coxon signed-rank test). Despite no significant difference in rim area ($P = 0.2$), the rim volume was smaller in the affected eyes ($P = 0.002$). The RNFL thickness measured by GDx VCC was significantly smaller in the NAION eyes in all three parameters (temporal-superior-nasal-inferior-temporal average, superior average, and inferior average; $P<0.0001$). Most differences were still significant after Bonferroni corrections for multiple comparisons.

When the same parameters were compared between the unaffected fellow eyes of patients with NAION and the age- and refraction-matched normal control eyes, the disc area was significantly smaller in the NAION fellow eyes ($P = 0.002$, Mann–Whitney *U* test; Table 3). All cup parameters were smaller in the NAION fellow eyes ($P<0.033$, Mann–Whitney *U* test), whereas the rim area and the rim volume were not significantly different. The disc area and the mean cup depth differed significantly even after correction for multiple comparisons by Bonferroni's method. The RNFL thickness by GDx VCC did not differ between the fellow eyes and the normal control eyes (Table 3).

Discussion

The absence of cupping or smaller cupping after NAION compared with arteritic anterior ischemic optic neuropathy[6,13] and glaucoma[12,23] has been reported. However, comparisons of cupping between eyes in which NAION had developed and normal eyes have been inconsistent in previous studies. Using fundus photography, Jonas and Xu reported significantly smaller cupping in eyes after the development of NAION.[5] Danesh-Meyer et al[6] reported no significant difference in cupping on fundus photographs, and Nagai-Kusuhara et al[7] found no significant difference in cup area using the HRT. However, differences between eyes in which NAION has developed and normal eyes cannot be entirely attributed to the occurrence of the disease because eyes prone to NAION are believed to have characteristic morphologic features that differ distinctly from typical normal eyes.[8–10,24] Therefore, comparing NAION eyes with the as yet unaffected fellow eyes seems to be a more appropriate comparison to investigate the changes after the development of the disease.

Previous reports have compared optic disc morphologic features between eyes in which NAION has developed and the unaffected fellow eyes. Quigley and Anderson[12] found no significant difference in cupping on optic disc photographs. Danesh-Meyer et al[13] reported a slight but significantly greater cup-to-disc area ratio in the eyes in which NAION had developed using the HRT, whereas there were no significant differences in cup area or cup volume. Contreras et al[14] found a significant difference in cup-to-disc area ratio but not in optic disc area using OCT. In the current study, the authors found a significantly greater cup area, cup-to-disc area ratio, and cup volume using the HRT. However, the difference in the rim area was not significant and the rim volume was smaller by approximately 20% ($P = 0.002$). The discrepancy among the previous reports may be the result of an inability to quantify minute changes in cupping on optic disc photographs. Although the study by Danesh-Meyer et al[13] also did not find significant differences in cup area or cup volume using the HRT in a series of eyes in which NAION had developed, the cup-to-disc ratio increased significantly by 42%, and it is possible that the eyes in which NAION had developed in the current study were investigated later, after the onset of NAION, resulting in more evident cupping.

It is also noteworthy that there was no difference in cup area or cup-to-disc area ratio when the eyes in which NAION had developed and the normal control eyes were compared (cup area, 0.56±0.56 vs. 0.58±0.32; $P = 0.9$; cup-to-disc area ratio, 0.26±0.22 vs. 0.27±0.13; $P = 0.9$, Mann–Whitney *U* test). The current findings suggested that after the development of NAION there is mild enlargement of cupping compared with the premorbid state; despite that, however, the cupping did not exceed that of normal eyes.

Furthermore, to the authors' knowledge, the current study is the first to compare the peripapillary RNFL thickness between eyes in which NAION has developed and the unaffected fellow eyes by scanning laser polarimetry. A thinner RNFL was observed in eyes with NAION in all three parameters investigated ($P<0.0001$). Between the eyes with NAION and the unaffected fellow eyes, the differences in polarimetry were more obvious compared with the HRT results, suggesting that the peripapillary RNFL thickness was more notably affected compared with the intrapapillary morphologic features after development of the disease.

