Macular and Peripapillary Retinal Nerve Fiber Layer Measurements by Spectral Domain Optical Coherence Tomography in Normal-Tension Glaucoma

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PURPOSE. To evaluate and compare the glaucoma discrimination ability of macular inner retinal layer (MIRL) thickness with that of peripapillary retinal nerve fiber layer (pRNFL) thickness measured by spectral-domain optical coherence tomography (RTVue-100; Optovue Inc, Fremont, CA) in patients with normal-tension glaucoma (NTG).

METHODS. Sixty-five healthy subjects and 102 with NTG were enrolled. MIRL thickness provided by a ganglion cell complex (GCC) scan and pRNFL thicknesses measured by the NHM4 (RNFL1) and RNFL 3.45 (RNFL2) modes of the RTVue-100 system were analyzed. The areas under the receiver operating characteristic curves (AUCs) of MIRL and pRNFL thicknesses for discriminating patients with NTG from control subjects were determined. The AUCs were compared between patients with central visual field (VF) defects (VF: ≤10° of fixation) and peripheral VF defects (>10° from fixation).

RESULTS. The average MIRL thickness showed a strong correlation with both RNFL1 and 2 thicknesses ($R^2 = 0.773, 0.774$, both $P < 0.0001$). The AUCs for average MIRL, RNFL1, and RNFL2 thicknesses were not significantly different at 0.945, 0.973, and 0.976, respectively. However, the AUCs of the average and superior MIRL thicknesses were significantly less than that of the pRNFL thickness in eyes with moderate-to-advanced glaucoma and eyes with peripheral VF defects.

CONCLUSIONS. The average MIRL thickness showed a strong correlation with pRNFL thickness, because patients with NTG at an early stage showed paracentral VF defects near the fixation point. MIRL thickness showed glaucoma discrimination ability comparable to that of pRNFL thickness in patients with NTG with early VF defects. In eyes with advanced or peripheral VF defect, pRNFL measurement showed a better glaucoma diagnostic ability than did MIRL measurement. (Invest Ophthalmol Vis Sci. 2010;51:1446–1452) DOI:10.1167/iovs.09-4258

Reports have suggested that macular thickness assessment could be a valuable surrogate measure in evaluating glaucomatous structural change, because such damage occurs in retinal ganglion cells (RGCs), which are multilayered and most dense in the macular region.1–4 Furthermore, RGC bodies residing in the inner nuclear layer are known to be 10- to 20-fold thicker than their axons.5,6 Studies have consistently shown that both peripapillary retinal nerve fiber layer (pRNFL) thickness and macular volume are lower in glaucomatous eyes.1–6 Therefore, it can be speculated that improvement in the resolution of imaging technologies may increase segmentation in the macula, which can be useful for detection of glaucoma at earlier stages.

Newer versions of optical coherence tomography (OCT) that incorporate spectral domain (SD) technology provide higher scan resolution and scan speed than conventional time domain (TD) OCT. The basic principles of SD-OCT have been described elsewhere.7–8 The RTVue-100 OCT (Optovue, Inc., Fremont, CA) is one of the commercially available OCT devices that use SD technology. It has an axial resolution of 5 μm in tissue and a scan speed of 26,000 A-scans/s, whereas the Stratus OCT (Carl Zeiss Meditec, Inc., Dublin, CA) has an axial resolution of 8 to 10 μm and a scan speed of 400 A-scans/s. The RTVue-100 OCT includes a ganglion cell complex (GCC) scan mode that measures macular inner retinal layer (MIRL) thickness from the internal limiting membrane to the inner nuclear layer, and possibly also to a level somewhat more posterior, to assess RGC dendrites. The GCC scan is centered on the fovea and covers a square grid on the central macula of 7 × 7 mm. MIRL thickness measured by the RTVue-100 OCT may provide improved diagnostic ability for glaucomatous change compared with TD OCT, owing to the higher scan resolution and enhanced segmentation of the MIRL from the other macular layers.

