Comparative Assessment for the Ability of Cirrus, RTVue, and 3D-OCT to Diagnose Glaucoma

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PURPOSE. We compared the ability of circumpapillary retinal nerve fiber layer (cpRNFL) thickness and macular parameters obtained by three spectral-domain optical coherence tomography (SD-OCT) instruments to detect glaucoma.

METHODS. We enrolled 87 normal eyes and 145 glaucomatous eyes (75 early glaucomatous eyes [EGs], mean deviation > −6 dB). Each participant was imaged using Cirrus, RTVue, and 3D-OCT to evaluate the average and quadrant cpRNFL thicknesses. The macular retinal nerve fiber layer (mRNFL), ganglion cell layer plus inner plexiform layer (GCL/IPL), and mRNFL + GCL/IPL (ganglion cell complex [GCC]) thicknesses were analyzed. The areas under the receiver operating characteristic curves (AUCs) were compared among the instruments.

RESULTS. These instruments revealed similar AUCs for the average cpRNFL and GCC thicknesses in EGs, and total all-stage glaucomatous eyes (TGs). RTVue showed better performance in the nasal cpRNFL thickness than Cirrus and 3D-OCT, and better performance in the temporal cpRNFL thickness than 3D-OCT in TGs. RTVue had a higher AUC for the superior GCC thickness compared to Cirrus and 3D-OCT in EGs, and TGs. Cirrus had higher AUCs for GCL/IPL parameters in TGs, and lower AUCs for the mRNFL parameters in EGs and TGs compared to 3D-OCT.

CONCLUSIONS. The average cpRNFL and GCC thicknesses measured using these OCT instruments exhibited similar abilities in the diagnosis of glaucoma, and RTVue exhibited better diagnostic abilities than Cirrus and 3D-OCT for nasal cpRNFL, and superior GCC thicknesses. The diagnostic performance of Cirrus and 3D-OCT was different for GCL/IPL and mRNFL parameters. (http://www.umin.ac.jp/ctr number, UMIN000006900.)

Keywords: glaucoma, optical coherence tomography, ganglion cell layer, retinal nerve fiber layer thickness

Glaucoma is an optic neuropathy that is characterized by a specific and progressive injury to the optic nerve and retinal nerve fiber layer (RNFL).1 RNFL evaluation has an important role in the diagnosis and management of glaucomatosus patients. The recent introduction of spectral-domain optical coherence tomography (SD-OCT) has enhanced the scan resolution and provides better reproducibility for image acquisition compared to time-domain OCT (TD-OCT).2 SD-OCT allows for an automatic segmentation of retinal layers at the macula.3 Glaucomatously affected macula preferentially affects the macular inner retinal layers: the macular RNFL (mRNFL), ganglion cell layer (GCL), and inner plexiform layer (IPL). The ganglion cell complex (GCC) is defined as the sum of RNFL, GCL, and IPL thickness. Circumpapillary RNFL (cpRNFL) measurements were the parameters that were applied originally to OCT for glaucoma diagnosis, but recent studies have demonstrated that GCC thickness also exhibits good glaucoma-detecting ability that is comparable to cpRNFL thickness.4–6

The TD-OCT device is available from only one manufacturer (Carl Zeiss Meditec, Dublin, CA), but SD-OCT devices are available commercially from several different companies. The speed and resolution of image acquisition vary among instruments despite similar working principles. Two studies revealed that cpRNFL measurements obtained from healthy controls using several devices were different and not interchangeable.7,8 However, interinstrumental comparisons among SD-OCT devices for the diagnosis of glaucomatous optic neuropathy have been reported only in a single study to our knowledge, and Spectralis, Cirrus, and RTVue exhibited similar diagnostic performance in measurements of cpRNFL thickness in glaucoma detection.9 In addition, Cirrus and 3D-OCT recently have achieved segmentation between mRNFL and GCL/IPL.10–12 However, to our knowledge no studies have compared these macular parameters among SD-OCT instruments.

Our study assessed the diagnostic ability of cpRNFL thickness and macular parameters evaluated using Cirrus, RTVue, and 3D-OCT, which are commercially available SD-OCT instruments for the detection of glaucoma. We also performed a subanalysis for the comparison of the OCT instruments for diagnosing glaucomatous eyes with early visual field loss (EGs).

MATERIALS AND METHODS
Japanese subjects were recruited at the Kobe University Hospital (Kobe, Japan) for this observational cross-sectional...
study. The institutional review board of Kobe University approved the study protocol, which adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each subject after an explanation of the study protocol.

