Influences of the Inner Retinal Sublayers and Analytical Areas in Macular Scans by Spectral-Domain OCT on the Diagnostic Ability of Early Glaucoma

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Purpose. We investigated the influences of the inner retinal sublayers and analytical areas in macular scans by spectral-domain optical coherence tomography (OCT) on the diagnostic ability of early glaucoma.

Methods. A total of 64 early (including 24 preperimetric) glaucomatous and 40 normal eyes underwent macular and peripapillary retinal nerve fiber layer (pRNFL) scans (3D-OCT-2000). The area under the receiver operating characteristics (AUC) for glaucoma diagnosis was determined from the average thickness of the total 100 grids (6 × 6 mm), central 44 grids (3.6 × 4.8 mm), and peripheral 56 grids (outside of the 44 grids), and for each macular sublayer: macular RNFL (mRNFL), ganglion cell layer plus inner plexiform layer (GCL/IPL), and mRNFL plus GCL/IPL (ganglion cell complex [GCC]). Correlation of OCT parameters with visual field parameters was evaluated by Spearman’s rank correlation coefficients (rs).

Results. The GCC-related parameters had a significantly larger AUC (0.82–0.97) than GCL/IPL (0.81–0.91), mRNFL-related parameters (0.72–0.94), or average pRNFL (0.88) in more than half of all comparisons. The central 44 grids had a significantly lower AUC than other analytical areas in GCC and mRNFL thickness. Conversely, the peripheral 56 grids had a significantly lower AUC than the 100 grids in GCL/IPL inferior thickness. Inferior thickness of GCC (rs, 0.45–0.49) and mRNFL (rs, 0.43–0.51) showed comparatively high correlations with central visual field parameters to average pRNFL thickness (rs, 0.41, 0.47) even in the central 44 grids.

Conclusions. The diagnostic ability of macular OCT parameters for early glaucoma differed by inner retinal sublayers and also by the analytical areas studied.

Keywords: spectral-domain optical coherence tomography, inner macular parameter, diagnostic ability, differences by sublayers and analytical area

Glaucoma is an optic neuropathy characterized by loss of retinal ganglion cells. Ganglion cells and the retinal nerve fiber layer (RNFL) constitute 30% to 35% of the macular retinal thickness and are thickest in this region. Therefore, it was proposed that loss of ganglion cells can be more readily detected in the central macular region. Macular thickness evaluation has received increasing attention after Zeimer’s hypothesis1 that quantitative detection of glaucomatous damage at the posterior pole by retinal thickness mapping may provide a method for detection and monitoring for early glaucomatous damage.

The recent introduction of spectral-domain OCT (SD-OCT) allows imaging of the intraretinal microstructure at a much faster scan rate and at higher resolution than previous technologies. This advance enabled us to measure the inner retinal thickness of the macular region, which is known as ganglion cell layer plus inner plexiform layer (GCL/IPL) plus macular RNFL (mRNFL; ganglion cell complex [GCC]). Several reports, including ours, have assessed GCC measurements to detect glaucomatous damage using commercially available SD-OCT.2-5 In these reports, GCC thickness measurements had similar discrimination capabilities of glaucomatous visual field (VF) damage as peripapillary RNFL (pRNFL) thickness measurements. A recent version of SD-OCT software permitted separation of mRNFL and GCL/IPL measurements from GCC measurements. A few studies have compared the diagnostic ability of GCL/IPL measurements to pRNFL measurements and showed that GCL/IPL also had a high ability to discriminate between normal and early glaucomatous eyes.6-9 However, most of these findings were obtained using the Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA), which evaluates a 4 × 4.8-mm elliptical annulus region of the macula.