Studies have shown that eyes with normal-tension glaucoma (NTG) have visual field (VF) defects that are dense and more central than those in eyes with primary open-angle glaucoma, as determined by computerized threshold perimetry.9–11 Carprioli and Spaeth9 demonstrated that scotomas in the NTG group have steeper slopes and are significantly closer to the fixation point (a mean of 6.5° from fixation) and that the densest scotomas occur in the superior hemifield.9 This central area (within 10° from the fixation point) corresponds well with macular nerve fibers, as shown by the maps of Weber et al.12 and Garway-Heath et al.13 Thus, the detection ability for structural change of the inner retina, particularly in the central macular region, using the MIRL mode of the SD-OCT (RTVue-100) could be valuable in assessing damage caused by NTG.

With these considerations, we chose to evaluate the glaucoma discrimination ability of MIRL thickness measured by the GCC mode of the RTVue-100 OCT and to compare the data with pRNFL thickness measurements obtained with the same
instrument, in patients with NTG of different degrees of severity. Moreover, the ability of GCC scans to discriminate glaucomatous eyes from normal control eyes was assessed and compared with that of pRNFL thickness measurements in two groups of patients with NTG segregated according to differences in VF defect location (central VF defect versus peripheral VF defect).

METHODS

Subjects

All patients with glaucoma were recruited prospectively, in a consecutive manner, from the glaucoma clinic of the Asan Medical Center, Seoul, Korea. At initial evaluation, each subject underwent a complete ophthalmic examination, including medical, ocular, and family history; visual acuity (VA) testing; the Humphrey Field Analyzer (HFA) Swedish Interactive Threshold Algorithm (SITA) 24-2 test (Carl Zeiss Meditec, Dublin, CA); multiple intraocular pressure (IOP) measurements with Goldmann applanation tonometry (GAT); stereoscopic optic nerve photography; and RTVue-100 OCT scanning (Optovue, Inc.). All patients with glaucoma had undergone more than one HFA test. To minimize the learning effect, only the results of the second HFA test were used in the analysis. For inclusion in the study, all participants had to meet the following criteria: best corrected VA of 20/30 or better, with a spherical equivalent within ±5 D and a cylinder correction within ±3 D; presence of a normal anterior chamber and open-angle on slit-lamp and gonioscopic examinations; and reliable HFA test results with a false-positive error <15%, a false-negative error <15%, and a fixation loss <20%. Subjects with any other ophthalmic or neurologic condition that could result in HFA defects, or with a history of diabetes mellitus, were excluded. Age- and sex-matched healthy eyes formed the control group.

The controls consisted of hospital staff, staff family members, spouses of patients, or volunteers from the eye clinic and hospital, who had no history of ocular symptoms or disease and had not experienced intraocular or laser surgery. Each control eye had an IOP less than 22 mm Hg, with no history of IOP elevation and no perimetric defects. All NTG eyes were newly diagnosed; there had been no previous treatment. Such eyes were defined as those showing a maximum IOP of less than 22 mm Hg on GAT measurements, on at least three outpatient clinic visits as well as those showing a maximum IOP of less than 22 mm Hg (Tono-pen; Mentor Ophthalmics, Santa Barbara, CA), during subsequent in-hospital 24-hour IOP monitoring every 2 hours in the habitual position (upright between 8 AM and 10 PM and supine between 12 AM and 6 AM) before any antiglaucoma therapy; glaucomatous VF defects as confirmed by at least two reliable VF examinations; and the presence of a glaucomatous optic disc that showed increased cupping (a vertical cup-disc ratio >0.6), a difference in vertical cup-disc ratio of >0.2 between eyes, diffuse or focal neural rim thinning, disc hemorrhage, or RNFL defects. Eyes with glaucomatous VF defects were defined as those with a cluster of three points with probabilities of <5% on the pattern deviation map in at least one hemifield, including at least one point with a probability of <1% or a cluster of two points with a probability of <1% and a glaucoma hemifield test (GHT) result outside 99% of age-specific normal limits; or a pattern standard deviation (PSD) outside 95% of normal limits. One eye was randomly selected if both eyes were found to be eligible for the study. To discriminate between patterns of VF defects, all eyes with defects in only the central 10° of fixation were defined as the central group, whereas glaucomatous eyes with VF defects only outside the central 10° constituted the peripheral group.

