Comparison of retinal nerve fiber layer thickness measured by optical coherence tomography and scanning laser polarimetry (GDx)

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Abstract

Purpose: Optical coherence tomography (OCT) and scanning laser polarimetry (Nerve Fiber Analyzer, GDx) are optical devices that directly measure retinal nerve fiber layer (RNFL) thickness. In this study, we compared the RNFL thickness measured by these two instruments under the same conditions, and also investigated the relationship between the visual field and RNFL thickness. Methods: Thirteen eyes of 13 glaucoma patients, 4 eyes of 4 patients with ocular hypertension, and 6 eyes of 6 normal subjects were studied (mean age±standard deviation, 56.0±13.6 year). Mean deviation (MD) of the Humphrey Field Analyzer (HFA) was −3.8±4.9 dB in glaucoma patients. Three consecutive measurements of peripapillary RNFL thickness were performed by a single operator using OCT and GDx. The same circular scan area with a radius of 1.7 mm centered on the optic disc was used for the determination of RNFL thickness using both instruments. The mean RNFL thickness was calculated for the total area and for each quadrant (superior, nasal, inferior, temporal) of the scanned circle. Cases with a coefficient of variance (standard deviation divided by mean RNFL thickness) greater than 10% were excluded from analysis. Results: The mean overall RNFL thickness for OCT and GDx were $105.8\pm17.3~\mu m$ and $79.3\pm14.6~\mu m$, respectively, and a significant difference was observed (p < .0001). A significant correlation between RNFL thickness measured by OCT and GDx was obtained in the total area and superior and inferior quadrants, but not in nasal and temporal quadrants. A significant correlation between corrected pattern standard deviation (CPSD) determined by HFA and RNFL thickness was observed for OCT but not for GDx. Conclusions: The RNFL thickness obtained using OCT is generally greater than that using GDx. Furthermore, a better correlation between visual function and RNFL thickness was obtained for OCT compared with GDx.

I. Introduction

In glaucoma, structural alterations of the optic disc and retinal nerve fiber layer (RNFL) often precede visual field abnormalities, and the importance of the ocular fundus test is emphasized^{1,2)}. Although the cup-disc (C/D) ratio is commonly used as a glaucomatous parameter in the clinical setting, this ratio does not allow reliable identification of structural changes of

glaucoma because there is a broad overlap in distribution of glaucomatous and normal values and occasionally a lack of inter-observer reliability in measurement.

Recently, several imaging technologies have been applied to the diagnosis of glaucoma, and allow quantitative and objective analysis of the optic disc and RNFL thickness. Among the optic disc parameters, the relative RNFL height has been reported to be the most effective parameter to distinguish between glaucoma

Received March 17, 2004, Accepted May 6, 2004

Key words: Optical coherence tomography, Scanning laser polarimetry, Retinal nerve fiber layer thickness, Visual field **Corresponding author**: Kunio YAMADA, Department of Ophthalmology, Tokyo Medical University, 6-7-1, Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan

patients and normal subjects³⁻⁵⁾. High expectation has been held concerning quantitative measurement of RNFL thickness regarding improved diagnosis of early glaucoma and preperimetric stage glaucoma.

Both indirect and direct measurements using imaging devices are available for the evaluation of RNFL thickness. Indirect measurement of the RNFL thickness determines the relative height difference between a reference plane and the peripapillary retinal surface. This measurement depends on a reference plane that is subject to changes with progression of glaucoma⁶⁾. On the other hand, the absolute RNFL thickness can be obtained by the direct method, which is not influenced by the reference plane and is more desirable for the evaluation of RNFL thickness. Currently, direct measurement can be performed using scanning laser polarimetry (Nerve Fiber Analyzer, GDx; Laser Diagnostic Technologies, Inc., San Diego, CA, USA) or optical coherence tomography (OCT; Humphrey/Zeiss, Dublin, CA, USA). Both instruments measure RNFL thickness by applying the optical properties of the RNFL.

Several previous reports showed that the RNFL thickness measured by OCT and GDx correlated well with the histological measurement of RNFL thickness^{7–10}, but no exact comparison between measurement of RNFL thickness by OCT and GDx has yet been reported. In this study, we compared the peripapillary RNFL thickness measured by the two instruments under identical conditions. We also investigated the relationship of visual function and RNFL thickness measured by these instruments.