Three-dimensional OCT-2000 (3D-OCT, software version 8.00; Topcon, Inc., Tokyo, Japan) creates a 10 × 10 grid map and displays three parameters of the segmented inner retinal layer of a 6 × 6-mm square macular region: mRNFL, GCL/IPL, and GCC. At this stage, it is not clear which parameter is the most useful to evaluate the diagnostic ability or structure-function relationship in the early stages of glaucoma in clinical practice. The aim of this study was to carry out macular scans and pRNFL scans using 3D-OCT in patients with early glaucoma and normal participants, and to determine which parameter had the highest diagnostic ability and highest structure-function relationship among four parameters tested (mRNFL,
GCL/IPL, GCC, and pRNFL). In addition, we also examined the effects of the difference of the analytical area on the diagnostic ability of the macular parameters.

**MATERIALS AND METHODS**

**Participants**
This study met the Helsinki Declaration guidelines and was approved by the Ethical Committee of Koseiren Takaoka Hospital, Japan. Informed consent was obtained from each participant before enrollment. Early glaucoma participants included those with preperimetric glaucoma (PG) and primary open-angle glaucoma (POAG). One eye of each participant was examined in this study according to the eligibility criteria described below. If both eyes met the eligibility criteria, one eye was selected randomly. All participants had complete ophthalmologic examinations including best-corrected acuity, slit-lamp examination, IOP measurement using Goldmann applanation tonometry, gonioscopy, dilated fundus biomicroscopy using a 78-diopter (D) lens, stereoscopic optic disc photography, and standard automated perimetry (SAP) using a Humphrey field analyzer (HFA; Carl Zeiss Meditec) with the 30-2 Swedish Interactive Threshold Algorithm. Inclusion criteria were best corrected acuity ≥20/20, open angle, and no ocular pathology other than glaucoma. Exclusion criteria included cataract, large refractive errors (outside of ±6.00 D sphere or 2.00 D cylinder), and pupil diameter <3 mm. Only eyes with reliable SAP results, which were defined as false-negative and false-positive responses <5% and fixation loss <20%, were eligible for the study. Glaucomatous VF defects were determined according to Anderson’s criteria in which one of the following was present: having a cluster of 3 or more nonedge points with P <5% and at least one point with P < 1% in the pattern deviation probability plot, pattern standard deviation (PSD) of less than 5%, or a glaucoma hemifield test result outside normal limits. Early glaucoma patients and normal participants underwent SAP at least twice before this study was initiated. Normal participants had a normal optic nerve head appearance, IOP <21 mm Hg, and normal SAP results. The PG patients had glaucomatous optic disc abnormalities with a localized RNFL defect at areas of rim thinning, but without glaucomatous VF defects. The POAG patients had glaucomatous optic disc abnormalities with a localized RNFL defect at areas of rim thinning, but without glaucomatous VF defects. The POAG patients had glaucomatous optic disc abnormalities with a localized RNFL defect at areas of rim thinning, but without glaucomatous VF defects. In the early glaucoma group, the mean deviation (MD) was >−6 dB. All patients with POAG had a reproducible glaucomatous VF defect with SAP in at least two consecutive examinations.

**3D-OCT Measurements**

The 3D-OCT-2000 has an axial scanning speed of 27,000 A-scans per second at an axial resolution of 5 to 6 μm. Raster scanning of a 7×7-mm area centered on the fovea at a scan density of 512 (vertical)×128 (horizontal) scans was performed using 3D-OCT. A 6×6-mm square area centered on the fovea was measured using software embedded in the 3D-OCT instrument. The data were divided automatically into 10×10 grids, and average, superior, and inferior thickness of mRNFL, GCL/IPL, and GCC thicknesses were displayed (Fig. A). In this study, average, superior, and inferior thickness of GCC, GCL/IPL, and mRNFL parameters were evaluated. Furthermore, average, superior, and inferior thickness of the central 44 grids (within a 3.6×4.8-mm area), which correspond to the Cirrus OCT elliptical annulus region (4×4.8 mm), and those of the peripheral 56 grids were derived from 10×10 grids to examine the effects of the difference of the analytical area on the diagnostic ability (Fig. C). For pRNFL thickness measurements, a circular scan, each composed of 1024 A-scans, was obtained for each test. The 3D-OCT algorithm identified the center of the optic disc and automatically placed a 3.4-mm circle around it. The pRNFL thickness was assessed between the anterior and posterior margins of the RNFL as delineated by a computer algorithm. Average pRNFL thickness was evaluated in this study. Internal fixation was used for all scans. All images were obtained with image quality scores of at least 60 as recommended by the manufacturer. Eyes with segmentation errors in OCT measurements were excluded from this study.

