Abstract

Purpose: To evaluate the relationship between retinal nerve fibre layer (RNFL) thickness measured by optical coherence tomography (OCT) and light threshold values obtained with the Humphrey Field Analyser (HFA).

Methods: Thirty-one normal subjects and 72 glaucoma patients were included. Around the optic disc, RNFL thickness was measured with Stratus OCT scans and sensitivity evaluated with the Swedish Interactive Threshold Algorithm (SITA) Standard strategy at the same visit. The RNFL thicknesses at the inferior, superior, nasal and temporal regions were compared to retinal sensitivity values in the same areas.

Results: Correlation between RNFL thickness and retinal sensitivity in the regions of the optic nerve head using the Karl-Pearson’s correlation coefficient for the two groups showed significant correlation between structure and function loss at the inferior, superior and nasal regions in the glaucoma group.

Conclusions: There is significant structural and functional correlation for values around the optic nerve head in the glaucoma group.

Key words: Visual field, Optic nerve head, retinal nerve fiber layer, Optical coherence tomography
Introduction

The diagnosis of glaucoma despite the plethora of newer machines and imaging techniques rests on recognizable glaucomatous field changes on the gold standard automated perimetry. The hallmarks of glaucomatous progression are visual field deterioration and morphologic changes of the optic disc, including narrowing of the neuroretinal rim accompanied with deepening or widening of the optic cup, or both (1).

Structural changes occur before functional alterations in many types of glaucomas (2,3). To assess the structural changes several different modalities are available. Optic nerve head photography, retinal nerve fibre layer photography, Heidelberg retinal tomograph (HRT), Nerve fibre analyzer GDx, Retinal thickness analyzer and the Optical coherence tomography (OCT). Several studies with follow up show progression of retinal nerve fibre layer changes before visual field changes in glaucoma and ocular hypertensive patients (4,5). Similar studies have demonstrated significant correlation between structural parameters obtained with HRT and visual field indices either globally or regionally (6,7,8,9). With the GDx, equipped with variable corneal compensation (VCC), scanning laser ophthalmoscopy correlates better with mild glaucomatous changes correlate better with perimetry than those with fixed corneal compensation (FCC) (10,11).

Soliman et al studied the relationship between RNFL loss on OCT and visual field damage. This is non-linear, exponential and shows that a considerable amount is lost before development of detectable field damage. In early stages of glaucoma, field changes occurs before RNFL loss detected on OCT (12, 13).

White on White (W/W) perimetry is a generally accepted method for monitoring visual field damage in glaucoma patients and suspects.

Glaucma patients suffer a loss of about 40% of their retinal ganglion cells before this loss is picked up on W/W perimetry.

To detect the structural changes on the RNFL, we used OCT in this study and compared it to visual functional sensitivity on HFA using the Swedish Interactive Thresholding Algorithm (SITA) Standard strategy.

Aim of the Study

To evaluate the relationship between retinal nerve fibre layer (RNFL) thickness measured by optical coherence tomography (OCT) and light threshold values obtained with the Humphrey Field Analyser (HFA) using the Swedish Interactive Threshold Algorithm (SITA ) Standard strategy.

Materials and Methods

Subjects

Seventy – two glaucoma patients and 31 normal control subjects participated in a longitudinal, prospective study on visual field and optic disc change. Patients were recruited consecutively from the glaucoma clinic with the following inclusion criteria: (1) clinical diagnosis of open-angle glaucoma with notching or progressive thinning of the neuroretinal rim, (2) baseline visual field mean deviation between −2 and −10 dB, (3) open angles by gonioscopy, and (4) best-corrected visual acuity of 6/18 or better.