Previous studies also have compared the unaffected fellow eyes of patients with NAION with the eyes of normal subjects. Mansour et al[24] found a smaller disc area and shorter horizontal disc diameter in the unaffected fellow eyes on fundus photographs compared with eyes of a

Table 3. Comparison of Parameters of the Heidelberg Retina Tomograph II and the GDx with Variable Corneal Compensation between Unaffected Fellow Eyes of 31 Patients with Unilateral Nonarteritic Ischemic Optic Neuropathy and 62 Age- and Refraction-Matched Normal Control Eyes

	Unaffected Fellow Eyes of Patients with Nonarteritic Ischemic Optic Neuropathy	Normal Control Eyes	P Value*
HRT II parameters			
Disc area (mm²)	1.75±0.44	2.07±0.42	0.002
Cup area (mm²)	0.36±0.42	0.57±0.33	0.014
Rim area (mm²)	1.38±0.27	1.50±0.32	0.1
Cup-to-disc area ratio	0.18±0.17	0.27±0.13	0.011
Cup volume (mm³)	0.07±0.09	0.13±0.11	0.014
Rim volume (mm³)	0.41±0.15	0.41±0.15	0.9
Mean cup depth (mm)	0.16±0.09	0.23±0.08	<0.0001
Cup shape measure	−0.21±0.08	−0.18±0.05	0.033
GDx VCC parameters			
TSNIT average (μm)	55.6±9.3	53.3±5.1	0.1
Superior average (μm)	66.1±10.4	66.6±8.1	0.8
Inferior average (μm)	63.4±10.4	67.2±7.0	0.061

HRT II = Heidelberg Retina Tomograph II; GDx VCC = GDx with variable corneal compensation; TSNIT = temporal-superior-nasal-inferior-temporal.
The values are expressed as the mean±standard deviation.
*Comparison between the unaffected eyes of unilateral nonarteritic anterior ischemic optic neuropathy and age- and refraction-matched normal control eyes (Mann–Whitney *U* test).

refraction-matched normal control group. However, the patients with NAION in their study were older than the normal control subjects (mean±standard deviation, 75.0±9.9 vs. 63.1±15.0; $P = 0.03$), which weakened their conclusion about the premorbid optic disc characteristics in subjects with NAION because some previous studies suggested significant correlation between age and disc size,[18,19] although other studies could not find such correlation.[15,16,25–27] Feit et al[8] reported a smaller cup-to-disc area ratio in the unaffected fellow eyes on fundus photographs compared with age-matched control subjects. Also, a recent study by Contreras et al[14] using OCT revealed smaller cup-to-disc area ratio in comparison with normal controls. However, the refractive error was not considered in these studies, and the relationship between refraction and disc morphologic features[15,16] cannot be disregarded. Doro and Lessell[9] and Beck et al[10] also compared unaffected fellow eyes with normal control eyes and found a smaller cup-to-disc area ratio in the unaffected fellow eyes. However, neither age nor refraction was matched in these studies, and the possible effect of these factors on the results cannot be ignored.

In the current study, in which the authors assumed bilateral similarity in optic disc morphologic features within a subject,[11] the authors compared the unaffected fellow eyes of the patients with NAION with age- and refraction-matched normal control eyes to assess the premorbid characteristics of eyes in which NAION would develop in the future. The gender ratio was similar between the two groups. The disc area and cup parameters, including the cup area, cup-to-disc area ratio, and cup volume, were significantly smaller in the unaffected fellow eyes compared with age- and refraction-matched normal control eyes using the HRT. These tendencies were consistent with the results reported previously, and the current study confirmed the premorbid disc characteristics of patients with NAION after excluding the influence of age, refraction, and possibly gender. However, disc area was not necessarily smaller in NAION fellow eyes than in normal control eyes in all of the previous studies, including the most recent one by Contreras et al.[14] Although the exact reasons for this discrepancy between the results of Contreras et al and the present study may be difficult to explain, a few possible factors can be addressed. First, refraction that is known to have a correlation with disc size[15,16] was not matched in the normal controls in the study of Contreras et al.[14] Second, with the fast optic disc protocol of the Stratus OCT (Carl Zeiss Meditec, Dublin, CA), the disc contour is drawn automatically from 12 points decided by the machine. This automatic disc contour definition has been reported to be placed erroneously at a very high frequency,[28] and disc area determined by OCT is not as accurate as that measured by the HRT where the contour line is drawn by an experienced examiner with the guide of a stereophotograph of the optic disc.[28–30] Third, in the current study, 22 patients with NAION were excluded because of low reliability of measurements of HRT II, GDx VCC, or visual field, and this exclusion may have some influence on the current results and on the discrepancy with the results of Contreras et al.[14]

Moreover, this is the first report that there is no difference in the RNFL thickness between the unaffected fellow eyes of patients with NAION and normal control eyes by scanning laser polarimetry. In contrast with the RNFL thickness measurements obtained with the HRT, which measures the thickness at a given distance from the optic disc margin, GDx VCC measures the RNFL thickness along the same diameter (3.2 mm) regardless of the size of the disc. Thus, the present results showing similar RNFL thickness in NAION fellow eyes and normal control eyes indicate that the amount of RNFL is approximately equivalent between the 2 groups at the given diameter. If the disc is smaller, RNFL thickness increases as it approaches the disc margin, and the present results follow the well-believed thesis that the optic nerve becomes crowded at the smaller lamina cribrosa in NAION eyes with smaller discs or cup-to-disc area ratio.

