Comparative short-term predictive power of global structural measurements in glaucoma

Stuart K. Gardiner1, Pui Yi Boey2, Hongli Yang1, Claude F. Burgoyne3, Brad Fortune1, Shaban Demirel1
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Purpose: Retinal Nerve Fiber Layer Thickness (RNFLT), as measured using Optical Coherence Tomography (OCT), correlates well with functional measures from perimetry. However, a variety of data suggests that structural change within the optic nerve head may precede RNFL change. This study asks whether changes in the neuroretinal rim, as measured by the OCT parameter Minimum Rim Width (MRW; averaged around the neuroretinal rim), predict subsequent changes in RNFLT.

Methods: A structural equation model (SEM) was formed, as illustrated in the Figure. The principle is that each eye has two possibly correlated latent (unobservable) variables; baseline retinal ganglion cell (RGC) count, and rate of RGC loss. The observable values of MRWn and RNFLTn at time n are predicted by their values at time (n-1), and the values of the latent variables for that eye at time n. This model was fit using the lavaan software package for R, on data from 160 eyes of 160 participants with glaucoma or suspected glaucoma in the Portland Progression Project longitudinal study, tested every 6 months using the Spectralis OCT.

Results: The mean series length was 8.7 visits (range 5-11), over 4.3 years (range 2.5-5.1). The fit of the model was good, as seen in the Table. An increased baseline RGC count was correlated with more rapid RGC loss (r=-0.135, p<0.001). MRWn was predicted by MRWn-1 and RNFLTn (both p<0.001), RNFLT was predicted by RNFLTn-1 (p<0.001), but not MRWn-1 (p=0.251). Similar analyses using longer time lags of up to 3 years for MRW did not improve the fit of the model. When splitting the data into equal parts based on age, MRWn-1 did not improve predictions of RNFLTn in older eyes (p=0.301), but it is possible that it could help in younger eyes (p=0.075).

Conclusions: There was no evidence that MRWn-1 improved predictions of RNFLT measured 6 months later, compared with just using RNFLTn. It remains possible that the time lag between changes in these measures could be less than 6 months and so undetectable in this dataset, or much longer than was tested here. However, the results may be because MRW in its current form is more variable than RNFLT, reducing its utility as a predictor.

Table

<table>
<thead>
<tr>
<th>Measure</th>
<th>Value</th>
<th>Ideal value for good fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative chi-square</td>
<td>2.80</td>
<td>&lt; 3.0</td>
</tr>
<tr>
<td>Root Mean Square Error Approximation</td>
<td>0.106</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Tucker-Lewis Index (TLI)</td>
<td>0.963</td>
<td>&gt; 0.9</td>
</tr>
<tr>
<td>Comparative Fit Index (CFI)</td>
<td>0.962</td>
<td>&gt; 0.9</td>
</tr>
</tbody>
</table>

Goodness of fit of the SEM model. No single index or p-value is considered appropriate for assessing SEM models; instead, consideration of several indices is recommended.

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Macular SD-OCT Outcome Measures in Glaucoma: Comparison of Local Structure-Function-Relationships and Dynamic Range

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**Purpose:** There is scant evidence regarding comparative utility of various macular SD-OCT thickness parameters for detection of glaucoma progression. We have previously found the local variability for all macular parameters to be very low and uniform across the macula. The goal of this study is to compare the performance of inner macular thickness parameters with regard to local structure-function (SF) relationships and dynamic range of measurements.

**Methods:** One hundred fifteen glaucomatous eyes from 102 patients, including 17 eyes with intact achromatic visual field, and 16 normal eyes (8 subjects) with macular SD-OCT images (Spectralis) and 10-2 visual fields were enrolled. Macular images were segmented and inner plexiform layer (IPL), ganglion cell layer (GCL), and GC/IPL thicknesses were calculated for an 8x8 array of 3-degree superpixels. The main outcome measures used to compare macular parameters were: 1) local structure-function (SF) relationships within the central 18 degrees of the macula after adjusting for macular retinal ganglion cell displacement, and 2) dynamic range of measurements, defined as the difference between the median of the top highest 5% of measurements and the bottom plateau of OCT measurements (the intercept of Hood’s simple linear model) and the change point, i.e. the local total deviation value where the macular parameters reach the bottom plateau.