II. Subjects & Methods

Thirteen eyes of 13 glaucoma patients (primary openangle glaucoma: 5 eyes, normal-tension glaucoma: 8 eyes), 4 eyes of 4 patients with ocular hypertension, and 6 eyes of 6 normal persons were studied (mean age \pm standard deviation, 56.0 ± 13.6 year). All subjects were experienced with automated perimetry and had corrected visual acuity of at least 1.0 with refraction of more than -5 diopters spherical equivalent. No ocular media opacity was observed on slit-lamp examination. None of the subjects had a remarkable history of ocular disease.

Peripapillary RNFL of each subject was scanned consecutively three times using OCT and GDx. Image acquisition was performed by a single operator. GDx measurement was performed by the standardized method without pupillary dilation, while OCT measurement was performed after pupillary dilation. Informed consent was obtained from all subjects before testing.

OCT is a low-coherence interferometer that uses near-infrared, low-coherence illumination (wavelength,

840 nm) as a light source. By detecting the time delay of optical echoes of the reflected light beam and a reference beam, the cross-sectional information of the retinal internal microstructure is obtained. A cross sectional image of the retina is constructed based on the reflectivity of different layers of the retina. A highreflectance layer located just under the inner surface of the retina corresponding to the RNFL is measured with a computer algorithm to give RNFL thickness. In this study, a 360-degree circular scan with a radius of 1.7 mm centered on the optic disc was performed on each subject. The mean RNFL thickness in total area and each quadrant (superior, nasal, inferior, temporal) of the scanned circle was calculated by the computer software (version A6.1) for the OCT instrument. Images were excluded from analysis when the center of the scanned circle shifted away from the optic disc or when the signal-to-noise (S/N) ratio was less than 40 dB.

GDx is a scanning laser polarimeter that uses polarization-modulated diode laser (wavelength, 780 nm) as the light source. The polarized beam penetrates the nerve fiber layer and is divided into two parallel beams in varying polarization directions because of the birefringent properties of RNFL. These parallel beams penetrate the tissue at different speeds, and the reflected beams, which are caught by a polarization detector, show a time delay called retardation. The amount of retardation is proportional to the RNFL thickness. At a scanning angle of 15×15 degrees, GDx produces a retardation map consisting of 256×256 individual retinal positions (65,536 pixels), and the retardation for each pixel is measured. If the operator positions a circle or ellipse on the margin of the optic disc, a concentric peripheral measurement ellipse is automatically set at 1.75 times the disc diameter. The entire image is usually divided into four segments with the optic disc as center and at the following default settings: superior 120 degrees, inferior 120 degrees, nasal 50 degrees, and temporal 70 degrees. GDx software version used in this study was 3.0.00.

To compare the results of OCT and GDx under the same conditions, we adjusted the diameter of the peripheral measurement circle to 3.4 mm and the angle of each quadrant to 90 degrees in GDx measurement, which were identical to the conditions used in the OCT. GDx images with image quality less than 80% were excluded from analysis.

Program 24–2 of the Humphrey Field Analyzer (HFA; Humphrey/Zeiss, Dublin, CA) was performed on all subjects. Cases were excluded from analysis when fixation loss was greater than 33% or false positive errors were greater than 20%, or false negative errors greater than 20%.

The mean and standard deviation of RNFL thickness

from three images were calculated for OCT and GDx. Cases with coefficient of variance (standard deviation divided by mean RNFL thickness) greater than 10% were excluded. We compared the mean RNFL thickness in total area and in each quadrant (superior, nasal, inferior, temporal) obtained by the two instruments, and investigated the correlation between the results. We also analyzed the correlation between visual field and RNFL thickness measured by OCT and GDx.

III. Results

The mean overall RNFL thickness for OCT and GDx was $105.8\pm17.3~\mu m$ and $79.3\pm14.6~\mu m$, respectively; and the measurement for OCT was significantly greater than that for GDx (student's paired *t*-test, p<.0001). The correlation between the overall RNFL thickness determined by OCT (y) and GDx (x) is represented by y=0.59x+58.7 (Pearson correlation coefficient, r=0.50, p<0.001) (Fig. 1). The mean coefficients of variance for OCT and GDx were $4.3\pm2.5\%$ and $3.4\pm2.4\%$, respectively, with no significant difference between the two instruments (paired *t*-test, p=0.18).