The relatively small number of subjects is a limitation to this study. However, considering the low prevalence of NAION, it is difficult to conduct a study with more patients. The current study with 31 patients with NAION included approximately the same number[8,9,14] or more patients[6,7,24] compared with previous studies. All the disc contours of the HRT II images were outlined by one examiner (H.S.), referring to color photographs if necessary when determining the optic disc margin. Thus, another limitation is the possibility that the examiner was able to infer the diagnosis from the photographs and was not completely masked to the diagnosis when determining the disc margin. Furthermore, from the retrospective nature of this study, it is not possible to distinguish whether the larger cupping in eyes in which NAION had developed are truly acquired after the onset of the disease or whether the cupping was larger to begin with in eyes in which NAION developed. However, the authors believe that these conclusions are well supported by reports on bilateral similarity between eyes in each subject.[11] Also, if cupping truly were to be larger in NAION eyes, it would go against the theory of small cupping as a predisposing factor for the onset of the disease.

In summary, this study quantitatively investigated the optic disc morphologic features and peripapillary RNFL thickness of affected and unaffected eyes of patients with unilateral NAION and age- and refraction-matched normal control eyes using the HRT II and GDx VCC. The authors found a significantly greater cup area, cup-to-disc area ratio, and cup shape measure, smaller rim volume, and thinner RNFL in eyes after NAION compared with the unaffected fellow eyes, suggesting the acquired enlargement of the cupping after the onset of NAION. Furthermore, the disc area and cup parameter were smaller in the unaffected fellow eyes of patients with NAION, whereas the rim parameter and RNFL thickness did not differ compared with the normal control eyes, which imply that smaller disc area and cupping are risk factors for NAION.

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Scanning Laser Polarimetry With Enhanced Corneal Compensation in Patients With Open-angle Glaucoma

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Aims: To compare the retinal nerve fiber layer thickness (RNFLT) parameters obtained with newly introduced GDx with enhanced corneal compensation (ECC) and those with GDx with variable corneal compensation (VCC) and to evaluate their reproducibility and the correspondence with visual field damage (VFD) in total or sectorized fields in association with refractive errors in open-angle glaucoma (OAG) patients.

Patients and Methods: Measurement reproducibility was assessed in 30 normal and 30 OAG eyes. Correlation between the RNFLT parameters and the corresponding VFD was evaluated in 58 OAG eyes.

Results: All parameters of both GDx VCC and ECC showed high intraclass correlation coefficients among the repeated measurements (0.89 to 0.99), suggesting good reproducibility. All RNFLT parameters were significantly correlated between VCC and ECC (intraclass correlation coefficient = 0.58-0.92, $P < 0.001$) though they were significantly different. In OAG eyes, correlation between temporal, superior, nasal, inferior, temporal average and mean deviation of VFD was similar in both algorithms ($Rs = 0.58$ and 0.53, $P < 0.001$). When the OAG eyes were subgrouped by refractive error at -5 D, the correlation was significant for both ECC and VCC in the lower myopic group (> -5 D) ($Rs = 0.71$ and 0.74, $P < 0.0001$) but was significant only for ECC in the higher myopic group (≤ -5 D) (ECC: $Rs = 0.44$, $P = 0.016$, VCC: $Rs = 0.19$, $P = 0.309$). In all 58 OAG eyes, significant correlation between the sectorized VFD and the corresponding RNFLT was found in the superior arcuate, inferior arcuate, and inferior para-arcuate areas for both VCC and ECC in the sector analysis ($P < 0.01$), whereas the correlation was significant only for ECC ($Rs = 0.46$, $P < 0.001$) but not for VCC ($Rs = 0.30$, $P = 0.024$) in the superior para-arcuate.

Conclusions: The results of GDx ECC were well correlated with those of VCC and had good reproducibility equivalent to that of VCC. Introduction of the ECC algorithm should improve the correspondence with VFD at least in moderate to high myopic OAG patients.

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Glaucoma is characterized by progressive loss of the retinal ganglion cells and thinning of retinal nerve fiber layer (RNFL), both of which are believed to precede visual field damage (VFD).[1–5] Because glaucomatous damage is irreversible, it is of clinical importance to find glaucoma in early stages to appropriately start treatments.

