering (F), CenterVue (F), Optos (F), Carl Zeiss MediTec (F); Wolf M. Harmening, Heidelberg Engineering (F), CenterVue (F), Optos (F), Carl Zeiss MediTec (F); Monika Fleckenstein, Genentech/Roche (R), Heidelberg Engineering (F), Alcon/Novartis (C), Bayer (R), Alcon/Novartis (F), Allergan (F), Formycon (F), CenterVue (F), Optos (F), Heidelberg Engineering (R), Allergan (R), Carl Zeiss MediTec (F), Genentech/Roche (C), Genentech/Roche (F), Bayer (F); Frank G. Holz, NightstarX (F), Boehringer-Ingelheim (C), Carl Zeiss MediTec (R), Allergan (F), Thea (C), Allergan (R), Bioeq (C), CenterVue (F), Optos (F), Carl Zeiss MediTec (F), Acucela (F), Genentech/Roche (R), Novartis (C), Heidelberg Engineering (F), Novartis (R), Bayer (C), Bayer (R), Heidelberg Engineering (C), Novartis (F), Heidelberg Engineering (R), Acucela (C), Genentech/Roche (C), Genentech/Roche (F), Bioeq (F), Bayer (F); Steffen Schmitz-Valckenberg, Heidelberg Engineering (F), Alcon/Novartis (C), Bayer (R), Alcon/Novartis (F), Allergan (F), Formycon (F), CenterVue (F), Optos (F), Heidelberg Engineering (R), Allergan (R), Carl Zeiss MediTec (F), Bayer (F)

Support: BONFOR GEROK Program of the Faculty of Medicine, University of Bonn (Grant No O-137.0022 to MP)

Program Number: 2482

Presentation Time: 9:15 AM–9:30 AM

Two-Color (Red-Blue) Dark Adaptometry: Sensitivity, Specificity and Clinical Application

Jeff C. Rabin, Brooke Houser, Carolyn Talbert, Ruh Patel. Optometry, UIW Rosenberg School of Optometry, San Antonio, TX.

Purpose: Dark adaptometry (DA) is a sensitive test for diagnosis of retinal disease including retinitis pigmentosa (RP) and macular degeneration. Patients requiring flash electroretinograms (ERGs) often benefit from DA for proper diagnosis. Our purpose was to develop a new DA test administered during the 20 min. dark adaptation period of the standard flash ERG (www.iscev.org) using alternating red and blue stimuli to bias the response in favor of cones (red) or rods (blue). We report sensitivity and specificity of this test.

Methods: An ERG Ganzfeld (Diagnosys, LLC) was used to measure DA in 21 normal subjects and 21 patients with retinal disease: RP/Ushers syndrome, cone dystrophy, Bests, fundus albipunctatus, DUSN, macular dystrophy, Allagile syndrome. Each subject initially

underwent 75 sec. of pre-adaptation (1000 cd/m²) followed by 20 min. of DA during which the subject pressed a button each time she/he detected alternating 6 msec. flashes of red (630 nm) or blue (445 nm) light which diffusely illuminated the Ganzfeld. An adaptive staircase measured red and blue DA thresholds during DA. Final 20 min. and halfway (10 min.) red and blue thresholds were compared between groups.

Results: Mean (\pm 2SD) red and blue DA was computed across normal subjects for 25 points in time during the 20 min. DA period yielding separate red and blue DA curves. Subjects were initially 1.5 log units (32x) more sensitive to blue vs. red light and 2.5 log units more sensitive to blue after 20 min. DA ($p < 0.0001$) exemplifying greater sensitivity of rods to blue light. Both curves were flat at 15 min. indicating that absolute thresholds were achieved for parameters of this test. Combining 10 and 20 min. thresholds, 95% of patients were detected with DA (>2 SD below normal); a patient with macular dystrophy was borderline normal. The most sensitive single parameter was blue DA at 10 min. (86% sensitivity) reflecting both delay and sensitivity loss. In RP ($n=7$) mean elevation in final blue threshold was 2.3 log units (200x).

Conclusions: Two-color (red-blue) DA offers high sensitivity (95%) for detecting dysfunction in various retinal diseases with 100% specificity in normals thus far. It is expediently measured during the DA phase of ERGs providing definitive separation of rod and cone function. The test shows promise for improving diagnosis and revealing functional impairment in vision debilitating disease.