**VF Examination**

Correlations were analyzed by comparing the MD, PSD, central mean sensitivity (MS), and the central total deviation (TD) values measured by SAP to the average OCT parameters assessed by 3D-OCT. The central MS and central TD, which were assumed to correspond roughly to the retina within a 6×6-mm square area centered on the fovea, were defined as the average of 16 central data points. The VF sensitivity was evaluated using a logarithmic decibel scale.

**Statistical Analyses**

An independent sample t-test was used to compare differences in mean age, sex, refractive error, IOP, SAP-MD, SAP-PSD, inner macular thickness parameters, and pRNFL thickness between normal and early glaucomatous eyes. The receiver operating characteristics (ROC) curves were calculated to assess the ability of each testing parameter to differentiate early glaucoma from normal eyes. A value of 1.0 of the area under a ROC curve (AUC) represents perfect discrimination, whereas an AUC of 0.5 represents chance discrimination. The correlation between 3D-OCT measurements and VF parameters was expressed as a Spearman’s coefficient of correlation. Statistical analyses were performed using SPSS 16.0 software for Windows (SPSS Japan, Inc., Tokyo, Japan). The ROC curves were compared by the DeLong test. MedCalc, version 10.4.0, (MedCalc Software, Ostend, Belgium) was used to compare the ROC curves. A P value <0.05 was considered statistically significant.

**RESULTS**

We evaluated 111 eyes for this study. Five eyes were excluded due to failure of the segmentation algorithm and two eyes were excluded because the image quality scores were <60. Analysis was performed on 64 eyes of 64 early glaucoma and 40 normal subjects. The early glaucoma group included 40 POAG and 24 PG patients. The demographic and clinical information for each group is summarized in Table 1. There were no significant differences in age, sex, or refractive error. The MD and IOP were significantly lower, whereas PSD was significantly higher in patients with glaucoma than in normal subjects. Results of 3D-OCT macular and pRNFL parameters in early glaucoma and normal subjects are shown in Table 2. The thickness was significantly lower in patients with glaucoma than in normal subjects for all parameters.

The results of AUCs for detecting early glaucoma are shown in Table 3. The AUCs of superior thickness were significantly lower than those of average or inferior thickness regardless of the analytical area in almost all of the macular OCT parameters. In comparison, the areas of AUCs between different analytical areas, the central 44 grids had a significantly lower AUC than the total 100 grids or the peripheral 56 grids in GCC (except for GCC...
superior) and mRNFL thickness. Conversely, the peripheral 56 grids had a significantly lower AUC than the total 100 grids in GCL/IPL inferior thickness.

In terms of the differences in AUCs between different OCT parameters, average or inferior thickness of GCC had significantly higher AUCs than the corresponding thickness of GCL/IPL or average pRNFL thickness when comparing the total 100 grids and the peripheral 56 grids (Table 4). However, no differences were found regarding the central 44 grids of all GCC parameters (average, superior, and inferior) compared to GCL/IPL or pRNFL. In contrast, GCC thickness had significantly higher AUCs than the corresponding thickness of mRNFL except for GCC average thickness in the total 100 grids or the peripheral 56 grids. The GCL/IPL average or inferior thickness in the central 44 grids had significantly higher AUCs than the corresponding thickness of mRNFL, while all GCL/IPL parameters showed no significant differences when compared to the average pRNFL thickness regardless of the analytical area. All mRNFL parameters had significantly lower AUCs compared to average pRNFL thickness in the central 44 grids.

In an additional analysis, we compared the diagnostic ability using 40 POAG eyes excluding PG and normal subjects. The results were generally the same as those of 64 early glaucoma eyes including PG subjects.