The GDx (Carl Zeiss Meditec, Inc, Dublin, CA) is a scanning laser polarimeter (SLP) which noninvasively measures light retardation to quantify RNFL thickness (RNFLT).[5–10] The currently used GDx is equipped with a variable corneal compensation (VCC) to individually compensate for the birefringence of the cornea and the lens, resulting in improved performance in the evaluation of RNFLT compared with GDx with the fixed corneal compensation.[11–14] The enhanced corneal compensation (ECC) was developed as an alternative algorithm to the VCC method.[15–18] When retardance in the reflected light from the globe is low, sensitivity of the SLP detector in the GDx system is inherently low and becomes more susceptible to optical and electronic error likely to yield inaccurate results.[15] In ECC, a predetermined birefringence (bias retardance) is added to the raw birefringence signal to shift it into a more sensitive region of the SLP detector to improve on signal to noise ratio.[15]

Regarding the ECC system, studies on its reproducibility,[16] the prevalence of atypical retardation pattern (ARP), and comparison of the RNFLT parameters between normal and glaucomatous eyes[16,18] have been recently published. To our knowledge, however, neither the correlation between the RNFLT parameters obtained with ECC and those with VCC nor the correspondence of the RNFLT parameters measured by ECC with VFD in glaucomatous eyes have ever been studied. The aims of this study are to compare the RNFLT parameters obtained with GDx ECC and those with GDx with VCC, and to evaluate their reproducibility and the correspondence with VFD in total or sectorized fields in association with refractive errors in open-angle glaucoma (OAG) patients.

PATIENTS AND METHODS

All studies described below were carried out at the Department of Ophthalmology, University of Tokyo Graduate School of Medicine after obtaining written informed consent from the subjects or patients. The studies were approved by the Institutional Review Board and followed the declaration of Helsinki.

The ECC algorithm is a newly introduced software to the VCC system without any changes in the hardware. The principle of the ECC algorithm has been described in detail elsewhere[15-18] and is briefly summarized below. In both the VCC and ECC algorithms, an SLP image of the macula is first obtained to decide eye-specific anterior segment polarization and the corneal compensator is set to remove the anterior segment polarization. In the ECC algorithm, the bias retardance is further added to shift the polarization signal into a more sensitive region of SLP detector (approximately 55 nm with a vertical slow axis). After a precise measurement of the total retardance is carried out, the bias retardance is mathematically removed and then the RNFLT is calculated. As a consequence, the signal to noise ratio is increased by the enhancement of polarization signal, resulting in improvements on RNFLT measurement in eyes with considerable noise interference originating from optical (eg, stray light, sclera reflection) or electronic (eg, noise, digitization error) error.[15]

In the current study, GDx measurements with VCC and ECC were performed in 30 ophthalmologically normal eyes of 30 paid volunteers who were gathered to obtain a normative database and 58 eyes of 58 consecutive patients with OAG from the outpatient clinic at Tokyo University Hospital between March 2005 and August 2005.

Ophthalmologically normal eyes had no history of ocular diseases, intraocular pressure of 21 mm Hg or lower by Goldmann applanation tonometry, normal optic disc appearance based on clinical stereoscopic examination, and reliable and normal results of the Humphrey Field Analyzer (HFA) 24-2 Swedish Interactive Testing Algorithm (SITA) standard strategy (Carl Zeiss Meditec, Inc, Dublin, CA). The results of the HFA were judged as reliable when fixation loss was $<20\%$ and false positive/negative error $<33\%$. A visual field result was concluded as normal when it showed neither glaucomatous abnormalities according to the criteria described below nor other pathologic findings.

OAG was diagnosed based on normal open angles, typical glaucomatous optic disc appearances, VFD corresponding to the optic disc findings evaluated with reliable HFA results with 30-2 SITA standard strategy, the absence of apparent pale color of the optic disc, and the absence of any contributing ocular or specific systemic disorders. The visual field was judged to be abnormal according to the criteria described by Anderson and Patella.[19] Eyes with refractive error exceeding $+5$ or -10 D, eyes in which reliable GDx measurements with the VCC or ECC algorithm (quality score ≥ 8) could not be obtained, eyes with ocular diseases except OAG and slight cataract, eyes having history of intraocular surgeries, and eyes with peripapillary atrophy situated within the measurement circle (diameter 3.2 mm) of the GDx measurement were not included in this study. If both right and left eyes fulfilled the inclusion criteria, the data of right eye was used in the following analyses.