**Results:** The average visual field mean deviation was −6.8 (±4.4) dB in the glaucoma group. The strength of SF relationships was similar among all thickness measures (rho = 0.571, 0.519, and 0.578 for GCL, IPL, and GC/IPL, respectively; p >0.05 for the difference). The highest SF correlations coincided with the peak of the GCL thickness (rho = 0.610, 0.618, and 0.637). The dynamic range was highest for the GC/IPL (57μm) followed by GCL (36μm), and IPL (22μm)(Figure). The change points were very similar among all the parameters as follows: IPL=−8.4 dB, GCL=−8.7 dB, and, GC/IPL=−8.6 dB.

**Conclusions:** The strength of structure-function relationships and the latter’s point of change were similar for all inner macular parameters. Given the similar variability for the 3 macular parameters, the higher dynamic range, and the less demanding segmentation, GC/IPL provides the best compromise for detection of change over time with current SD-OCT technology.
texture enface images and the RNFL thickness map performed
significantly better than standard cpRNFL and intensity enface
images for discriminating between OAG eyes (mean ± SD visual
field MD =−3.07 dB (±4.35)) and healthy eyes (age-adjusted AUC
of 0.94, 0.93, 0.91 and 0.86, respectively). Among the 35 OAG
progressing eyes (mean visual field MD =−7.7 dB (±8.4)), 31 (89%)
eyes were identified as progressing by the RNFL thickness map,
30 (86%) eyes by texture enface image, 25 (71%) eyes by cpRNFL
and 14 (40%) eyes by intensity enface image.

Conclusions: Novel texture enface images and RNFL thickness maps
were significantly better than standard intensity enface images and
cpRNFL thickness for discriminating between healthy and OAG eyes
and for detecting progression. Deep learning methods show promise
for individualizing monitoring of glaucoma.

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Program Number: 5192
Presentation Time: 4:30 PM–4:45 PM
Early detection of visual field conversion using an unsupervised
machine-learning analysis of retinal nerve fiber layer thickness
measurements
Siamak Yousefi, Michael H. Goldbaum, Ehsan Shahrian
Varnousfaderani, Linda M. Zangwill, Felipe A. Medeiros, Robert
N. Weinreb, Christopher A. Girkin, Jeffrey M. Liebmann,
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University, New York, NY.

Purpose: To determine if glaucomatous visual field conversion can be
detected by machine-learning analysis of retinal nerve fiber layer
thickness (RNFLT) measurements prior to glaucomatous visual field
conversion

Methods: Study participants were recruited from the Diagnostic
Innovations in Glaucoma Study (DIGS) and the African Descent
and Glaucoma Evaluation Study (ADAGES). Longitudinal RNFLT
measurements (Spectralis RNFL circle scan protocol, 768 A-scans;
64 RNFL sectors were generated by averaging 12 contiguous
A-scans to reduce noise and any possible misalignment) from
74 eyes of 68 patients followed clinically (minimum 3 visits before
conversion date) for suspicion of glaucoma were analyzed using
Gaussian mixture model using expectation maximization (GEM)
progression of patterns (POP) prior to conversion to glaucoma
(conversion was defined as ≥3 consecutive abnormal SAP results
by GHT or PSD ≤0.05). Previous cross-sectional GEM analyses
of RNFLT measurements identified 7 glaucomatous RNFL patterns
(axes) of loss (Yousefi et al., ARVO 2015). To define the conversion
limit for GEM, longitudinal RNFLT measurements of 83 stable
glaucoma eyes (imaged once a week for approximately 5 weeks,
approximately 120 permuted series per eye) were analyzed across
each axis and the rate of change was approximated using linear
regression (LR). The conversion limit for each axis was adjusted
to result in an overall 95th percentile conversion limit. To detect
conversion, the longitudinal RNFLT measurements of patient eyes
were analyzed across each GEM axis and the rate of change was
approximated by LR. Conversion was assigned if the rate of change
in an eye, along any GEM axis, was greater than the conversion
limit for that axis; otherwise, no conversion was assumed. The
early detection rate (defined as percentage of convert eyes correctly
identified) of GEM was compared to that of LR of RNFLT global
average, using the same method for setting conversion limits.