Commercial Relationships: Jeff C. Rabin, None; Brooke Houser, None; Carolyn Talbert, None; Ruh Patel, None

Program Number: 2483

Presentation Time: 9:30 AM–9:45 AM

Video Scanpath with Central Vision Loss

Russell L. Woods^{1,2}, Francisco Costela^{1,2}, Dylan J. Rose¹, Daniel R. Saunders^{1,2}, Sidika Kajtezovic¹. ¹Schepens Eye Research Institute, Boston, MA; ²Ophthalmology, Harvard Medical School, Boston, MA.

Purpose: Most people with central vision loss (CVL) report difficulty watching video, on TV, computers and in the cinema. People with full sight look in about the same place most of the time when watching directed content such as “Hollywood” movies and TV programming. We asked whether people with CVL look in the same places and whether that is related to the reported difficulty.

Methods: Subjects with CVL ($n=16$), with normal vision (NV; $n=60$), and with NV that was blurred by defocus ($n=15$) watched short (30s) video clips. Blur reduced visual acuity to about 20/50, 20/125, 20/320, or 20/800, which matched the range of visual acuities of the CVL group. Scanpaths coherence was measured using the normalized scanpath salience (NSS) method that compares each scanpath to a control group. To test whether there was a disadvantage to the scanpath of a person with CVL, in a second study, 351 on-line participants with NV watched clips on which a restricted region was visible, and that matched either the scan path of the normal vision group or that of a person with CVL.

Results: Subjects with CVL made longer fixations and shorter saccades than the NV group. Subjects with CVL had lower NSS scores than the NV subjects, indicating that they were not looking in the same places at the same times. NSS scores of NV subjects with defocus were very similar to NSS scores without defocus and were higher than subjects with CVL with similar visual acuity. Thus, blurred vision alone is not the cause of the altered scanpath with CVL. When viewing the NV scanpath restricted-area clips, subjects were more able to follow the story than when viewing the CVL-scanpath clips. As, the CVL scanpath was less informative, it

suggests that the “poor” scanpath is related to the difficulty watching TV.

Conclusions: Difficulty with video content experienced by people with CVL seems to be caused by difficulty with eye movement control. This suggests that rehabilitation methods that rely on the person with CVL locating and looking at the objects of interest may not be successful.

Commercial Relationships: Russell L. Woods, None;

Francisco Costela, None; Dylan J. Rose, None;

Daniel R. Saunders, None; Sidika Kajtezovic, None

Support: R01EY019100

Program Number: 2484

Presentation Time: 9:45 AM–10:00 AM

Viewing Video with Homonymous Hemianopia

Francisco Costela, Daniel R. Saunders, Sidika Kajtezovic, Dylan J. Rose, Sarah S. Sheldon, Russell L. Woods. Ophthalmology, Schepens Eye Research Institute, Boston, MA.

Purpose: In three studies, we (1) characterized the reported difficulty of people with homonymous hemianopia while watching TV, (2) objectively measured the difficulty, and (3) propose and tested a novel rehabilitation aid.

Methods: (1) We conducted a survey about watching TV and movies with subjects with normal vision ($N=193$) or hemianopia ($N=93$). (2) We measured the ability to follow the story in video clips in a subset from both groups ($N=60$, 20, respectively), using a novel information acquisition (IA) measure that uses natural language processing to objectively scoring the subject’s descriptions of the clips (ability to follow the story). (3) The IA of subjects with hemianopia ($N=17$) was compared when viewing the videos with or without a superimposed dynamic cue that we called a content guide (see figure 1B), calculated from the gaze of subjects with normal vision (figure 1A).

Results: (1) Subjects with hemianopia were more likely to report difficulty watching TV, movies on a computer, and movies at the theater, and were less likely to take photographs or attend the theater, because of vision difficulties. (2) The hemianopia group had a significantly lower IA score, average 3.0, compared to 4.3 shared words of the normal-vision group (mixed-effects regression, $z=4.52$, $p < 0.001$). (3) Presence of the content guide significantly increased the IA score by 0.54 shared words ($z=4.67$, $p < 0.001$), and was higher in most (14/17) of the subjects with hemianopia.

Conclusions: In addition to reporting difficulty, people with hemianopia have measurable difficulty viewing video and related tasks, and interventions like the content guide can provide benefit.



Commercial Relationships: Francisco Costela, None; Daniel R. Saunders, Schepens Eye Research Institute (P); Sidika Kajtezovic, None; Dylan J. Rose, Schepens Eye Research Institute (P); Sarah S. Sheldon, None; Russell L. Woods, Schepens Eye Research Institute (P)
Support: NIH Grant EY019100

The content guide dynamically directs attention to areas that were fixated by the majority of normally-sighted viewers. A) Kernel density estimate of the gaze points for this particular frame. B) Illustration of the content guide as it appeared for the same frame.