GDx VCC and ECC measurements were performed on one GDx machine by switching the methods software within the apparatus. In every subject, VCC measurements were done first and ECC measurement followed. In all of the 30 normal subjects and the first consecutive 30 OAG patients of the 58 OAG patients enrolled in this study, VCC and ECC measurements were repeated twice with an interval of at least 5 minutes during which the subject was asked to remove his/her face from the head rest to evaluate measurements reproducibility. Same anterior segment birefringence data was applied to both VCC and ECC measurements. All scans were checked for quality and scans with a Q score lower than 8 were excluded from the study. The default measurement ring size (diameter 3.2 mm) was used throughout the study, and the automatic disc edge identification was checked for each scan and manually adjusted when necessary. The GDx parameters investigated in this study were ellipse average [temporal, superior, nasal, inferior, temporal (TSNIT) average], superior average, inferior average, TSNIT standard deviation, and Nerve Fiber Index. Typical scan score (TSS)[16-18] was also obtained to evaluate the typicality of the polarimetry images. HFA measurements were obtained within 3 months from the GDx measurements.

Correlation coefficients between TSNIT average and mean deviation (MD) were determined in the 58 OAG eyes. To investigate the influence of myopia, the 58 eyes were divided into 2 groups by refractive error. The median of the refractive error (spherical equivalent), -5 D, was chosen as the dividing value, yielding one group with 30 eyes which had spherical refractive error > -5 D (lower myopic group) and another group with 28 eyes which had refractive error ≤ -5 D (higher myopic group).

Correlation between the sectorized peripapillary RNFLT and the corresponding sectorized VFD was also studied in the 58 OAG eyes. According to the classification proposed by Garway-Heath et al,[20] visual field results obtained with the HFA 30-2 SITA standard strategy were divided into 5 sectors including paracentral area, superior arcuate area, superior para-arcuate area, inferior arcuate area, and inferior para-arcuate area and total deviation values within each area were averaged (Fig. 1A). Peripapillary RNFLT measured by GDx VCC and ECC was also averaged within the corresponding angle with the visual field areas (Fig. 1B).

Statistical Analyses

The differences in means or figures between 2 groups were evaluated using Wilcoxon signed rank test, Mann-Whitney test, or χ^2 test. Statistical correlation was evaluated by intraclass correlation coefficients (ICCs) for

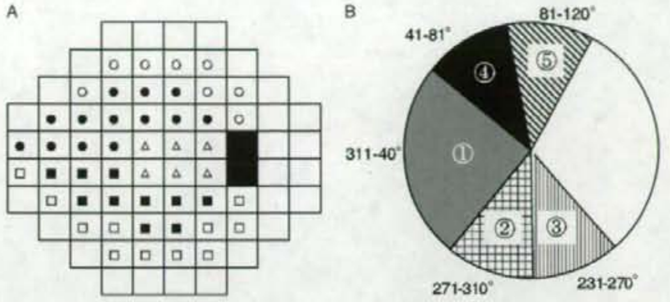

FIGURE 1. A and B, A division of the visual field (A) and optic nerve head (B) into 5 sectors. The visual field was divided into the paracentral area (white triangle), superior arcuate area (black circle), superior para-arcuate area (white circle), inferior arcuate area (black square), and inferior para-arcuate area (white square). The optic nerve head was divided into the sectors 1, 2, 3, 4, and 5 corresponding with the paracentral area, superior arcuate area, superior para-arcuate area, inferior arcuate area, and inferior paraarcuate area, respectively, in the visual field.

the GDx VCC and ECC results, and Spearman rank correlation coefficient was used to determine correlation between VFD and the corresponding GDx parameters. A P value of <0.05 after the correction for multiple tests with the Bonferroni's method was considered statistically significant. The statistical analyses were performed using SPSS 14.0J for Windows (SPSS Japan, Inc, Tokyo, Japan).

RESULTS

In 30 eyes of 30 normal subjects and 58 eyes of 58 OAG patients, age averaged 51.7 ± 14.4 (mean ± standard deviation) and 52.3 ± 9.9 years, refractive error -1.5 ± 2.3 and -4.0 ± 3.0 D, untreated intraocular pressure 14.0 ± 1.8 and 19.4 ± 4.1 mm Hg, and MD of the HFA -0.0 ± 1.1 and -7.6 ± 7.3 dB, respectively.

All RNFLT parameters and TSNIT standard deviation of both VCC and ECC were significantly smaller in OAG eyes than in normal eyes (all $P < 0.001$, Mann-Whitney tests) (Table 1). Nerve Fiber Index was significantly greater in OAG eyes ($P < 0.001$). All parameters were significantly correlated between VCC and ECC (ICC, all $P < 0.001$). In normal eyes and OAG eyes, TSNIT average and superior average were significantly greater in VCC than ECC ($P < 0.002$, Wilcoxon signed rank test), whereas inferior average and TSNIT standard deviation were smaller in VCC ($P < 0.008$).