All subjects received a full ocular examination. The Humphrey Field Analyzer 30-2 SITA standard program (HFA; Carl Zeiss Meditec) was used to perform the visual field (VF) test. Subjects with a best-corrected visual acuity of 20/40 or better, a spherical refraction higher than 6.0 diopters (D), a cylinder correction within ±3.0 D, and gonioscopically open angles were included. Axial length was acquired using an IOL Master (Carl Zeiss Meditec). No subjects had undergone any ocular surgeries. VF tests and measurements obtained with the three SD-OCT instruments were performed within 6 months of each other.

Glaucomatous optic neuropathy (GON) is defined as neuroretinal rim damage, an increased cup-to-disc ratio, rim thinning, and notches with or without RNFL defects. The glaucomatous VF defect was defined based on liberal criteria: two or more contiguous points with a pattern deviation sensitivity loss of P < 0.01, three or more contiguous points with sensitivity loss of P < 0.05 not crossing the horizontal meridian line, or a 10-dB difference across the nasal horizontal midline at two or more adjacent locations, and an abnormal result on the glaucoma hemifield test. Furthermore, EG was selected based on Anderson and Patella’s classification when the mean deviation (MD) was > −6 dB. All-stage glaucomatous eyes were defined as total glaucoma (TG). Self-reported healthy subjects at least 20 years of age also were invited to participate in the study. The exclusion criteria for normal eyes were as follows: intraocular pressure > 21 mm Hg, unreliable HFA results (fixation loss, false positive, or false negative > 3%), abnormal findings in HFA suggestive of glaucoma as mentioned above, any abnormal VF loss due to vitreoretinal diseases, and optic nerve or RNFL abnormality unrelated to glaucomatous optic neuropathy.

### cpRNFL Measurements

The optic disc cube protocol was adopted for Cirrus HD-OCT (software version 6.1.0.96; Carl Zeiss Meditec). This protocol is based on a 3-dimensional scan of a 6 × 6 mm² area centered on the optic disc. A 3.46 mm diameter circular scan was performed automatically around the optic disc, which provided measurements of parapapillary RNFL thickness. Images with signal strength < 3 were excluded. RNFL thickness values at 256 measurement points on the circular scan were exported and evaluated as described below.

The optic nerve head map protocol was applied for RTVue-100 (software version 4.0.5.39; Optovue, Inc., Fremont, CA). This protocol generated an RNFL thickness map that was measured along a circle 3.45 mm in diameter and centered on the optic disc. 3D disc protocol was used to register the edge of the optic nerve head. Only good quality images, as defined by a signal strength index > 30, were accepted. RNFL thickness parameters calculated by the original software were used.

3D OCT-2000 (software version 8.00; Topcon, Inc., Tokyo, Japan) used a 7 × 7 mm scan disc protocol. The magnification effect in each eye was corrected according to the formula (modified Littman’s method) provided by the manufacturer, which was based on the refraction, corneal radius, and axial length, to obtain more accurate circle sizes during measurements. Images with a quality factor > 60 were used for analyses. RNFL thickness data with 1024 points of resolution on a 3.46 mm circle diameter were exported by the software provided by Topcon, Inc., and evaluated as described below.

The RNFL thicknesses at 256 points from Cirrus and 1024 points from 3D-OCT were converted to the following parameters. The mean 360° RNFL thickness was defined as the average of RNFL thicknesses. Starting from a point on the temporal margin, which was designated as 0°, the mean quadrant RNFL thickness between 315° and 45° was defined as the temporal RNFLT: between 45° and 135° was superior, between 135° and 225° was nasal, and between 225° and 315° was inferior.

### Macular Inner Retinal Layer Thickness Measurements

The ganglion cell analysis (GCA) was used to process the data when Cirrus OCT was used. GCA detects and measures the thickness of the mRNFL, GCL/IPL, and GCC within a 14.13 mm² elliptical annulus area that is centered on the fovea. The special software provided from the manufacturer (OCT XML Reader; Carl Zeiss Meditec) was used to export the data. The superior (0°–180°) and inferior (180°–360°) segment was calculated from the corresponding sectors.

The GCC was measured when the RTVue-100 OCT was used. The GCC protocol explores parameters within a circle with a 6 mm diameter; the center of the GCC scan was shifted approximately 1 mm temporal to the fovea to improve the sampling of temporal peripheral nerve fibers. The variables generated by the GCC analysis included the average, superior, and inferior hemi-retinas.