Results: GEM detected 88% of converted eyes prior to the first of 3
consecutive abnormal SAP results and linear regression of average
RNFLT detected 62%. Fifty-seven percent of converted eyes were
detected by both methods.

Conclusions: Analysis of patterns of RNFLT using GEM can detect
glaucoma in more eyes than linear regression of global average
RNFLT before the onset of repeatable SAP abnormality.

Figure 1. RNFLT measurements from a sample eye (before VF conversion) and the first GEM axis (second dashed box on top row). Color-coded RNFL loss overlaid on an en face for better visualization. Top row: RNFLT measurements analyzed across GEM axes and identified change before the VF conversion onset.
Bottom row: Linear regression of Average RNFLT measurements detect no change in RNFLT measurements of the eye.

Figure 2. Venn diagram of the number of eyes detected by each method. GEM identified 65 eyes while linear regression of average RNFLT measurement of the standard instrument detects 46 eyes as converted to glaucoma.

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Clinical Trial: NCT00221923

Program Number: 5193

Presentation Time: 4:45 PM–5:00 PM

Optic Nerve Head Characterization in Chronic Angle Closure Glaucoma Detected by Swept-Source OCT

Dejiao Li1, Elise Taniguchi1, Zi-Ning Choo1, Taibo Li1, Marissa K Shoji1, Haobing; Wang1, Scott H. Greenstein1, Stacey C. Brauner1, Angela Turalba1, Louis R. Pasquale1,2, Lucy Q. Shen1

1Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, MA; 2Channing Division of Network Medicine, Brigham and Women’s Hospital, Boston, MA.

Purpose: To identify differences in optic nerve head (ONH) structures in chronic angle closure glaucoma (CAGC) compared to primary open angle glaucoma (POAG) and controls using swept-source optical coherence tomography (SS-OCT).

Methods: Patients with CAGC, age-matched POAG patients and healthy control subjects underwent radial and volume B-scans of the ONH by SS-OCT. MM-OCT (Morpheus, Carl Zeiss Meditec Inc) was used to obtain a 6x6 mm volumetric angiography scan of the macula. The split-spectrum amplitude decorrelation angiography (SSADA) algorithm was used. A novel algorithm was used to detect macular circulation defects in glaucoma using OCT angiography.

Results: [SSADA] algorithm was used. A novel algorithm was used to detect macular circulation defects in glaucoma using OCT angiography. Figure. SS-OCT Images of ONH Prelaminar Defects. Multiple large holes in CAGC (A); one small hole in POAG (B); wedge defect extending to LC in POAG (C).

Table. Comparison of Demographic Characteristics and Optic Nerve Head Parameters Among Studied Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Eyes (N = 25)</th>
<th>POAG Eyes (N = 40)</th>
<th>CAGC Eyes (N = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.96 ± 7.97</td>
<td>66.48 ± 8.01</td>
<td>67.93 ± 8.54</td>
</tr>
<tr>
<td>VF MD (dB)</td>
<td>-</td>
<td>-7.95 ± 5.96</td>
<td>-6.77 ± 2.96</td>
</tr>
<tr>
<td>VF PD (dB)</td>
<td>-</td>
<td>5.79 ± 1.4</td>
<td>5.83 ± 2.4</td>
</tr>
<tr>
<td>IOP (mm Hg)</td>
<td>16.40 ± 2.10</td>
<td>13.90 ± 2.64</td>
<td>13.93 ± 3.64</td>
</tr>
<tr>
<td>IOP (mm Hg)</td>
<td>15.20 ± 1.80</td>
<td>20.65 ± 4.64</td>
<td>20.17 ± 15.73</td>
</tr>
</tbody>
</table>

Conclusions: While SS-OCT evaluation of the ONH revealed thinner BMO-MRW in both CAGC and POAG groups compared to controls, prelaminar holes were most frequent in CAGC patients suggesting this may be a distinguishing feature of CAGC.

