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Effect of Glaucomatous Damage on Repeatability of Confocal Scanning Laser Ophthalmoscope, Scanning Laser Polarimetry, and Optical Coherence Tomography

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Abstract

Purpose—To determine and compare the effect of the severity of glaucomatous damage on the repeatability of retinal nerve fiber layer (RNFL) thickness with GDx-VCC (variable corneal compensation) and StratusOCT (optical coherence tomography; both produced by Carl Zeiss Meditec, Inc., Dublin, CA), and optic nerve head (ONH) topography with HRT-II (retinal tomograph; Heidelberg Engineering GmbH, Heidelberg, Germany) and StratusOCT.

Methods—With each of these techniques, two measurements were obtained from 41 eyes of 41 control subjects and 98 glaucomatous eyes (37 patients with early, 29 with moderate, and 32 with severe field loss). To evaluate test–retest variability at each stage, limits of agreement (Bland–Altman plots) and repeatability coefficients (RCs) were obtained from pairs of measurements. Comparisons of within-subject variances were used to compare repeatability of GDx-VCC versus StratusOCT for global RNFL and HRT-II versus StratusOCT for global ONH topography. Effects from age, visual acuity, and lens status were also included in the analysis as covariates.

Results—Test–retest variability of RNFL using GDx-VCC and StratusOCT were consistent through all stages of disease severity. Repeatability results of GDx-VCC were better than those of StratusOCT, except in severe cases. Test–retest variability of ONH topography using HRT-II and StratusOCT increased with increasing disease severity for rim area, cup area, and cup-to-disc (C/D) area ratio. In contrast, vertical C/D ratio from HRT-II, and horizontal C/D ratio from StratusOCT showed stable test–retest variability through all stages. Regardless of disease severity, repeatability results of HRT-II were better than those of StratusOCT.

Conclusions—GDx-VCC and HRT-II showed better repeatability than StratusOCT. Although test–retest variability increased with disease severity for rim area, the variability for vertical C/D ratio (HRTII) and global RNFL (GDx-VCC) was stable across disease severity. These parameters, rather than rim area, may be more useful in detection of progression in patients with glaucoma who have more advanced field loss.

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Studies evaluating the reproducibility of recent versions of the confocal scanning laser ophthalmoscope (HRT-II; Heidelberg Engineering, Heidelberg, Germany), scanning laser polarimetry (GDx-VCC; Carl Zeiss Meditec, Inc., Dublin, CA), and optical coherence tomography (StratusOCT; Carl Zeiss Meditec, Inc.) have shown that each of these imaging techniques obtains measurements with a high degree of reproducibility.^{1–5} However, most of these studies were performed in healthy eyes or in eyes of patients with glaucoma with predominantly early field loss and did not include cases with more advanced stages of field loss.^{3,5–7} Hence, evaluation of reproducibility for glaucoma cases has been performed in cohorts with a truncated range of field loss ranging from none to early loss, and reproducibility is unknown in cases with more advanced field loss.

Although it has been argued that observation and documentation of the optic disc becomes less important at more advanced stages of disease, this has never been rigorously evaluated with subjective and objective techniques. Furthermore, the “floor” effect in cases of advanced glaucoma also impairs the utility in visual fields, which become increasingly variable in advanced disease.^{8,9} Indeed, no validated technique has been developed to observe patients with advanced glaucoma.

Although a floor effect has been reported using GDx-VCC in eyes of patients with end-stage glaucoma,⁸ it is unknown whether a similar effect is likely to be present in less damaged eyes with severe field loss and good central visual acuity. In addition, higher test–retest variability of the confocal scanning laser ophthalmoscope (HRT) has been reported in locations of the optic disc topography with steep contour, such as the optic disc cup.¹⁰ Thus, test–retest variability is likely to be altered by variation in the surface contour of the optic disc as the disease advances. The purpose of the study was to determine and compare the effect of degree of field loss on the repeatability (two replicated scans) of nerve fiber layer measured with GDx-VCC and StratusOCT and on optic nerve head (ONH) topography measured with HRT-II and StratusOCT within the same study population of healthy eyes and glaucomatous eyes with diverse degrees of field loss.

Methods

Data were obtained from the University of Alabama at Birmingham (UAB) Optic Nerve Imaging Center database, consisting of patients with glaucoma and control subjects who had undergone optic disc imaging and visual function testing between February 2003 and October 2005. All participants were recruited as part of longitudinal glaucoma studies currently being conducted at the UAB. Patients with glaucoma were obtained from the Glaucoma Service and control subjects were obtained primarily from referrals and university employees. All aspects of the protocol adhered to the tenets of the Declaration of Helsinki. Human Subjects Committee approved all methodology, and informed consent was obtained from all participants. Forty-one control subjects with healthy eyes, 37 glaucoma patients with early field loss, 29 patients with moderate, and 32 patients with severe field loss were selected from the cohort in these studies based on the following inclusion criteria.

Normal participants were included if they had a bilateral highest documented intraocular pressure (IOP) of 22 mm Hg or less, bilateral normal eye examination findings, including dilated fundus examination, and bilateral normal results in a SITA 24-2 standard visual field test.¹¹ Patients with glaucoma were included if they had glaucomatous visual field loss (defined as pattern standard deviation outside 95% normal limits or glaucoma hemifield test [GHT] results outside of 99% normal limits and at least one cluster of three abnormal points within the same GHT sector in the pattern deviation probability plot) confirmed with a second visual field, and glaucomatous optic neuropathy as classified by three masked graders (see below). One fellowship-trained glaucoma specialist (CAG, JEDO, or BEM)

verified that visual field defects were consistent with glaucoma. Classification of severity of visual field loss was done using the criteria of Hodapp, et al.¹² All visual field tests and imaging acquisitions were made within 3 weeks (0.5 ± 0.6 weeks; mean $\pm$ 1 SD). One eye per participant was included, selected randomly except for patients with bilateral glaucoma, in whom the worse eye was selected.