The reproducibility of repeated GDx measurements was also evaluated with ICC. All parameters of both normal and OAG groups showed ICC higher than 0.85 and were almost equivalent between VCC and ECC (Table 2). There was no significant difference between the first and second measurements for both VCC and ECC in the reproducibility study ($P < 0.3$, Wilcoxon signed rank test).

In all 58 OAG eyes, TSS was significantly greater in the measurements with ECC than VCC (98.8 ± 4.1 vs. 88.5 ± 17.0, $P < 0.001$, Wilcoxon signed rank test). When ARP was defined as a TSS lower than 80,[17] 12 eyes (21%) scanned by VCC and no eyes (0%) by ECC demonstrated ARP ($P < 0.0001$, χ^2 test). Additionally, of the 30 normal eyes, 4 eyes (13%) with VCC and 1 eye (3%) with ECC demonstrated ARP ($P = 0.1$, χ^2 test).

TSNIT average was significantly correlated with MD in both VCC and ECC in similar strengths ($Rs = 0.58$ and 0.53, respectively, $P < 0.001$). In the lower myopic group, TSS was higher with ECC than VCC (99.8 ± 0.9 vs. 94.1 ± 12.2, $P < 0.001$). Correlation coefficients between TSNIT average and MD were statistically significant for both VCC and ECC ($Rs = 0.71$ and 0.74, respectively, $P < 0.001$) (Fig. 2). In the higher myopic group, TSS was also higher with ECC than VCC (96.7 ± 5.4 vs. 82.5 ± 19.5, $P < 0.001$). Correlation coefficient between TSNIT average and MD was significant for ECC ($Rs = 0.44$, $P = 0.016$) but not for VCC ($Rs = 0.19$, $P = 0.309$) (Fig. 3). Between the higher myopic and lower myopic groups, TSS was significantly higher in the latter than the former for both VCC and ECC ($P = 0.022$ and 0.002, respectively, Mann-Whitney test).

Significant correlation between the sectorized VFD and the corresponding RNFLT ($P < 0.05/5 = 0.01$ determined according to the Bonferroni's method) was found in the superior arcuate, inferior arcuate, and inferior para-arcuate areas for both VCC and ECC in the sector analysis in all 58 OAG eyes (Table 3). Regarding the superior para-arcuate, the correlation was significant only for ECC ($Rs = 0.46$, $P < 0.001$) but not for VCC ($Rs = 0.30$, $P = 0.024$).

DISCUSSION

In the current study on repeatability, ICCs of the repeated measurements of GDx VCC or ECC were approximately 0.9 or more for all parameters (Table 2). These results were well coincident with a previous study on reproducibility of GDx VCC and ECC measurements,[16] indicating good performance in finding small changes in the RNFLT in the follow-up of glaucoma eyes.

TABLE 1. Averages of the Parameters of GDx With VCC and ECC and Their Correlations

		Normal	OAG	P†
No. eyes		30	58	
TSS	VCC	93.3 ± 11.8	88.5 ± 17.0	0.224
	ECC	99.2 ± 3.9	98.3 ± 4.1	0.257
	P*	0.004	< 0.001	
TSNIT average	VCC	55.3 ± 4.2	44.4 ± 8.5	< 0.001
	ECC	52.5 ± 4.0	42.8 ± 7.8	< 0.001
	P*	< 0.001	< 0.001	
	ICC(P)	0.74 (0.53-0.87) (< 0.001)	0.84 (0.75-0.9) (< 0.001)	
Superior average	VCC	66.6 ± 8.5	52.9 ± 12.3	< 0.001
	ECC	64.5 ± 7.9	52.6 ± 11.9	< 0.001
	P*	0.002	0.063	
	ICC(P)	0.89 (0.78-0.95) (< 0.001)	0.92 (0.86-0.95) (< 0.001)	
Inferior average	VCC	64.3 ± 6.2	49.2 ± 11.5	< 0.001
	ECC	66.9 ± 4.7	51.4 ± 11.3	< 0.001
	P*	0.008	< 0.001	
	ICC(P)	0.58 (0.28-0.77) (< 0.001)	0.83 (0.72-0.89) (< 0.001)	
TSNIT standard deviation	VCC	21.8 ± 3.8	16.8 ± 5.1	< 0.001
	ECC	25.1 ± 3.1	19.7 ± 5.0	< 0.001
	P*	< 0.001	< 0.001	
	ICC(P)	0.63 (0.36-0.81) (< 0.001)	0.7 (0.54-0.81) (< 0.001)	
Nerve Fiber Index	VCC	18.7 ± 7.6	53.1 ± 22.7	< 0.001
	ECC	19.2 ± 7.8	46.8 ± 22.7	< 0.001
	P*	0.34	0.001	
	ICC(P)	0.8 (0.61-0.9) (< 0.001)	0.83 (0.72-0.9) (< 0.001)	

Data are shown as mean ± standard deviation.