Normal control subjects were recruited among volunteers with the following inclusion criteria: (1) clinically normal appearance of the optic disc and fundus, (2) intraocular pressure of less than 22 mmHg, and (3) best-corrected visual acuity of 6/12 or better. Common exclusion criteria were: (1) systemic disease like diabetes, neurological diseases or systemic medication known to affect the visual field, (2) refractive error exceeding 5 diopters (D; equivalent sphere) of myopia or hyperopia or 3 D of
astigmatism, and (3) contact lens wear. Additionally, patients were excluded if there was concomitant ocular disease, and controls were excluded if there was any ocular disease. One eye was chosen randomly as the study eye for the controls and also for the patients if both eyes were eligible.

Methods

A detailed medical and surgical history was elicited from the patients, all of whom underwent a complete ophthalmic examination that included slit-lamp biomicroscopy, visual acuity testing with refraction, ONH examination with slit lamp biomicroscopy, applanation tonometry, gonioscopy, HFA perimetry using the Swedish Interactive Thresholding Algorithm (SITA) standard strategy and OCT evaluation of RNFL.

Instrumentation

Optical Coherence Tomography

Optical coherence tomography uses low-coherence interferometry to image intraocular structures cross-sectionally. It is analogous to ultrasound B-mode imaging, except that it uses light rather than sound and provides in vivo tissue sampling with axial resolution of the current commercially available unit in the range of ~10 μm. Cross-sectional images of tissue microstructure are obtained by measuring the echo time delay and magnitude of light backscattered from internal tissue microstructure. Optical coherence tomography has been shown to obtain accurate and reproducible NFL and retinal thickness measurements. Detailed descriptions of OCT have been previously published (14,15). Optical coherence tomography enables cross-sectional imaging of the macula, peripapillary and ONH regions. The peripapillary scan is a circular scan with a diameter of 3.4 mm centered on the ONH.

Optical coherence tomography was performed by using Stratus OCT, model 3000(Carl Zeiss Meditec Inc, Dublin, CA, USA). The results were analyzed with Version 4.0.1 software. After dilatation to a minimum of 5 mm, a patch was placed over the other eye. Three hundred and sixty degrees circular scans with a diameter of 3.4 mm, centered on the optic disc were performed using the Fast RNFL thickness protocol.

The RNFL thickness was defined as the number of pixels between the anterior and posterior edges of the RNFL. Each scan consisted of 100 individual A-scan samples evenly distributed along a circle circumference. Three circular scans, each 3.4 mm in diameter centered on the optic disc, were obtained from each test eye. The best quality, properly aligned scan was chosen for analysis. Average RNFL thickness was calculated globally and separately for superior, inferior, temporal and nasal quadrants. Good quality OCT scans were defined as scans with a signal-noise ratio of 40 dB.

SITA Standard HFA 30-2

W/W perimetry was performed with HFA (Zeiss Humphrey Systems, Model 750) by using SITA-standard test strategy 30-2 program. A reliable test was defined as having fewer than 33% false-positive or false-negative scores and fewer than 20% fixation losses. Test was repeated to establish baseline in most subjects. The dB threshold values around the blind spot were taken at the inferior, superior, nasal and temporal for sectoral analysis.

Statistical analysis

The parameters compared were average RNFL thickness of the entire circumference of the optic disc and quadrant thickness consisting of superior (46 to 135 degrees), nasal (136 to 225 degrees), inferior (226 to 315 degrees) and temporal (316 to 345 degrees) quadrant areas between the three groups.

To compare similar areas on the fields, decibel light threshold sensitivity at the superior, inferior,
nasal and temporal quadrants were obtained thus. Three points are obtained for superior and inferior areas of the disc and four points for nasal and temporal sides. For instance, the peripheral two points for superior are halved. Therefore, sum of one central point and two halved peripheral points divided by two gives threshold value at superior quadrant and similarly for the inferior area. For the 4 nasal points, sum of two central and two peripheral points divided by three gives threshold nasal sensitivity.