Table 1 compares the mean RNFL thickness measured by the two instruments at each quadrant in normal persons (6 eyes). The RNFL thickness measured by OCT was significantly greater than that obtained by GDx in all four quadrants. This difference was remarkable in the superior quadrant. Table 2 compares the mean RNFL thickness measured by the two instruments at each quadrant in all subjects. The RNFL thickness measured by OCT was significantly greater than that obtained by GDx at the superior, inferior, and temporal quadrants.

A significant correlation between RNFL thickness determined by OCT and GDx was observed for the superior and inferior quadrants, but not for the nasal and temporal quadrants. The correlation between the RNFL thickness determined by OCT (y) and GDx (x) is represented by y=0.80x+62.2 (Pearson correlation coefficient, r=0.55, p<0.001) for the superior quadrant, y=0.63x+58.4 (Pearson correlation coefficient, r=0.43, p<0.01) for the inferior quadrant, y=0.32x+56.8 (Pearson correlation coefficient, r=0.16, p=0.46) for the nasal quadrant, and y=0.40x+68.3 (Pearson correlation coefficient, r=0.29, p=0.17) for the temporal quadrant (Fig. 2).

The average mean deviation (MD) of glaucoma patients was -3.8 ± 4.9 dB. No significant correlation was observed between the mean deviation (MD) determined by HFA and overall RNFL thickness when measured by both OCT and GDx. A significant correlation between the corrected pattern standard deviation (CPSD) determined by HFA and overall RNFL thickness was observed when measured by OCT but not when

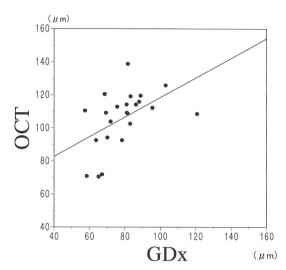


Fig. 1 Correlation between retinal nerve fiber layer (RNFL) thickness measured by OCT and GDx for the whole scanned circle

Table 1. Comparison of mean RNFL thickness measured by OCT and GDx in each quadrant in normal persons (6 eyes)

	OCT	GDx	<i>t</i> -test
Superior	$138.7 \pm 19.1 \mu\text{m}$	$83.6 \pm 15.7 \mu\text{m}$	p < 0.0001
Nasal	$88.1 \pm 19.8 \ \mu \text{m}$	$69.7 \pm 14.2 \mu\text{m}$	p = 0.032
Inferior	$130.0\pm~9.6~\mu\mathrm{m}$	$105.6 \pm 14.3 \ \mu \text{m}$	p = 0.012
Temporal	$83.8 \pm 12.8 \ \mu \text{m}$	$62.1 \pm 10.1 \; \mu \mathrm{m}$	p = 0.031

Table 2. Comparison of mean RNFL thickness measured by OCT and GDx in each quadrant in all subjects (23 eyes)

	OCT	GDx	t-test
Superior	$129.2 \pm 27.4 \mu{\rm m}$	$83.3 \pm 18.9 \ \mu \text{m}$	p < 0.0001
Nasal	$79.2 \pm 24.7 \ \mu \text{m}$	$69.7 \pm 12.3 \ \mu \text{m}$	p = 0.09
Inferior	$121.5 \pm 26.3 \mu\text{m}$	$101.1 \pm 18.1 \; \mu \mathrm{m}$	p < 0.001
Temporal	92.9 \pm 19.1 μ m	$61.3 \pm 14.1 \mu\text{m}$	p < 0.0001

measured by GDx. The correlation between CPSD by HFA (x) and overall RNFL thickness measured by OCT (y) is represented by y=-2.1x+111.4 (Pearson correlation coefficient, r=0.45, p<0.05). The correlation between CPSD by HFA (x) and overall RNFL thickness measured by GDx (y) is represented by y=-1.1x+82.7 (Pearson correlation coefficient, r=0.28, p=0.20).