All participants gave written informed consent before enrollment. All procedures conformed to the Declaration of Helsinki, and the study was approved by the Institutional Review Board of the Asan Medical Center at the University of Ulsan, Seoul, Korea.

Optical Coherence Tomography

MIRL thickness using the GCC scan protocol and pRNFL thickness employing two scanning modes, NHM4 and RNFL 3.45, were measured with the RTVue-100 OCT (software version A4, 0, 0, 143; Optovue, Inc.). The GCC scan covered a 7° × 7-mm scan area centered on the fovea. RNFL thickness was determined by both NHM4 (RNFL1) and RNFL 3.45 modes (RNFL2). The RNFL 3.45 mode measures pRNFL thickness along a circle 3.45 mm in diameter around the optic disc, as does the fast RNFL mode of Stratus OCT (Carl Zeiss Meditec, Inc.), whereas the NHM 4 mode measures pRNFL thickness by recalculating data along a circle 3.45 mm in diameter around the optic disc, guided by a map created from en face imaging of 6 circular and 12 linear data inputs. Average, superior, and inferior hemiretinal MIRL data and information from the two modes of pRNFL thickness measurement, were used for analysis. Images with signal strength index (SSI) less than 40 or with overt misalignment of the surface detection algorithm on at least 10% of consecutive A-scans or 15% of cumulative A-scans or with overt decentration of the measurement circle location (assessed subjectively) were excluded from further analysis. Pharmacologic dilation was performed if the pupil was smaller than 3.0 mm. All images were acquired by a single well-trained operator (HEH) who was masked to the diagnosis and other clinical findings, including location and severity of VF defect during the same patient visit.

According to the criteria, of 179 eyes that qualified for initial inclusion, 12 were excluded because of poor image quality. Seven of those eyes had SSI less than 40, and 8 had overt misalignment of the surface detection algorithm; 3 eyes were disqualified by both criteria. The final analysis thus included the remaining 167 eyes.

Statistical Analysis

The Wilk-Shapiro test was used to test distribution of numerical data. Normally distributed data of healthy subjects and patients with glaucoma were compared by the unpaired t-test. The χ² test was used to compare categorical data. The relationships between MIRL and each pRNFL measurement were assessed by Pearson correlation analysis and coefficients of determination (R²) were calculated. To compare the discrimination capability between MIRL and pRNFL thickness measurements in healthy and glaucomatous eyes, we calculated and analyzed the areas under the receiver operating characteristics (ROC) curves (AUCs), including those for the average, superior, and inferior retinal regions. To compare glaucoma discrimination capabilities between MIRL and pRNFL thickness measurements at different stages of glaucoma, we divided the subjects with glaucoma into two groups—an early group (EG group) and a moderate to advanced group (AG group)—according to the Hodapp-Anderson-Parrish (HAP) grading scale of VF severity. This staging system is described in detail elsewhere. By HAP criteria, 56 eyes had early VF defects (EG group), whereas 46 eyes had moderate-to-advanced defects (AG group).

Eyes with NTG often exhibited scotomas closer to the fixation point in our series of NTG eyes. Thus, to test the diagnostic capabilities of MIRL and pRNFL thickness assessment with respect to VF defect location in glaucoma, we selected consecutive eyes with VF defect clusters confined to the central 10° only (24/102 eyes, 24%, central group) and eyes with VF defect clusters outside the central 10° (33/102 eyes, 32%, peripheral group) from the total of 102 glaucomatous eyes (45/102 eyes, 44% with VF defect clusters overlapping the border at 10°). Patients with both central and peripheral VF defects were excluded from each group in this analysis. The AUCs of these subgroups were also determined. The method of DeLong et al. was used to evaluate statistical differences between AUCs. Sensitivities at fixed specificities of 80%, 90%, and 95% were calculated from ROC curves for the entire group and for each subgroup (SPSS, ver. 15.0; SPSS Inc., Chicago, IL; and MedCalc, ver. 9.6; MedCalc, Mariakerke, Belgium).