Table 5 summarizes the correlation coefficients between VF parameters and OCT parameters in all participants. Although significant correlations were found between all VF parameters and most of the OCT parameters, inferior thickness generally showed better correlation compared to average or superior thickness. When looking at good correlations, which have \( r^2 \geq 0.4 \) and \( P < 0.05 \), average pRNFL thickness had good correlations with all VF parameters, while no macular OCT parameters had good correlations with MD. The GCC inferior and mRNFL inferior thickness had good correlations with PSD and central VF parameters except for the correlation between the central 44 grids and PSD. In contrast, GCL/IPL inferior thickness had a good correlation between the central 44 grids and central VF parameters.

**DISCUSSION**

In our study, the diagnostic ability of macular OCT parameters to detect early glaucoma differed by inner retinal sublayers and also by the analytical areas studied. Among the four OCT parameters examined, GCC-related thickness had a higher AUC than the corresponding thickness of GCL/IPL, mRNFL, or average pRNFL in more than half of all comparisons. Macular OCT parameters other than GCC had high AUCs that were comparable to pRNFL except for mRNFL thickness in the central 44 grids, which had lower AUCs compared to the other OCT parameters. Several studies have shown that GCC thickness had a similar diagnostic power as pRNFL thickness for the diagnosis of early glaucoma.\(^2\)\(^-\)\(^5\) In other reports using Cirrus OCT, Mwanza et al.\(^6\) reported that average pRNFL (AUC = 0.935) was comparable to GCC thickness in more than half of all comparisons. Macular OCT parameters other than GCC had high AUCs that were comparable to pRNFL except for mRNFL thickness in the central 44 grids, which had lower AUCs compared to the other OCT parameters. The only available study comparing the diagnostic ability among GCC, GCL/IPL, mRNFL, and pRNFL thickness by a single OCT device (Cirrus OCT) was reported by Kotowski et al.\(^8\) They showed that average GCC and GCL/IPL (AUC =

### Table 1. Clinical Characteristics of the Participants

| Age, y (range) | 61.5 ± 9.4 (36–81) | 64.2 ± 9.5 (43–82) | 0.07* |
| Sex, male/female | 21/19 | 27/37 | 0.24† |
| Refractive error, D | −0.9 ± 1.8 | −1.1 ± 2.3 | 0.62* |
| SAP.MD, dB (range) | −0.6 ± 1.0 (−2.5–1.9) | −1.4 ± 0.9 (−3.0–0.3) | <0.001* |
| SAP.PSD, dB (range) | 1.8 ± 0.5 (1.2–3.0) | 2.9 ± 1.4 (1.5–8.5) | <0.001* |
| IOP, mm Hg | 13.9 ± 2.4 | 12.6 ± 2.8 | 0.02* |

Values are mean ± SD. P indicates P value in comparison of means or frequency among normal and early glaucoma groups.

* With an independent t-test.
† With \( \chi^2 \) test.