Raster scanning of a 7 mm² area centered on the fovea with a scan density of 512 (vertical) × 128 (horizontal) scans was performed using 3D-OCT. The built-in 3D-OCT measured a 6 × 6 mm area that was centered in the fovea using embedded 3D-OCT measurement software (3D OCT-2000 software version 8.00; Topcon, Inc.). The data divided in 10 × 10 grids were exported by the software provided by Topcon, Inc. The average thickness, and superior and inferior hemi-retina thicknesses of mRNFL, GCL/IPL, and GCC were calculated.

Table 1 summarized the protocol for the measurements in each instrument.
Table 2. Characteristics of the Studied Eyes (Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Normal Eyes, n = 87</th>
<th>EG, n = 75</th>
<th>TG, n = 145</th>
<th>P Value Normal vs. EG</th>
<th>P Value Normal vs. TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>43.5 ± 12.8</td>
<td>48.3 ± 10.6</td>
<td>47.6 ± 9.4</td>
<td>0.016*</td>
<td>0.006*</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>60.9</td>
<td>46.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refraction, D</td>
<td>−2.25 ± 1.97</td>
<td>−2.78 ± 2.00</td>
<td>−2.75 ± 1.96</td>
<td>0.058*</td>
<td>0.219†</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>24.8 ± 1.13</td>
<td>25.2 ± 1.17</td>
<td>25.2 ± 1.20</td>
<td>0.092*</td>
<td>0.073*</td>
</tr>
<tr>
<td>Mean deviation, dB</td>
<td>−0.02 ± 1.59</td>
<td>−2.61 ± 2.29</td>
<td>−7.12 ± 6.62</td>
<td>0.055*</td>
<td>0.058*</td>
</tr>
</tbody>
</table>

* Unpaired t-test.
† Fisher’s exact test.

Statistical Analysis

All numerical data had normal distributions confirmed by the Kolmogorov-Smirnov test. Bilateral eyes were included in the analyses if they matched the inclusion criteria. Because measurements from both eyes of the same subject were likely to be correlated, the standard statistical method for parameter estimation could lead to underestimation of standard errors (SEs). To account for potential correlation between eyes, the cluster of the data for the subject was considered as the unit of resampling when calculating SEs. This procedure has been used in the literature to adjust for the presence of multiple correlated measurements from the same unit. Receiver operating characteristic (ROC) curves were constructed for cpRNFL, GCC, GCL/IPL, and mRNFL thickness to investigate the ability of the devices to differentiate eyes with glaucoma from normal eyes. The area under the ROC curve (AUC) was calculated for each parameter. ROC curves were adjusted for differences in age using covariate-adjusted ROC curves, as demonstrated by Pepe. A bootstrap resampling procedure was used in the literature to adjust for the presence of multiple correlated measurements from the same unit. Receiver operating characteristic (ROC) curves were constructed for cpRNFL, GCC, GCL/IPL, and mRNFL thickness to investigate the ability of the devices to differentiate eyes with glaucoma from normal eyes. The area under the ROC curve (AUC) was calculated for each parameter. ROC curves were adjusted for differences in age using covariate-adjusted ROC curves, as demonstrated by Pepe. A bootstrap resampling procedure was used in the literature to adjust for the presence of multiple correlated measurements from the same unit.

The sensitivities of the detection of early glaucomatous eyes was determined using the average cpRNFL thickness and the average GCC, as measured by each instrument, with a target specificity of ≥95%.

Statistical analyses were performed using computer programs (Stata ver. 12.0; StataCorp., College Station, TX; and Medcalc version 11.6.1.0; Medcalc, Mariakerke, Belgium). A P value less than 0.05 was considered statistically significant.

RESULTS

We enrolled 87 normal eyes and 145 TGs, including 75 EGs. Table 2 shows the demographics and ocular characteristics of the subjects. There were no significant differences in refraction or axial length between normal eyes versus EGs or normal eyes versus TGs. However, the age of patients in the glaucomatous groups was significantly higher than in patients with normal eyes.