RESULTS

A total of 167 subjects including 65 healthy individuals and 102 patients with glaucoma were enrolled in the study. As expected, the VF mean deviation (MD) and PSD were significantly different between control and glaucomatous eyes at various stages. The average, superior, and inferior hemiretinal...
MIRL thickness, and thicknesses measured by the two RNFL modes demonstrated statistically significant differences between healthy and glaucomatous eyes (Table 1).

The association between MIRL and pRNFL thickness as measured by NHM4 (RNFL1) and RNFL 3.45 (RNFL2) scanning was assessed with Pearson’s correlation analysis. The average MIRL thickness showed a strong correlation with average pRNFL thickness measured by both scan protocols (MIRL versus RNFL1, $R^2 = 0.773$; MIRL versus RNFL2, $R^2 = 0.774$). The superior and inferior hemiretinal MIRL thicknesses also showed strong correlations with the corresponding superior and inferior pRNFL thicknesses measured by both scan protocols (superior MIRL versus RNFL1, $R^2 = 0.635$; superior MIRL versus RNFL2, $R^2 = 0.635$; inferior MIRL versus RNFL1, $R^2 = 0.797$; inferior MIRL versus RNFL2, $R^2 = 0.801$).

The overall and subgroup ROC curves and AUCs are shown in Figures 1 and 2. Overall, the AUCs for average MIRL and pRNFL thickness measured by both protocols, to discriminate between healthy and glaucomatous eyes, were 0.945, 0.976, and 0.973, and there were no significant differences (Fig. 1a). RNFL1 and -2 showed higher AUCs than that of MIRL in the superior hemiretina (Fig. 1b). However, the AUCs of MIRL, RNFL1, and RNFL2 did not show significant differences in the inferior hemiretina (Fig. 1c).

The AUCs for MIRL and pRNFL thickness, to discriminate between healthy and glaucomatous eyes, did not differ significantly in any sector, including the overall average, in eyes with early glaucoma (EG, Figs. 1d–f). However, in patients with moderate-to-advanced glaucoma (AG), the AUC of MIRL average thickness was significantly less than that of the pRNFL average thickness. AUCs from the superior hemiretina showed similar results (Figs. 1g–i).

In eyes with central VF defects (the central group), the AUCs of average and superior MIRL and pRNFL thickness (RNFL1 and -2) did not show statistically significant differences, whereas in the inferior hemiretina, RNFL2 showed a significantly greater AUC than did MIRL (Figs. 2a–c). In the peripheral group, however, the AUCs of both pRNFL thicknesses, overall and in the superior retina, were greater than those of the MIRL thicknesses (Figs. 2d–f).

Table 2 shows sensitivities (%) at fixed specificities of the three assessed methods for glaucoma discrimination. There was a uniform trend for MIRL thickness measurement to be less sensitive at fixed specificities of ≥80%, ≥90%, and ≥95%, when compared with RNFL1 and -2 assessments. This trend was more pronounced in the moderate-to-advanced glaucoma group (AG) and in patients with peripheral VF defects (the peripheral group).

Figure 3A illustrates a clinical case in which the central VF defect in a patient with early glaucoma was detected by both MIRL and pRNFL scanning. Figure 3B illustrates a patient with advanced glaucoma with both superior and inferior field defects, in whom an inferior VF defect was detected by the superior pRNFL mode, whereas the superior MIRL scan yielded a normal finding.

### Discussion

After Zeimer et al. suggested the importance of macular thickness measurements in evaluation of glaucomatous damage, several studies were performed to determine the effectiveness of such a thickness assessment for glaucoma detection. These studies showed that macular thickness measurements were able to detect glaucomatous damage. However, the measurements had not better predictive value than pRNFL thickness assessment. The reason may be that total macular thickness was assessed, rather than that of the RGC layer, thus decreasing the specificity of macular thickness for glaucoma diagnosis.