### Table 2. Comparisons of Thickness in OCT Parameters Between Glaucoma and Normal Subjects

<table>
<thead>
<tr>
<th>Analytical Areas</th>
<th>Total 100 Grids</th>
<th>Central 44 Grids</th>
<th>Peripheral 56 Grids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness, ( \mu )m</td>
<td>GCC</td>
<td>GCL/IPL</td>
<td>mRNFL</td>
</tr>
<tr>
<td>GCL/IPL average</td>
<td>89.5 ± 6.7</td>
<td>105.7 ± 6.8</td>
<td>89.5 ± 6.4</td>
</tr>
<tr>
<td>GCL/IPL inferior</td>
<td>91.1 ± 10.7</td>
<td>104.6 ± 6.9</td>
<td>93.8 ± 10.2</td>
</tr>
<tr>
<td>GCL/IPL superior</td>
<td>87.9 ± 9.4</td>
<td>106.4 ± 7.6</td>
<td>94.8 ± 10.2</td>
</tr>
<tr>
<td>mRNFL average</td>
<td>60.2 ± 4.3</td>
<td>68.4 ± 4.4</td>
<td>73.0 ± 6.3</td>
</tr>
<tr>
<td>mRNFL inferior</td>
<td>61.4 ± 6.1</td>
<td>68.7 ± 4.5</td>
<td>74.0 ± 8.4</td>
</tr>
<tr>
<td>mRNFL superior</td>
<td>59.0 ± 5.0</td>
<td>67.9 ± 4.6</td>
<td>71.4 ± 7.3</td>
</tr>
<tr>
<td>pRNFL average</td>
<td>29.3 ± 3.8</td>
<td>37.0 ± 4.3</td>
<td>23.6 ± 2.9</td>
</tr>
<tr>
<td>pRNFL inferior</td>
<td>29.7 ± 5.8</td>
<td>36.2 ± 4.7</td>
<td>24.1 ± 3.6</td>
</tr>
<tr>
<td>pRNFL superior</td>
<td>28.9 ± 6.0</td>
<td>37.8 ± 4.6</td>
<td>23.4 ± 3.9</td>
</tr>
<tr>
<td>pRNFL average</td>
<td>88.4 ± 10.6</td>
<td>103.9 ± 8.6</td>
<td>88.4 ± 10.6</td>
</tr>
</tbody>
</table>

Mean (±SD) and SD values of each parameter are shown. P value of t-test to evaluate the differences between glaucoma and normal.
had similar discriminating ability for early glaucomatous eyes to mean pRNFL (AUC = 0.900). Furthermore, the AUC of average mRNFL (AUC = 0.832) was significantly lower than that of average GCC or pRNFL. In contrast, Kanamori et al.\textsuperscript{12} reported that mRNFL had similar AUCs (0.846–0.949) for early glaucoma to GCL/IPL (0.819–0.912) using the same OCT device, 3D-OCT, as our study, which was consistent with our results. In this regard, the same study group showed lower AUCs for early glaucoma in the mRNFL parameters with Cirrus OCT (0.713–0.829) than with 3D-OCT (0.808–0.904) and speculated that the difference was due to the advantage of a wider analytical area of 3D-OCT (6 \times 6-mm square area) than Cirrus OCT (4 \times 4.8 mm elliptical area). This would allow more chances to include the thick portion of the RNFL along the vascular arcades and RNFL defects originating from a more perpendicular portion of the disc.\textsuperscript{13} However, to our knowledge, direct comparison of different analytical areas using the same OCT has not yet been reported. We provided evidence that the default analytical area of 3D-OCT (total 100 grids) had higher AUCs than the smaller Cirrus-like analytical area (central 44 grids) in mRNFL thickness. Furthermore, the peripheral 56 grids also had higher AUCs than the central 44 grids in mRNFL thickness indicating that the analytical area of the peripheral 56 grids