Paired comparisons for all significant mean defects were conducted. To evaluate the strength of the association of W/W perimetry, correlations between RNFL thickness and visual field parameters were assessed by correlation coefficients (Karl-Pearson’s r) and significance calculated using the Student t-test. Data were reported as mean ± standard deviation (SD). A P value of less than 0.05 was considered statistically significant.

**Results**

Seventy two patients and 31 normals were enrolled. There was no difference between the groups with regard to gender as depicted in Table 1.

**Table 1 represents the demographic features of the two groups.**

<table>
<thead>
<tr>
<th></th>
<th>Glaucoma</th>
<th>Normal</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60.17 ± 12.27</td>
<td>47.96 ± 12.35</td>
<td>0.003</td>
</tr>
<tr>
<td>Gender(M/F)</td>
<td>1.05</td>
<td>0.93</td>
<td>0.81</td>
</tr>
<tr>
<td>CD ratio</td>
<td>0.61 ± 0.18</td>
<td>0.49 ± 0.15</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Mean age of normals was 47.96 ± 12.35 years. The mean age of patients in the glaucoma group was 60.17 ± 12.27 years. The mean vertical CD ratio was 0.49 ± 0.15 and 0.61 ± 0.18 in normal and glaucomatous eyes respectively (P <0.05) The RNFL thickness was greatest in the inferior and superior quadrants and thinner in the nasal and temporal quadrants in the normal group. The RNFL profile demonstrated the “double hump” pattern. These results are consistent with those of earlier studies. (16)

The RNFL thickness in glaucomatous eyes differed significantly from normal eyes in all parameters (P <0.001). Representative OCT recordings in patients with glaucoma and normal subject are depicted Figure 1 and Figure 2 respectively.

Mean RNFL thickness was thinner in glaucomatous eyes (78.35 ± 19.46 mm) than the normals (94.75 ± 12.6 mm) and this was statistically significant at p<0.001. The RNFL was thinner in glaucomatous eyes in the inferior (98.5±31.25 mm), superior (93.34±27.58 mm), and temporal (56.51±13.92 mm) quadrants when compared to normals (P <0.01) except in the nasal aspect as tabulated in Table 2.

**Table 2 shows RNFL thickness average and in each sector for the two study groups.**

<table>
<thead>
<tr>
<th>RNFL Thickness</th>
<th>Glaucoma(mm)</th>
<th>Normal(mm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>78.35 ± 19.46</td>
<td>94.75 ±12.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferior</td>
<td>98.5±31.25</td>
<td>128.58 ±15.06</td>
<td>0.001</td>
</tr>
<tr>
<td>Superior</td>
<td>93.34±27.58</td>
<td>115.71±22.62</td>
<td>0.007</td>
</tr>
<tr>
<td>Nasal</td>
<td>66.44±21.65</td>
<td>70.55 ±16.71</td>
<td>0.942</td>
</tr>
<tr>
<td>Temporal</td>
<td>56.51±13.92</td>
<td>66.32 ±12.08</td>
<td>0.002</td>
</tr>
</tbody>
</table>
With reference to global indices in glaucoma W/W perimetry, mean deviation (MD) was \(-7.94 \pm 5.93\) and pattern standard deviation (PSD) was \(5.23 \pm 3.89\); and for normal group mean deviation (MD) was \(-3.01 \pm 1.31\) and pattern standard deviation (PSD) was \(1.84 \pm 0.49\). The mean RNFL thickness in glaucomatous eyes was \(78.35 \pm 19.46\) mm, which was thinner than the normals \(94.75 \pm 12.6\) mm and this was statistically significant at \(p<0.001\). Hoh et al (18) reported that the mean RNFL thickness measured with OCT was significantly less in glaucomatous eyes \(56.9 \pm 21.5\) mm than in ocular hypertensive \(83.70 \pm 16.57\) mm and normal \(90.86 \pm 14.17\) mm; although RNFL thickness tended to be greater in normal than in ocular hypertensive eyes, this difference was not statistically significant.