IV. Discussion

Only a few studies have compared the RNFL thickness determined by histological measurement with that determined by OCT and GDx. Huang et al.⁷⁾ used eye bank specimens with the cornea and lens removed, and reported that the actual thickness of retina and RNFL

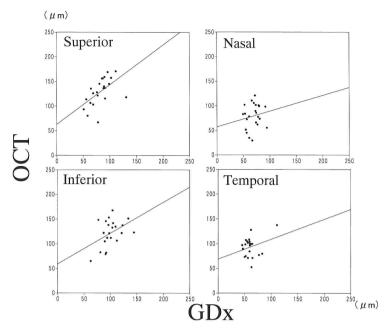


Fig. 2 Correlation between retinal nerve fiber layer (RNFL) thickness measured by OCT and GDx in each quadrant

closely matched those determined by OCT. Toth et al.⁸⁾ reported that the retinal thickness measured by light microscopy was on average 4–12% greater than the corresponding OCT image of *Macaca mulatta* macula, but the retinal morphology correlated well with macular OCT imaging. On the other hand, Weinreb et al.⁹⁾ reported an excellent correlation (r=0.83) between histological measurement of RNFL thickness and retardation measured by Fourier-ellipsometry using argon laser beam (wavelength: 514 nm).

The study reported by Hoh et al.11) showed that although a significant correlation was observed between GDx parameters (neural network number, maximum modulation, ellipse modulation, ellipse average, total integral) and RNFL thickness determined by OCT, the correlation coefficient between ellipse average and RNFL thickness measured by OCT was small (r = 0.29). Although their study objective was similar to ours, the methodology was quite different. In their study, GDx measurement was performed on a concentric ellipse placed at a 1.75-disc diameter from the disc edge, and OCT measurement was performed on a circular area with a diameter of 3.4 mm centered on the disc. Therefore, their OCT and GDx measurements did not measure identical areas on the retina. In the present study, we used a 3.4-mm diameter circle for both OCT and GDx measurements, and a better correlation (r=0.50) was obtained between the RNFL thickness measured by OCT and that measured by GDx. Moreover, there was no significant difference in reproducibility between the instruments. Shauman et al.12) reported better reproducibility for OCT measurement using a 3.4-mm diameter circle compared with a 2.9- or 4.5-mm diameter circle. Our search of the literature failed to find the reason why a 1.75-disc diameter area of the optic disc was chosen for the GDx testing in the previous study. For the GDx Access with a variable corneal compensator (VCC) that has become commercially available recently, a 3.2-mm diameter circle is used for the measurement, which is closer to the circle size used in the present study. Therefore, we believe that a 3.4-mm diameter circle was appropriate to compare the RNFL thickness using these instruments.

Although the number of normal subjects (n=6) was small, the mean RNFL thickness determined by OCT was significantly greater than that measured by GDx for each quadrant as shown in Table 1. Varma et al.¹³⁾ histologically measured the RNFL thickness in normal human eyes and reported that the mean RNFL thickness was the greatest in the superior quadrant at the margin of the optic disc quadrants, followed by the inferior, nasal, and temporal quadrants. They also showed that there was a significant negative correlation between the distance from the disc margin and RNFL thickness. The areas of RNFL thickness measurement in their study were not identical to ours, and direct comparison of RNFL thickness cannot be done. However, their ranking of histologic RNFL thickness for the four quadrants agrees with that of the RNFL thickness measured by OCT, but not with that measured by GDx: the RNFL thickness for the superior quadrant was less than that for the inferior quadrant in GDx measure-This result implies that measurement using GDx may not reflect the actual RNFL thickness, and a marked discrepancy in RNFL thickness is found in the superior quadrant. The same tendency was observed in

the measurements of all the subjects, not only for the superior quadrant but also for the temporal quadrant as shown in Table 2. A possible reason for this difference is birefringence of the cornea. In this study, we used GDx with a fixed compensator to correct the retardation value of the cornea. In human eyes, birefringence values of the cornea vary greatly¹⁴, and the fixed compensator used in the GDx is known to be inadequate to compensate the birefringence of the cornea in all subjects¹⁵).

A significant correlation between OCT and GDx measurements of RNFL thickness was obtained for the total area as well as for the superior and inferior quadrants, but not for the nasal and temporal quadrants. The lack of correlation in the nasal and temporal quadrants may be due to the fact that values obtained by GDx in these quadrants were less variable and relatively constant compared with OCT as shown in Fig. 2.

Weinreb et al. 16) reported that the mean retardation obtained by the Nerve Fiber Analyzer was significantly greater in normal eyes than in glaucomatous eyes in the inferior and superior quadrants, but not in the temporal and nasal quadrants. Lee and Mok¹⁴⁾ also reported that the peripapillary RNFL thickness in the temporal and nasal regions were similar in normal and glaucoma groups, and that parameters of superior/nasal (S/N) and inferior/nasal (I/N) ratio were effective for the diagnosis of early glaucoma. Morgan et al.10) also reported that regional comparison of RNFL thickness obtained by microscopy and Nerve Fiber Analyzer showed the best correlation in the inferior region (r=0.76), followed by superior (r=0.52), temporal (r=0.49), and nasal (r=0.49)0.06) regions. This evidence suggests that in the temporal and nasal regions, the RNFL thickness determined by GDx does not reflect the actual histological thickness, which might explain why we found no correlation between OCT and GDx measurements of RNFL thickness in the temporal and nasal quadrants.