\begin{table}[h]
\centering
\caption{Comparison of AUC Between Different OCT Parameters}
\begin{tabular}{llcccc}
\hline
OCT Parameters & Analytical Area & AUC & vs. GCL/IPL & vs. mRNFL & vs. pRNFL \\
\hline
GCC average & Total 100 grids & 0.97 & 0.90, 0.005 & 0.92, 0.062 & 0.88, 0.002 \\
& Central 44 grids & 0.91 & 0.76, <0.001 & 0.88, 0.002 \\
& Peripheral 56 grids & 0.97 & 0.84, 0.28 & 0.79, 0.04 & 0.88, 0.05 \\
GCC superior & Total 100 grids & 0.84 & 0.87, 0.001 & 0.94, 0.136 & 0.88, 0.002 \\
& Central 44 grids & 0.82 & 0.72, 0.01 & 0.88, 0.13 & \\
& Peripheral 56 grids & 0.86 & 0.81, 0.02 & 0.88, 0.63 & \\
GCC inferior & Total 100 grids & 0.96 & 0.91, 0.02 & 0.89, 0.004 & 0.88, 0.008 \\
& Central 44 grids & 0.91 & 0.76, <0.001 & 0.88, 0.38 & \\
& Peripheral 56 grids & 0.96 & 0.86, 0.002 & 0.90, 0.02 & 0.88, 0.01 \\
GCL/IPL average & Total 100 grids & 0.90 & 0.92, 0.61 & 0.88, 0.43 & \\
& Central 44 grids & 0.91 & 0.76, 0.001 & 0.88, 0.41 & \\
& Peripheral 56 grids & 0.87 & 0.94, 0.11 & 0.88, 0.84 & \\
GCL/IPL superior & Total 100 grids & 0.85 & 0.79, 0.39 & 0.88, 0.22 & \\
& Central 44 grids & 0.81 & 0.72, 0.07 & 0.88, 0.09 & \\
& Peripheral 56 grids & 0.81 & 0.80, 0.87 & 0.88, 0.08 & \\
GCL/IPL inferior & Total 100 grids & 0.91 & 0.90, 0.59 & 0.88, 0.31 & \\
& Central 44 grids & 0.91 & 0.76, 0.001 & 0.88, 0.30 & \\
& Peripheral 56 grids & 0.86 & 0.90, 0.42 & 0.88, 0.67 & \\
mRNFL average & Total 100 grids & 0.92 & 0.92, 0.61 & 0.88, 0.26 & \\
& Central 44 grids & 0.91 & 0.76, 0.001 & 0.88, 0.10 & \\
& Peripheral 56 grids & 0.94 & 0.88, 0.01 & \\
mRNFL superior & Total 100 grids & 0.79 & 0.88, 0.07 & 0.88, 0.002 & \\
& Central 44 grids & 0.72 & 0.88, 0.07 & 0.88, 0.01 & \\
& Peripheral 56 grids & 0.80 & 0.88, 0.03 & \\
mRNFL inferior & Total 100 grids & 0.89 & 0.88, 0.82 & 0.88, 0.61 & \\
& Central 44 grids & 0.76 & 0.88, 0.03 & \\
& Peripheral 56 grids & 0.90 & 0.88, 0.61 & \\
\hline
\end{tabular}
\end{table}
may fit the topography of mRNFL thickness abnormality better in early glaucoma than the central 44 grids.

In contrast to mRNFL thickness, no reports have shown a difference in the diagnostic ability for detecting early glaucoma concerning GCL/IPL or GCC parameters by the different analytical areas. Akashi et al.13 showed that AUCs of GCL/IPL or GCC parameters were not different between Cirrus and 3D-OCT for early glaucoma. In this study, GCL/IPL inferior thickness had a lower AUC in the peripheral 56 grids than in the total 100 grids, whereas GCC parameters (except for GCC inferior thickness) had lower AUCs in the central 44 grids than in the total 100 grids, whereas GCC parameters were not different between Cirrus and 3D-OCT.

Our results showed that GCC was the most reliable predictor and measurements based on the peripheral area were good predictors. However, these results might be influenced by inaccurate segmentation of the boundaries between the retinal sublayers, especially the RNFL/GCL boundary, since it is the hardest to delineate. This could have caused less accurate measurements in RNFL and GCL/IPL, or in the foveal area where RNFL and GCL are very thin. However, this possibility was dismissed because we excluded eyes with obvious segmentation errors and a supplemental analysis excluding the 4 central foveal squares did not change the results.

There are several reports regarding the correlation between VFs and SD-OCT macular parameters.5,6,19–23 Mwanza et al.6 showed that average GCL/IPL had a significant correlation with 24-2 SAP MD ($r = 0.36$), which was in line with our results. Although significant correlations were found between all VF parameters and most of the OCT parameters, inferior thickness generally showed better correlation compared to average or superior thickness in our study. Houd et al.15 identified the region of the disc adjacent to the inferior vascular arcades to be particularly susceptible to glaucomatous damage and named the region the “macular vulnerability zone (MVZ) of the disc.” On the contrary, RNFL bundles in the corresponding portion of the superior macula to MVZ enter the disc within the temporal quadrant, which usually is less affected by early glaucomatous damage. The difference in glaucomatous damage between inferior and superior macular region concerning the MVZ may account for the difference in the correlation of macular OCT parameters with VF parameters and also for the difference in AUCs between inferior and superior hemiretina.