The correlation between RNFL thickness on OCT to the corresponding retinal sensitivity values obtained on the white on white SITA standard perimetry in the four common sectoral regions of the optic nerve head using the Karl- Pearson’s correlation coefficient for the two groups are as depicted in Table 4.

### Table 3 correlates RNFL thickness on OCT to the global indices on the perimetry for the two groups using Karl – Pearson’s correlation.

<table>
<thead>
<tr>
<th></th>
<th>RNFL(mm)</th>
<th>MD</th>
<th>Correlation</th>
<th>PSD</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaucoma</td>
<td>78.35±19.46</td>
<td>(-7.94 \pm 5.93)</td>
<td>(r=0.68, p&lt;0.01)</td>
<td>5.23±3.89</td>
<td>(r=-0.61)</td>
</tr>
<tr>
<td>Normal</td>
<td>94.75±12.6</td>
<td>(-3.01 \pm 1.31)</td>
<td>(r=-0.08)</td>
<td>1.84±0.49</td>
<td>(r=-0.03)</td>
</tr>
</tbody>
</table>

Discussion

Optical coherence tomography helps in obtaining objective and reproducible measures of RNFL thickness and detects focal defects independent of the visibility of RNFL. Sommer et al (17) in a 10-year follow-up study reported that RNFL thinning is a sensitive indicator of the extent of glaucomatous damage and that RNFL loss precedes measurable ONH and visual field damage approximately six years before any detectable visual field defects. Thus, the possibility of detecting these defects in areas of physiological decreased visibility is enhanced when OCT, rather than a conventional method, is used.
when compared to normals (P <0.01) except in the nasal aspect as tabulated in Table 2. Guedes et al (19) reported that the inferior RNFL was the only parameter in which a statistically significant difference was observed between normal subjects and glaucoma suspect groups. Pieroth et al reported a specificity of 81% and sensitivity of 65% in detecting focal defects solely through statistical analysis of OCT measurements and also noted that focal RNFL defects are located in the inferotemporal and superotemporal regions of the RNFL.

Teesalu et al. demonstrated that among patients with glaucoma, 38% of apparently normal W/W perimetry hemifields were classified as abnormal using SWAP hemifield data while 52% were classified as abnormal using HRT data, thus suggesting that eyes with seemingly healthy W/W perimetry hemifields may, in fact, already be affected by glaucoma. Subjects with abnormal SWAP values had thinner RNFLs than those with normal SWAP values. Therefore, assessment of RNFL by OCT may be as sensitive as SWAP in early detection of glaucoma and before a specific W/W perimetry defect has occurred (4).

The mean RNFL on OCT correlated to the global indices on the W/W perimetry- mean deviation (MD r= 0.68, p<0.01) and did not show correlation to the PSD (r= -0.61) (Table3). Soliman and associates 12 reported a significant correlation (correlation coefficient r = 0.557) between average RNFL thickness and mean deviation on W/W perimetry. Parisi et al and Zangwill et al have also reported a significant correlation between average RNFL thickness and MD. Kanamori et al showed that the highest correlation coefficient in all parameters was 0.729 at the average RNFL thickness, suggesting that average RNFL thickness was most useful for monitoring glaucoma.

Table 4 represents sector-wise correlation of RNFL thickness and retinal sensitivity values for glaucoma subjects and normals. Statistically significant correlation occurs for the former group where as not so for the normal subjects. This is possibly due to smaller number of patients in the normal group. Localized RNFL defects can be clinically detected if more than 50% of the thickness of RNFL is lost (20).

Therefore, we conclude that OCT gives fairly good structural correlation to the visual sensitivity functional loss in the glaucomatous optic nerve head. This can form an adjunct to diagnosis and management of glaucoma patients especially, in certain individuals who are unable to perform conventional standard perimetry.

References


6. Weinreb RN, Shakiba S, Sample PA et al. Association between quantitative nerve fibre layer measurement and visual field loss in