The axons, bodies, and dendrites of RGCs are believed to reside in the RNFL, the ganglion cell layer, and the inner plexiform layer, respectively. Therefore, it may be more accurate to measure the thickness of these specific layers rather than total macular thickness, to detect glaucomatous change. Ishikawa et al. developed a macular segmentation algorithm for the Stratus OCT and showed that the thickness of the inner retinal complex (macular RNFL, ganglion cells, and inner plexiform and inner nuclear layers) was the best measure for discriminating healthy from glaucomatous eyes, with reliability similar to that of pRNFL thickness evaluation. Tan et al. in a multicenter clinical trial in which the Stratus OCT was used, also demonstrated that thickness measurement of a combination of the three innermost layers of the macula was the best measure for glaucoma diagnosis in the macular region and offered a glaucoma discrimination power similar to that of pRNFL.

The loss of RGCs and thinning of the RNFL have been shown to precede development of a glaucomatous VF defect. Thus, detection of such early structural changes may be crucial for timely diagnosis. As RGC bodies are multilayered in the macular area, detection of RGC loss may be easier in that region than in the peripheral retina.

**Table 1. Baseline Characteristics and MIRL and pRNFL Thicknesses**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Healthy ($n = 65$)</th>
<th>EG ($n = 56$)</th>
<th>AG ($n = 46$)</th>
<th>$P1$</th>
<th>$P2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>52.7 ± 12.1</td>
<td>53.4 ± 11.7</td>
<td>56.4 ± 11.1</td>
<td>0.303</td>
<td>0.090</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>33/32</td>
<td>29/27</td>
<td>20/26</td>
<td>0.528</td>
<td>0.343</td>
</tr>
<tr>
<td>Spherical equivalent, D</td>
<td>-0.79 ± 1.97</td>
<td>-0.47 ± 2.01</td>
<td>-0.45 ± 1.89</td>
<td>0.64</td>
<td>0.55</td>
</tr>
<tr>
<td>VF MD, dB</td>
<td>-0.76 ± 1.29</td>
<td>-2.62 ± 1.72</td>
<td>-12.1 ± 4.40</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VF PSD, dB</td>
<td>1.56 ± 0.52</td>
<td>3.45 ± 2.03</td>
<td>10.1 ± 3.55</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MIRL, µm</td>
<td>Average</td>
<td>95.6 ± 4.63</td>
<td>82.4 ± 7.70</td>
<td>75.7 ± 10.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Superior</td>
<td>95.4 ± 5.44</td>
<td>84.5 ± 6.83</td>
<td>80.5 ± 12.7</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inferior</td>
<td>95.8 ± 4.45</td>
<td>80.3 ± 11.1</td>
<td>70.9 ± 10.9</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RNFL1, µm</td>
<td>Average</td>
<td>111.8 ± 7.84</td>
<td>88.9 ± 10.6</td>
<td>78.7 ± 11.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Superior</td>
<td>112.5 ± 9.44</td>
<td>90.2 ± 10.8</td>
<td>80.9 ± 14.7</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inferior</td>
<td>111.0 ± 8.59</td>
<td>87.6 ± 13.2</td>
<td>75.4 ± 12.6</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RNFL2, µm</td>
<td>Average</td>
<td>111.7 ± 7.64</td>
<td>88.5 ± 11.1</td>
<td>77.4 ± 10.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Superior</td>
<td>113.1 ± 9.18</td>
<td>90.9 ± 11.3</td>
<td>81.1 ± 14.6</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inferior</td>
<td>110.4 ± 8.25</td>
<td>86.2 ± 14.5</td>
<td>73.7 ± 10.9</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SD. P1, healthy vs. EG; P2, healthy vs. AG. Student’s $t$-test and $\chi^2$ test.
The disc changes of NTG are typically progressive and may present in a variety of characteristic disc appearances among different ethnic groups. Although the definition of a glaucomatous optic disc was based on multiple disc change patterns in the present study, the disc change associated with our Korean NTG eyes was primarily focal atrophy of the disc and corresponding RNFL defect. Initially, bundles of axons were selectively destroyed in the inferotemporal region close to the center of the fovea. With the advancement of glaucoma, neural rim tissue loss was found in the superotemporal sector that led to enlargement of the cup in a vertical direction. The loss of axonal bundles, which led to the neural rim changes of glaucomatous optic atrophy, produced visible defects in the RNFL, close to the center of fovea inferiorly, followed by superior RNFL damage somewhat remote from the fixation point, thus in the periphery. Therefore, we found that average, superior, and inferior thickness measurements using the three scanning protocols showed significant differences between healthy and glaucomatous eyes. These findings agree with previous studies demonstrating significantly thinner pRNFL and macular thicknesses in glaucomatous eyes.6,25–27