ICC (P) indicates intraclass correlation coefficient with interval of confidence and P value in parenthesis; normal, ophthalmologically healthy eyes; OAG, yes with OAG; P* = P value between the measurements with GDx VCC and those with ECC (Wilcoxon signed rank test); P†, P value between the normal and OAG groups (Mann-Whitney test).

In OAG eyes, RNFLT was significantly correlated with VFD in similar strength for both algorithms (Table 3). When correlation was assessed after stratifying the eyes into 30 eyes with refractive error > −5 D and 28 eyes with refractive error ≤ −5 D, relatively higher correlation coefficients were found in lower myopic eyes for both VCC and ECC. By contrast, in higher myopic eyes correlation coefficient was significant only for ECC. These results imply improved performance of ECC in eyes with moderate or high myopia. Introduction of the ECC algorithm substituting for VCC should improve the correspondence to VFD at least in moderate to high myopic OAG eyes. Because high myopic eyes are relatively common in Japan[21] or other Asian countries[22,23] and probably more common among OAG patients,[24] improved performance of ECC in high myopic eyes would bring some benefits for our OAG patients.

TABLE 2. ICCs of the Repeated Measurements of GDx With VCC and Those With ECC in 30 Normal and 30 OAG Eyes

		Normal	OAG
No. eyes		30	30
TSNIT average	VCC	0.96 (0.93, 0.98)	0.98 (0.96, 0.99)
	ECC	0.97 (0.94, 0.99)	0.95 (0.90, 0.98)
Superior average	VCC	0.97 (0.93, 0.99)	0.98 (0.96, 0.99)
	ECC	0.98 (0.95, 0.99)	0.97 (0.94, 0.99)
Inferior average	VCC	0.85 (0.69, 0.93)	0.98 (0.96, 0.99)
	ECC	0.89 (0.77, 0.95)	0.97 (0.94, 0.99)
TSNIT standard deviation	VCC	0.89 (0.76, 0.95)	0.94 (0.87, 0.97)
	ECC	0.88 (0.75, 0.94)	0.96 (0.92, 0.98)
Nerve Fiber Index	VCC	0.96 (0.92, 0.98)	0.97 (0.93, 0.98)
	ECC	0.98 (0.95, 0.99)	0.96 (0.91, 0.98)

Data are ICCs with 95% confidence interval in the parenthesis.

All parameters of both VCC and ECC in both normal and OAG groups showed ICC higher than 0.85, suggesting good reproducibility. All ICCs were almost equivalent between VCC and ECC.

Normal indicates ophthalmologically healthy eyes; OAG, eyes with open-angle glaucoma.

GDx VCC scans often demonstrate ARP,[16-18,25] which is a phenomena in which the brightest areas of the retardation maps are not consistent with the histologically thickest peripapillary RNFL portions. ARP is associated with the presence of low signal to noise ratio resulting from diminution of refractivity from the retinal epithelium and occurs more commonly in eyes with myopia or older subjects.[26] ARP is quantitatively assessed by TSS; a value calculated to yield values between 0 (maximally atypical) and 100 (completely typical). In OAG eyes of the current study, ARP was significantly less frequent in ECC scans than in VCC scans. Also, TSS was

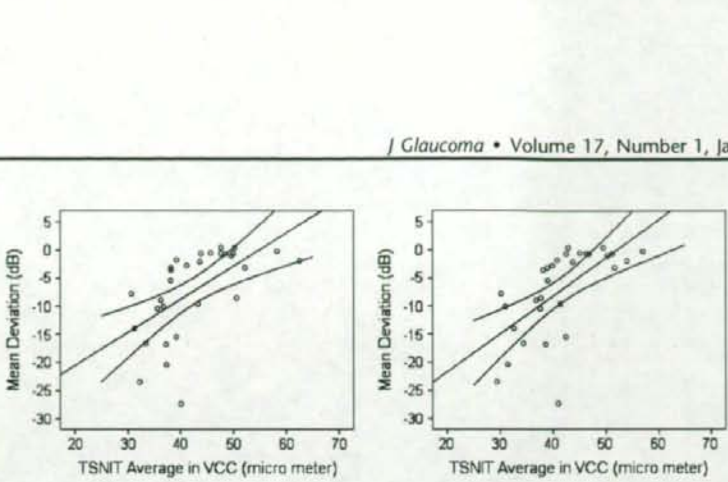

FIGURE 2. Correlation between TSNIT average measured with GDx VCC (left) and that with ECC (right) in 30 OAG eyes with refractive error > -5 D. For both VCC (left) and ECC (right) measurements, the correlation was significant (Spearman rank correlation coefficient, $Rs = 0.71$, $P < 0.001$ for VCC and $Rs = 0.74$, $P < 0.001$ for ECC).