In TGs and EGs, the average cpRNFL thickness had the highest AUC among all parameters for each instrument. Table 3 presents the age-adjusted AUCs of the different parameters for each instrument for the detection of TGs. The AUCs for the average cpRNFL thicknesses were 0.964, 0.968, and 0.957 for Cirrus, RTVue, and 3D-OCT, respectively. No significant differences in the average cpRNFL thicknesses were observed among the instruments. RTVue had a significantly higher AUC for the nasal cpRNFL compared to Cirrus (P = 0.02) and 3D-OCT (P = 0.019). Additionally, RTVue had a higher AUC for the temporal cpRNFL thickness than 3D-OCT (P = 0.008). Regarding macular parameters, no significant differences were observed in the average GCC thickness among the instruments. RTVue exhibited a significantly higher AUC for the superior hemifield GCC thickness compared to Cirrus (P < 0.001) and 3D-OCT (P = 0.019). Cirrus had higher AUCs for the average (P = 0.009) and inferior hemifield GCL/IPL thickness (P = 0.009) compared to 3D-OCT. 3D-OCT had significantly higher AUCs for the average, superior, and inferior hemifield mRNFL measurements compared to Cirrus (P = 0.002, <0.001, and 0.024, respectively). Figure 1 illustrates the ROC curves for the average cpRNFL, GCC, GCL/IPL, and mRNFL thicknesses measured by each instrument for detecting TGs.

We also evaluated the age-adjusted AUCs of the different parameters for each instrument for the detection of EGs (Table 4). The AUCs for the average cpRNFL thicknesses were 0.940, 0.944, and 0.929 for Cirrus, RTVue, and 3D-OCT, respectively. No significant differences in the average and quadrant cpRNFL thicknesses were observed among the instruments. Also, no significant differences were observed in the average GCC thickness among the instruments. RTVue exhibited a significantly higher AUC for the superior hemifield GCC thickness compared to Cirrus (P < 0.001) and 3D-OCT (P = 0.019). Cirrus had higher AUCs for the average (P = 0.009) and inferior hemifield GCL/IPL thickness (P = 0.009) compared to 3D-OCT. 3D-OCT had significantly higher AUCs for the average, superior, and inferior hemifield mRNFL measurements compared to Cirrus (P = 0.005 and 0.002, respectively). Figure 2 illustrates the ROC curves for detecting EGs.

The sensitivities of each parameter in EGs were calculated with target specificities ≥95%. We constructed Venn diagrams of the average cpRNFL and GCC thicknesses for each 3D-OCT instrument in the early glaucoma groups to investigate whether macular parameters could diagnose glaucomatous abnormalities in eyes that were negative based on cpRNFL thickness. The sensitivities of the average cpRNFL thickness determined using Cirrus, RTVue, and 3D-OCT were 76% (n = 57/75), 76%, and 73.3% (n = 55/75), respectively (Fig. 3). The sensitivities of the average GCC thickness were 60% (n = 45/75), 69.3% (n = 52/75), and 64% (n = 48/75), respectively. The agreement between the average cpRNFL thickness and the average GCC thickness was 55% (n = 41/75), 60% (n = 45/75), and 55%, respectively. In contrast, 19%, 15%, and 17% of the
Why RTVue had higher diagnostic performance for the detection of early glaucomatous eyes, respectively, could not be detected by either the average cpRNFL thickness or the average GCC thickness.

**DISCUSSION**

In our study, the ability of average cpRNFL thickness measurements to diagnose glaucoma was not significantly different among the three 5D-OCT instruments. These results are consistent with a previous report that compared cpRNFL measurements of RTVue, Cirrus, and Spectralis. We also demonstrated that RTVue exhibited a higher capability than Cirrus and 3D-OCT in the measurement of the nasal quadrant of cpRNFL thickness. This finding agreed with the study by Leite et al. in which RTVue (AUC 0.71) and Spectralis (0.70) had higher AUCs than Cirrus (0.60) for measuring nasal cpRNFL thickness. Why RTVue had higher diagnostic accuracy in the nasal quadrant measurement is not fully understood. Each instrument’s software is based on similar principal algorithms for distinguishing the RNFL from the retinal ganglion cell layer. One possibility is the location of the alignment center of the scan areas. Our previous study demonstrated the superiority of RTVue over Cirrus in the nasal quadrant measurement for the detection of compressive optic neuropathy due to chiasmal tumors, in which the temporal and nasal quadrants mainly were damaged.