In comparison between different OCT parameters, average pRNFL thickness showed good correlations ($r ≥ 0.4$ and $P < 0.05$) with all VF parameters, whereas macular parameters

### Table 5. Correlation Between VF Parameters and OCT Parameters in All Patients

<table>
<thead>
<tr>
<th>OCT Parameters</th>
<th>Analytical Areas</th>
<th>MD</th>
<th>PSD</th>
<th>cMS</th>
<th>cTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCC average</td>
<td>Total 100 grids</td>
<td>0.34</td>
<td>0.0004</td>
<td>0.37</td>
<td>0.0001</td>
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<tr>
<td></td>
<td>Central 44 grids</td>
<td>0.26</td>
<td>0.0008</td>
<td>0.25</td>
<td>0.0004</td>
</tr>
<tr>
<td>GCC superior</td>
<td>Total 100 grids</td>
<td>0.29</td>
<td>0.0023</td>
<td>0.20</td>
<td>0.0036</td>
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<tr>
<td></td>
<td>Central 44 grids</td>
<td>0.21</td>
<td>0.0030</td>
<td>0.13</td>
<td>0.0173</td>
</tr>
<tr>
<td>GCC inferior</td>
<td>Total 100 grids</td>
<td>0.29</td>
<td>0.0029</td>
<td>0.42</td>
<td>&lt;0.0001</td>
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<tr>
<td></td>
<td>Central 44 grids</td>
<td>0.25</td>
<td>0.0010</td>
<td>0.46</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>mRNFL average</td>
<td>Total 100 grids</td>
<td>0.29</td>
<td>0.0003</td>
<td>0.38</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Central 44 grids</td>
<td>0.29</td>
<td>0.0002</td>
<td>0.26</td>
<td>0.0007</td>
</tr>
<tr>
<td>mRNFL superior</td>
<td>Total 100 grids</td>
<td>0.31</td>
<td>0.0014</td>
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<td>0.0366</td>
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<td></td>
<td>Central 44 grids</td>
<td>0.26</td>
<td>0.0077</td>
<td>0.16</td>
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<tr>
<td>mRNFL inferior</td>
<td>Total 100 grids</td>
<td>0.28</td>
<td>0.0036</td>
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<td></td>
<td>Central 44 grids</td>
<td>0.26</td>
<td>0.0065</td>
<td>0.26</td>
<td>0.0017</td>
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<tr>
<td>pRNFL average</td>
<td>Total 100 grids</td>
<td>0.29</td>
<td>0.0003</td>
<td>0.38</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Central 44 grids</td>
<td>1.00</td>
<td>0.29</td>
<td>0.18</td>
<td>0.06</td>
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<tr>
<td></td>
<td>Peripheral 56 grids</td>
<td>0.32</td>
<td>0.0008</td>
<td>0.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GCC average</td>
<td>Total 100 grids</td>
<td>0.22</td>
<td>0.00272</td>
<td>0.18</td>
<td>0.0595</td>
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<tr>
<td></td>
<td>Central 44 grids</td>
<td>0.05</td>
<td>0.6341</td>
<td>0.04</td>
<td>0.7196</td>
</tr>
<tr>
<td>GCC superior</td>
<td>Total 100 grids</td>
<td>0.26</td>
<td>0.0067</td>
<td>0.22</td>
<td>0.0237</td>
</tr>
<tr>
<td></td>
<td>Central 44 grids</td>
<td>0.15</td>
<td>0.1188</td>
<td>0.27</td>
<td>0.0051</td>
</tr>
<tr>
<td>GCC inferior</td>
<td>Total 100 grids</td>
<td>0.27</td>
<td>0.006</td>
<td>0.47</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Central 44 grids</td>
<td>0.43</td>
<td>&lt;0.0001</td>
<td>0.44</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Notes:**