Both pRNFL thickness measurement protocols showed strong correlations with MIRL thickness ($R^2 = 0.773$ and 0.774 for RNFL1 and -2, respectively). Although direct comparison with other studies is problematic because different devices and study designs were used, the correlation of MIRL thickness with pRNFL thickness was found to be stronger than that in previous studies in which the correlation between total macular thickness and pRNFL thickness was evaluated. Wollstein et al.17 reported that the $R^2$ coefficient was 0.54 when macular and pRNFL thickness measurements obtained by a prototype OCT were compared. Greenfield et al.6 found a low correlation ($R^2 = 0.38$) between mean macular and pRNFL thicknesses, as determined by OCT1. The seemingly stronger correlation found in the present study may be attributable mainly to the correlation between the thickness of specific layers of the macula (MIRL) and the pRNFL, rather than to total macular thickness.

The improved scan resolution of updated SD-OCT versions may affect correlations between macular and pRNFL thicknesses. However, as measurement accuracy is determined by both segmentation algorithms and scan resolution and as detailed information on segmentation software or other possible factors attributable to RTVue-100 OCT operation is scarce, it would be premature to describe the effect of scan resolution or quality on the correlation between MIRL and pRNFL thickness measurements.

The overall AUCs for discriminating healthy from glaucomatous eyes were not significantly different when average MIRL and pRNFL thicknesses obtained by either scanning protocol were compared. These results are consistent with the findings of Ishikawa et al.4 and Tan et al.,3 in that evaluations of MIRL thickness showed a glaucoma discrimination ability similar to that of pRNFL analysis with the Stratus OCT (Carl Zeiss Meditec, Inc). This ability was most obvious in the inferior retinal data of our study. However, comparisons between the AUCs of MIRL thickness in the superior retina and the corresponding pRNFL thicknesses (RNFL1 and -2) showed that the latter two modes offered significantly better diagnostic abilities ($P = 0.016, 0.024, 0.016$).

FIGURE 1. ROC curves and AUCs of MIRL and RNFL thicknesses for discriminating between healthy and glaucoma groups at different stages. All eyes: average (a), superior (b), inferior (c); EG: average (d), superior (e), inferior (f); and AG: average (g), superior (h), inferior (i). x-Axis: 1 − specificity; y-axis: sensitivity; $P_1$: comparison between MIRL and RNFL1; $P_2$: comparison between MIRL and RNFL2; $P_3$: comparison between RNFL1 and -2. RNFL1 by NHM4 mode; RNFL2 by RNFL 3.45 mode.

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respectively). The most likely explanation for the better diagnostic ability of pRNFL assessment, compared with MIRL data, is that RNFL damage in NTG eyes usually occurs closer to the center of the fovea, with associated VF defects that are often found in the superior hemifield close to the fixation point, and thereafter spread both peripherally and inferiorly.9,28 VF loss close to the fixation point was often noted as an isolated finding, most frequently in patients with early-stage NTG.9 With disease progression, as in the AG group of our study, superior pRNFL damage remote from the fixation point—thus in the periphery—was frequently noted, similar to that in patients with high-tension glaucoma (HTG), because NTG eyes may become more susceptible to IOP-related damage with disease progression.29,30 Thus, in our series of NTG eyes, the pattern of VF defects described may explain the decreased sensitivity of MIRL measurements of superior hemiretina in detection of inferior VF defects.