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Presentation Time: 5:00 PM–5:15 PM

OCT Angiography of Macular Ganglion Cell Complex Circulation in Glaucoma

Hana L. Takusagawa, John C. Morrison, Yali Jia, Liang Liu, Beth Edmunds, Lorinna Lombardi, Rebecca Armour, Ellen Davis, David Huang. Casey Eye Institute, Oregon Health & Science University, Portland, OR.

Purpose: To detect macular circulation defects in glaucoma using optical coherence tomography (OCT) angiography.

Methods: One eye of each participant was imaged using a 70 kHz 840 nm wavelength spectral OCT system (RTVue-XR, Optovue, Inc) to obtain a 6x6 mm volumetric angiography scan of the macula. The split-spectrum amplitude decorrelation angiography (SSADA) algorithm was used. A novel algorithm was used to detect macular circulation defects in glaucoma using optical coherence tomography (OCT) angiography.

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Glaucoma preferentially affects vessel density in the GCC. The GCC vessel density has high diagnostic accuracy in glaucoma.

Conclusions:

Quantitative Speckle-variance Optical Coherence Tomography of Radial Peripapillary Capillaries in Glaucoma

Zaid Mammo1, Morgan Heisler2, Chandra Bala2, Sieun Lee2, Paul MacKenzie2, Steven Schendel1, Andrew Merkur1, Eduardo Navajas1, William H. Morgan3, Mariniko V. Sarunic2.

1University of British Columbia, Vancouver, BC, Canada; 2Simon Fraser University, Burnaby, BC, Canada; 3Lions Eye Institute, Perth, WA, Australia.

Purpose: To demonstrate the utility of speckle-variance Optical Coherence Tomography (svOCT) in imaging the Radial Peripapillary Capillaries (RPC) and assessing their role as a vascular parameter of glaucoma damage.

Methods: Thirty two eyes from 17 subjects were imaged with svOCT (1060-nm, 100-kHz custom built-system). Unilateral glaucoma subjects (Group A): 5 subjects (10 eyes), glaucoma suspects (Group B): 3 subjects (6 eyes); Normal subjects (Group C): 9 subjects (16 eyes). Automated 30-2 Humphrey Visual Field (HVF), optic disc photos, spectral-domain OCT (SD-OCT) and svOCT peripapillary imaging were done for Groups A and B. For group A, the imaged region was chosen based on the combination of focal optic nerve damage and corresponding HVF loss, the same region in the fellow eye was imaged. For group B, the peripapillary area with retinal nerve fiber layer (RNFL) thinning and normal HVF were imaged with svOCT. All peripapillary areas were imaged in Group C. Manual tracing was used to quantify the RPC density. Mean capillary density (CD) was compared across different groups. Correlations between CD, RNFL thickness, and Visual Field Index (VFI) values were explored.

Results: The CD per imaged area in the glaucomatous eye of Group A (0.09+-0.05) was significantly lower than the fellow eye in Group A (0.30+/-.06), Group B (0.28+/-.01) and Group C (0.33+/-.04) (P<0.001), no other statistically significant differences were found otherwise. Overall, a statistically significant correlation was found between CD and RNFL thickness (Slope=0.0010, p=0.0001). A statistically significant correlation was found between CD and VFI (Slope=0.0056, p=0.0012).

Conclusions: Using svOCT, reduced RPC density was noted in subjects with glaucomatous optic neuropathy. The CD showed strong correlation with VFI and RNFL thickness. Quantitative svOCT could be an adjunct modality in the evaluation of glaucoma patients.

Optic nerves of subject with left-sided glaucoma (Right=A and Left=B). Preserved visual field function is noted in the right eye (C) with significant loss is noted in the left eye (D). On svOCT, preserved RPCs capillaries are noted in the right eye (F) with significant loss is found in the left eye (H). The Outer Plexiform/Inner Nuclear Layer (OPL/INL) capillaries are preserved in both eyes (G&I)
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