Several reports showed a significant relationship between RNFL thickness and visual field in glaucoma¹⁶⁻²¹⁾, but other reports indicated that this relation became weaker when advanced glaucoma cases were excluded²²⁾. Although this means that it is difficult to obtain a good correlation between visual field and RNFL thickness in early-stage glaucoma cases alone, Asaoka et al.²³⁾ reported that sectorial division analysis of peripapillary RNFL thickness was effective in evaluating the early glaucomatous visual field. The CPSD is a visual field index which is indicative of early visual field damage. In this study, although the average MD of glaucoma cases was -3.8 dB, and the majority of cases were early to moderate glaucoma, CPSD correlates significantly with RNFL thickness determined by OCT, but not with RNFL thickness measured by GDx.

Hoh et al.¹¹⁾ also reported a better correlation between HFA visual field indices and RNFL thickness determined by OCT compared with GDx. A recent comparative study of imaging technologies and psychophysical tests by Bowd et al.²⁴⁾ showed that OCT ranked first in the ability to diagnose early glaucoma, followed by frequency-doubling technology (FDT) perimetry, GDx, and short-wavelength automated perimetry (SWAP). These reports indicate that among the potentially useful devices for diagnosing glaucoma, OCT has better abilities to discriminate glaucoma patients from normal persons. These may also be reflected in our result that compared with GDx determinations; OCT measurements correlate better with visual field loss.

In conclusion, the RNFL thickness obtained using OCT is generally greater compared with GDx. Our results indicate that the RNFL thickness in the nasal and temporal quadrants determined by GDx does not correlate with that obtained by OCT, probably reflecting previous findings that RNFL thickness determined by GDx does not represent the actual histological thickness. Although the correlation between visual function and RNFL thickness is also better in OCT measurements than in GDx measurements, we cannot definitely state that OCT correlates better with histological RNFL thickness at this point, and further investigation is needed to clarify this assumption.

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光干渉断層計 (OCT) およびスキャニングレーザーポラリメーター (GDx) を用い測定した網膜神経線維層厚の比較

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【要旨】 目的:光干渉断層計 (OCT) およびスキャニングレーザーポラリメーター (Nerve Fiber Analyzer, GDx) は網膜神経線維層 (RNFL) 厚を直接的に測定できる光学機器である。今回、OCT と GDx を用いて同一条件で測定した RNFL 厚の比較を行い、視野と RNFL 厚との相関性についても検討した。方法:対象は緑内障患者 13 例 13 眼、高眼圧症例 4 例 4 眼、正常者 6 例 6 眼である(平均年齢:56.0±13.6 歳)。緑内障患者におけるハンフリー視野の mean deviation (MD) の平均値は -3.8 ± 4.9 dB であった。同一検者によって視神経乳頭周囲の RNFL 厚を OCT と GDx を用いて 3 回連続で測定した。測定は乳頭を中心とした半径 1.7 mmの円周上で行い、全象限および上側、鼻側、下側、耳側の各象限における RNFL 厚の平均値を算出した。変動係数(RNFL 厚の標準偏差/平均)が 10%以上の症例はあらかじめ除外した。結果:全象限の平均 RNFL 厚は OCT で $105.8\pm17.3~\mu$ m、GDx で $79.3\pm14.6~\mu$ m となり、有意差があった (p<.0001)。全象限および上側、下側の象限では、OCT と GDx の RNFL 厚の間に有意な相関性が得られたが、鼻側、耳側の象限ではなかった。また、ハンフリー視野計の corrected pattern standard deviation (CPSD) と OCT の RNFL 厚との間には有意な相関性が得られたが、CPSD と GDx との間にはなかった。結論:OCT で得られた RNFL 厚は GDx と比べ全般的に大きくなり、視機能との相関性も GDx と比べ良かった。

〈Key words〉 光干渉断層計、スキャニングレーザーポラリメーター、網膜神経線維層厚、視野