When assessed with respect to the degree of glaucoma severity, all three measurements showed similar AUCs in patients with early glaucoma. In patients with moderate-to-advanced glaucoma, the average MIRL thickness was of significantly lower diagnostic value than was afforded by either of the two pRNFL thickness measurements (P = 0.032 and 0.029 for RNFL1 and RNFL2, respectively). When evaluated separately for each hemiretina, diagnostic abilities did not differ among the three scan types in the inferior retina, but the superior retinal MIRL thickness measurement offered a poorer discrimi-
inatory ability than did either of the pRNFL modes. The difference between the two hemiretinal MIRL thickness measurements in discrimination of moderate-to-advanced glaucoma may be attributable to the commonly noted sparing of the inferior VF, near the fixation point, until late in the course of glaucoma. Conversely, that there is a lack of any significant difference among the three modes in discrimination of early glaucoma may be because patients with NTG tend to show early VF defects near the fixation point, correlating well with inferior inner macular damage close to the fovea, which MIRL measurement effectively detects.

As the MIRL thickness measurement includes the RGC layers of the posterior pole, we hypothesized that it may be more sensitive in detection of VF defects close to the fixation point than were the peripapillary modes (RNFL1 and -2). However, we found that all three thickness measurement modes had an equivalent diagnostic ability for discriminating eyes with central glaucoma may be because patients with NTG tend to show early VF defects near the fixation point, correlating well with inferior inner macular damage close to the fovea, which MIRL measurement effectively detects.

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Turning to detection of peripheral VF defects, both pRNFL thickness protocols showed better performance than did the MIRL thickness assessment in average and superior retinal measurements, perhaps because peripheral glaucomatous VF defects tend to occur inferiorly, with superior RNFL defects being more frequent outside the posterior pole.28,29 Thus, MIRL thickness measurements may miss peripheral VF defects. This finding contrasts with the inferior RNFL defects in NTG, where such defects are often found at early stages of glaucoma and the pattern of RNFL damage shows involvement of both central and peripheral regions.28,29

There was a uniform trend toward decreased sensitivity in MIRL measurements at specificities of both 80%, 90%, and 95%, in discrimination of glaucomatous from control eyes. The relatively lower sensitivity of MIRL measurements was more pronounced in the superior retina among patients with all degrees of glaucoma severity. Koseki et al.10 emphasized that NTG VF defects more commonly begin in the superior hemifield near the fixation point. The similar sensitivity of MIRL and pRNFL assessment in the corresponding inferior hemiretina is thus understandable. Often, the inferior VF near the fixation point is spared until late in the course of NTG. Again, this sparing may explain the decreased sensitivity of MIRL measurements of the superior hemiretina as well as the average thickness measurement.
Limitations of the present study include the use of a homogeneous population. Data from a single ethnic group may not be generalized to other races. Also, as we did not include an HTG group in our study, we may not automatically apply our findings in NTG eyes to those in HTG eyes. Inclusion of normal subjects, based on normal optic nerve appearance and VF at initial clinical examination would overestimate the diagnostic accuracy of the various RTVue-100 OCT modes tested. However, such limitations are common to all case-control studies of this type. In addition, the relatively small sample size may limit the discriminating power of our subgroup analysis, which was based on VF defect location (central versus peripheral). However, our study was exploratory and comparative, evaluating both macular and pRNFL measurements in detection of glaucoma, by using SD-OCT in an NTG population. Therefore, this work may be valuable in guiding further studies.

In conclusion, our observation of macular thinning, as reflected by both MIRL and pRNFL exploration modes, in our NTG eyes, suggests that both GCC and pRNFL thickness modes can be useful in the detection of glaucoma. In our subgroup analysis, the diagnostic performance of the GCC mode was similar to that of the pRNFL thickness measurement in patients with early-stage NTG and in those eyes in which VF defects were close to the fixation point. However, the GCC mode (MIRL) of RTVue-100 OCT was not as sensitive as the pRNFL measurement modes (NHM4 and RNFL3.45) at fixed specificities (80%, 90%, and 95%). MIRL thickness measured by SD-OCT may be a good alternative to pRNFL thickness assessment for detection of glaucoma, in circumstances that pRNFL measurements may be unreliable, especially in eyes with unusually small or large optic discs or in those with peripapillary atrophy or a tilted optic disc.

References