Evidence is accumulating that measurements of the inner retinal layers in the macular region may be additional parameters for glaucoma detection. Previous studies have shown that GCC and cpRNFL thickness exhibit similar diagnostic performance for the detection of early glaucoma. The first report by Schulze et al. using RTVue (mean MD in the glaucomatous eyes = −1.76 dB) demonstrated that the AUCs of the average cpRNFL and GCC thickness were 0.828 and 0.789, respectively. Using RTVue, Rao et al. (mean MD in the early glaucomatous eyes = −2.6 dB) demonstrated that the AUCs for cpRNFL thickness and GCC thickness were 0.799 and 0.735, respectively. Our results are consistent with these previous reports, although direct comparisons are impractical because of the differences in the study populations. However, to our knowledge no reports have compared the diagnostic performance of macular parameters measured using several 5D-OCT instruments in the same population. Our study demonstrated that the use of average GCC thickness in the diagnosis of early glaucoma was not significantly different among the three 5D-OCT instruments.
and all-stage glaucoma was not significantly different among the three SD-OCT instruments. However, RTVue exhibited better performance in measuring the superior hemifield GCC thickness than Cirrus and 3D-OCT. The reason for the higher performance of RTVue in the diagnosis of glaucoma in this cohort is not clear, but one possibility is the difference in scan protocols of the three SD-OCT instruments. The circular shape of the scan area of RTVue is de-centered against the fovea toward 0.75 mm temporally. The scan area of Cirrus and 3D-OCT is centered symmetrically on the fovea in the nasal-temporal direction. The scanning area placement of RTVue may fit better in the detection of early glaucomatous damage in the macular region, which preferentially affects temporal sites in the parafoveal region. Cirrus and 3D-OCT scan an oval area and a square area (14.13 mm$^2$ and 36 mm$^2$), respectively, which is centered on the fovea (Fig. 4). These discrepancies in scanning protocols also might have affected the differences in the AUCs of macular measurements among instruments.

The recent versions of Cirrus and 3D-OCT allow for the separation of RNFL from GCL at the macula.\textsuperscript{10–12} We also compared mRNFL and GCL/IPL measurements between Cirrus and 3D-OCT. Unfortunately, RTVue was not included in this analysis because the software in this instrument does not separate RNFL and GCL. Only one study on the diagnostic ability of GCL/IPL thickness measurement by Cirrus for the diagnosis of glaucoma has been reported to our knowledge. Mwanza et al. used Cirrus (mean MD in the early glaucoma

\begin{table}[h]
\centering
\caption{Area Under the ROC Curve Analysis Using Cirrus, RTVue, and 3D-OCT for Early Glaucomatous Eyes (Means ± SE)}
\begin{tabular}{|l|c|c|c|c|c|}
\hline
\textbf{Measured Thickness Parameters} & \textbf{SD-OCT Instruments (±SD)} & & & & \\
\hline
& \textbf{Cirrus} & \textbf{RTVue} & \textbf{3D-OCT} & \textbf{Cirrus vs. RTVue} & \textbf{RTVue vs. 3D-OCT} & \textbf{Cirrus vs. 3D-OCT} \\
\hline
\textbf{CpRNFL} & & & & & \\
Average & 0.940 (±0.020) & 0.944 (±0.019) & 0.929 (±0.023) & 0.67 & 0.34 & 0.48 \\
Superior & 0.872 (±0.035) & 0.876 (±0.033) & 0.864 (±0.037) & 0.82 & 0.53 & 0.62 \\
Temporal & 0.772 (±0.041) & 0.793 (±0.038) & 0.750 (±0.045) & 0.36 & 0.14 & 0.34 \\
Inferior & 0.923 (±0.024) & 0.910 (±0.026) & 0.925 (±0.023) & 0.40 & 0.40 & 0.91 \\
Nasal & 0.660 (±0.048) & 0.732 (±0.043) & 0.662 (±0.051) & 0.063 & 0.10 & 0.97 \\
\hline
\textbf{GCC} & & & & & \\
Average & 0.860 (±0.037) & 0.895 (±0.031) & 0.884 (±0.031) & 0.057 & 0.57 & 0.17 \\
Superior & 0.783 (±0.045) & 0.847 (±0.036) & 0.796 (±0.035) & 0.007* & 0.023* & 0.51 \\
Inferior & 0.859 (±0.037) & 0.880 (±0.033) & 0.884 (±0.033) & 0.26 & 0.86 & 0.17 \\
\hline
\textbf{GCL/IPL} & & & & & \\
Average & 0.844 (±0.038) & N.A. & 0.826 (±0.041) & 0.31 & & \\
Superior & 0.789 (±0.043) & N.A. & 0.763 (±0.046) & 0.22 & & \\
Inferior & 0.855 (±0.039) & N.A. & 0.831 (±0.040) & 0.30 & & \\
\hline
\textbf{mRNFL} & & & & & \\
Average & 0.825 (±0.041) & N.A. & 0.904 (±0.028) & 0.005* & & \\
Superior & 0.713 (±0.055) & N.A. & 0.808 (±0.040) & 0.002* & & \\
Inferior & 0.829 (±0.041) & N.A. & 0.878 (±0.034) & 0.079 & & \\
\hline
\end{tabular}
\end{table}