- MD: mean deviation
- PSD: pattern standard deviation
- cMS: central mean sensitivity
- cTD: central total deviation

1. Akashi et al.
2. Houd et al.
3. Mwanza et al.
4. Kotowski et al.
5. OCT: optical coherence tomography
6. VF: visual field
7. SD-OCT: spectral domain optical coherence tomography
8. MVZ: macular vulnerability zone
9. GCL/IPL: ganglion cell layer/inner plexiform layer
10. GCC: ground curvature contour
11. RNFL: retinal nerve fiber layer
12. AUC: area under the curve
13. Correlation coefficients: $r$
14. Statistical significance: $P$
correlated only under limited conditions. In particular, no macular parameters had good correlation with MD. The results may be explained by the partial coverage of the 24-2 SAP area by the macular parameters in contrast to the full coverage by pRNFL.

Recently, the structure–function relationship for glaucomatous damage was examined using macular OCT parameters and VF parameters of SAP 10-2. Among them, Raza et al. recently showed a strong relationship between loss in 10-2 SAP sensitivity and decreases in local GCL/IPL thickness. When looking at the correlations with central VF parameters, which were derived from the area corresponding to SAP 10-2 (i.e., total 100 grids), inferior thickness of GCC and mRNFL showed comparably high correlations with central VF parameters to average pRNFL thickness even in the central 44 grids. Conversely, the inferior thickness of the central 44 grids was the only GCL/IPL-related parameter that showed a comparably high correlation to the pRNFL parameter. The GCL/IPL parameters failed to show superiority over GCC or mRNFL in the structure–function relationship of early glaucomatous damage in the macular area corresponding to SAP 10-2 test points. In this regard, Ohkubo et al. recently reported that mRNFL and GCC thickness had more SAP 10-2 test points where the layer thickness had good correlations ($r_s \geq 0.4$ and $P < 0.05$) with visual sensitivity than GCL/IPL. Further studies will clarify the best choice of retinal sublayer and analytical area to examine the nature of the structure–function relationship in the macula of eyes with glaucomatous damage.

Our study had several limitations. First, our study included a relatively small sample size. A larger sample size would allow us to examine PG and POAG separately. The SD-OCT detected parafoveal glaucomatous damage more easily because macular damage was included in the central scan area. The relative proportion of glaucomatous eyes with parafoveal and peripheral damage in the total sample size may influence the diagnostic ability. Further studies with a larger number of subjects using a wider scanning area will define the diagnostic ability of macular retinal sublayers more accurately to

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**FIGURE.** Inner retinal thickness analysis in the macula by 3D-OCT. (A) Top: Thickness map of each retinal sublayer. GCL+, GCL/IPL, GCL++; RNFL. Bottom: Average thickness values of superior, inferior, and total retinal area. (B) Significance map of GCL+ thickness in a 6 x 6 mm area centered on the fovea divided into 10 x 10 grids. Significant thinning is shown as red (<1%) or yellow (<5%) in each grid. (C) The area of the central 44 grids was similar to the Cirrus OCT elliptical annulus region (pink) and the peripheral 56 grids (red).
discriminate early glaucoma from normal eyes. Second, although we used the central 44 grids to simulate the analytical area of the Cirrus OCT, a direct comparison between 3D-OCT and Cirrus OCT still is not possible because the analytical area is not exactly the same and thickness data are derived from 10 × 10 grids in 3D-OCT and from pixel by pixel in Cirrus OCT. In conclusion, the diagnostic ability of macular OCT parameters for early glaucoma differed by inner retinal sublayers and also by the analytical areas studied. The GCL/ IPL parameters failed to show superiority over GCC or mRNFL parameters in the structure–function relationship of early glaucomatous damage similar to the diagnostic ability based on AUCs. More studies are needed to explore the best combination of retinal sublayer and analytical area for better understanding of the nature of the structure–function relationship of glaucomatous macular damage.

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References