significantly smaller in higher myopic eyes than lower myopic eyes, suggesting that increasing ARP due to myopia should be partly responsible for the disappearance of the correlation between TSNIT average and MD in high myopic eyes. Other than myopia, thin RNFL (in advanced glaucoma, etc.) or media opacities such as cataract which can lead to reduction of retardance or signal diminution should be additional factors that may affect the agreement of the VCC and ECC measurements or their correlation with visual field defect.

In the analyses of correlation between the sectorized VFD and the corresponding peripapillary RNFLT, regarding superior arcuate, inferior arcuate, and inferior para-arcuate areas in visual field, RNFLT was well correlated with the corresponding VFD for both VCC and ECC. Regarding superior para-arcuate area, correlation was significant only for ECC but not for VCC. Although it is difficult for us to speculate the reason of this finding at present, this suggests that ECC may have a better potential to evaluate the RNFLT in the nasal-inferior peripapillary region which is one of the areas suffered in early glaucoma.[27]

Most studies investigating the sensitivity and specificity of glaucoma diagnosis programs have limited their study patients to early stage glaucoma. However, because the primary purpose of our study was to evaluate the correlation between VFD and GDx parameters given by VCC or ECC, glaucomatous patients were not limited to those in the earlier stage of the disease. Therefore, glaucoma sensitivity and specificity by GDx VCC and ECC was not investigated in the current study. Comparison of the diagnostic ability between GDx VCC and ECC is, however, also an important issue and deserves further investigation. Another limitation of this study is that the numbers and the reasons of excluded glaucoma patients or normal subjects were not considered. In this study, if we found a glaucoma patient who fulfilled the inclusion criteria, we asked him/her to join this clinical study day by day. The normal subjects were paid volunteers of whom the eligibility was confirmed before visiting our hospital, and therefore the number and reasons of exclusion could not be specified.

In the current study, GDx VCC and ECC measurements demonstrated high correlation between each other. However, the values were significantly different between the 2 methods implying difficulty in interchanging the VCC results with the ECC results. Ideally, long-term measurement of RNFLT by the GDx is expected to lead to quantitative assessment of glaucoma progression. However, in order for a continuous observation to be

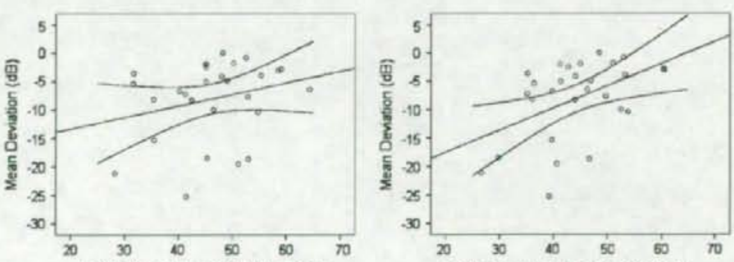

FIGURE 3. Correlation between TSNIT average measured with GDx VCC (left) and that with ECC (right) in 28 OAG eyes with refractive error < -5 D. The correlation coefficients were 0.44 ($P = 0.016$, Spearman rank correlation) and 0.19 ($P = 0.309$), respectively.

TABLE 3. Correlation Between the Sectorized Visual field Damage and the Corresponding RNFLT Evaluated With GDx With VCC and That With ECC in 58 OAG Eyes

Visual Field Area	VCC	ECC
Paracentral	0.01 (0.93)	0.17 (0.21)
Superior arcuate	0.50 (< 0.001)*	0.57 (< 0.001)*
Superior para-arcuate	0.30 (0.024)	0.46 (< 0.001)*
Inferior arcuate	0.66 (< 0.001)*	0.65 (< 0.001)*
Inferior para-arcuate	0.55 (< 0.001)*	0.54 (< 0.001)*

Data are shown as Spearman rank correlation coefficient with P value in the parenthesis. Visual field areas are indicated in Figure 1A.

*indicates significant correlation with P value $< 0.05/5$ ($= 0.01$) which is determined according to the Bonferroni's correction for multiple tests.

pursued, RNFLT measurement is required to be performed by the same method. There is still room for argument on justifying total replacement of the VCC method with the GDx ECC method. The nature and characteristics of the GDx VCC and ECC measurements still need to be explored before we can make any decisive conclusions.

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