\* $P < 0.05$.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{ROC curves of average cpRNFL thickness (A), average GCC thickness (B), average GCL/IPL thickness (C), and average mRNFL thickness (D) measured using Cirrus, RTVue, and 3D-OCT for discriminating early glaucomatous eyes.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Venn diagrams illustrate the percentage of eyes that were judged as having glaucoma based on the criteria of the average cpRNFL thickness and average GCC from Cirrus, RTVue, and 3D-OCT at a fixed specificity of 95% for eyes with early glaucoma.}
\end{figure}
However, the opposite may also be true, as recently reported by Garvin et al. These investigators established an excellent correlation map between RNFL thickness from the parafoveal area only entered the temporal side at the optic nerve head 12 o'clock sectors in some cases. However, the opposite also may be true, as recently reported by Garvin et al. These investigators established an excellent correlation map between RNFL thickness from the parafoveal area only entered the temporal side at the optic nerve head 12 o'clock sectors in some cases.

Figure 4. A schema for macular scanning area using Cirrus (red), RTVue (green), and 3D-OCT (blue) merged with a retinal photograph.

The Venn diagram analyses demonstrated the combination of GCC and cpRNFL thicknesses for the detection of early glaucoma (Fig. 5). More than half of early glaucomatous eyes detected with the cpRNFL thickness also were confirmed by the average GCC thickness measured by the three instruments. However, some populations were detected only with GCC or cpRNFL thickness. A study using fundus photography demonstrated that RNFL defects preferentially occurred in the 7 and 11 o'clock sectors, but these defects also appeared in the 6 and 12 o'clock sectors in some cases. This observation indicated that local RNFL thinning may occur at variable locations, and therefore, macular parameters may miss the structural damage that converges into the superior or inferior pole of the optic disc. However, the opposite also may be true, as recently reported by Garvin et al. These investigators established an excellent correlation map between RNFL thickness from the superotemporal to inferotemporal area, and GCL/IPL thickness in macular grid regions, as measured with Cirrus in patients with glaucoma.

Axons that originated from the parafoveal area only entered the temporal side at the optic nerve head according to their map. The temporal cpRNFL thickness is much thinner than superior and inferior quadrants; therefore, the cpRNFL profile has a "double-hump" pattern. Localized RNFL thinning at the parafoveal area without diffuse RNFL loss might be underdetected in average cpRNFL measurements. Macular parameters may indicate structural damage near the fovea better than cpRNFL. The most damaged area likely determines which parameter is able to detect early glaucoma in an individual eye. Additionally, we observed that cpRNFL and GCC thicknesses missed approximately 20% of early glaucomatous eyes by any of the three instruments.

Our study had some limitations. First, HFA and OCT measurements were not performed on the same day in most subjects. However, these examinations were performed within 6 months. All glaucomatous eyes exhibited stable intraocular pressure, and the treatment modality was not altered during our study. Therefore, the reduction in examined parameters during the examination periods was likely negligible. Second, our patients were Japanese, and our results may not be applicable to other ethnic groups. Finally, our study’s design was a case-control study including patients with well-established glaucoma, and using a separate group of normal subjects as hospital based-controls could overestimate the diagnostic performance substantially.

In conclusion, we demonstrated that the diagnostic performances of average cpRNFL thickness and average GCC thickness to identify early glaucoma and all-stage glaucoma were similar among Cirrus, RTVue, and 3D-OCT measurements in our study population. RTVue yielded a higher AUC value for nasal cpRNFL thickness than Cirrus and 3D-OCT in the detection of glaucoma. Overall, Cirrus exhibited higher AUCs for GCL/IPL measurements than 3D-OCT. Conversely, 3D-OCT had higher AUCs for mRNFL measurements than Cirrus. Macular and cpRNFL analyses could be used complimentarily, but a combined use of these parameters still could not detect structural damage in some early glaucomatous eyes.

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