Participants were excluded if they had a best corrected visual acuity less than 20/40, a spherical refraction outside ± 5.0 D, cylinder refraction outside ± 3.0 D, or unreliable visual fields (defined as fixation losses, false positive and negative responses exceeding 33%; the latter criteria was not used for cases with severe field). In addition, subjects using medications known to affect visual sensitivity at the time of visual field testing, those with comorbid ophthalmic or neurologic disease, and those with inadequate stereo photograph or imaging quality were also excluded.

Two scans were acquired with each technique. GDx-VCC imaging was acquired first through an undilated pupil, as per the manufacturer's recommendations. After full pupil dilation, HRT-II, StratusOCT imaging, and ONH stereo photographs (Nidek 3-Dx fundus camera; Nidek Technology America, Inc., Greensboro NC) were acquired. Two masked experienced graders (JEDO, BEM) independently classified the stereo photographs as normal or glaucomatous optic disc appearance, whereas a third, senior grader (CAG) adjudicated cases of disagreement. Quality of the stereo photograph was evaluated at the time of masked grading. All participants had adequate quality of stereo photographs.

RNFL thickness was evaluated with the StratusOCT and with GDx-VCC (both by Carl Zeiss Meditec Inc.). Details of StratusOCT operation have been described elsewhere.^{13–15} Data included in the analysis were for global RNFL. The landmark option was used for all scan acquisitions. Images were excluded if the video image had a poor quality, the circular scan beam was not centered on ONH, scans with signal strength lower than 8, scan image too low or too high within the window, or low analysis confidence or if subject blinked or was unable to maintain stable fixation during acquisition. Two patients were excluded for inadequate quality.

Details of the GDx-VCC operation have been described,^{16–18} and parameters studied were TSNIT (temporal, superior, nasal, inferior, and temporal) referred to herein as global RNFL, and nerve fiber indicator (NFI). NFI is a support vector machine-derived parameter indicating the likelihood that an eye has glaucoma.¹⁹ Good quality was defined as adequate fixation, minimal eye movement, good illumination, lack of artifacts/unusual patterns on the retardance image, residual retardance less than 12, and scans with quality score higher than 7, which resulted in the exclusion of two patients. Furthermore, atypical birefringence pattern (ABP) was defined on the basis of a typical scan score (TSS) of ≥ 60 and subjective evaluation of the retardation map (defined as alternating peripapillary circumferential bands of low and high retardation, variable areas of high retardation arranged in a spoke-like peripapillary pattern, or splotchy areas of high retardation nasally and temporally).²⁰ Scans from nine eyes were classified as having ABP, with the following distribution: two (5.4%) eyes had early field loss, four (13.8%) had moderate, and three (9.4%) eyes had severe field loss. None of the eyes in the control group showed ABP. While three eyes had a TSS ≥ 30 (one with score of 0, which also showed a high degree of ABP), the rest had scores of 30 to 60 and mild ABP.

ONH topography was obtained with the confocal scanning laser ophthalmoscope (HRT-II, Heidelberg Engineering, Heidelberg, Germany). Details of the HRT-II operation have been described before.^{15,21,22} Experienced operators (JDDO, SNA) evaluated image quality and outlined the disc margin while viewing stereoscopic photographs of the ONH. The following

software-determined parameters were evaluated: rim and cup area, cup-to-disc area ratio, and horizontal and vertical cup-to-disc ratio. Topographies with acquisition sensitivity above 90%, computed topography with SD greater than 35 μm , decentered ONH, excessive movement during acquisition, floaters over/adjacent to the ONH, poor clarity of image and/or images with framing were excluded (2 patients).

Automated ONH measurements were also obtained with the StratusOCT. The following software-determined parameters were evaluated: cup and rim area, cup-to-disc area ratio, and vertical and horizontal cup-to-disc ratio. Inadequate quality of images was defined as blurred video image, ONH inadequately centered, subject had fixation losses or blinked during acquisition, and/or scans with signal strength lower than 8. Two patients were excluded because of poor imaging quality. The automated ONH algorithm correctly identified the retinal pigment epithelium (RPE) and vitreous-retinal interface in most of the scans; however, for 12 eyes (one scan on first and second observations) it was necessary to make a manual adjustment of the retinal surface sensitivity because the algorithm failed to identify the vitreous-retinal boundary accurately. Posterior vitreous detachment with high-reflectivity bodies located above the retinal surface was the reason for such errors. In addition, for two of six scans in one of these eyes (first and second observations), the operator (JEDO) had to identify the edge of RPE.

One-way analysis of variance was used to compare controls and cohorts of patients with glaucoma with respect to continuous variables (age, logMAR visual acuity,²³ refraction, IOP, and Lens Opacity Classification System (LOCS III) scores²⁴). Similar group comparisons were conducted for categorical variables (gender and self-reported race) by using χ^2 tests. The α level was set at 0.05. Multiple comparisons were controlled with Tukey HSD (honest significant difference) tests.

An operator obtained two replicate measurements with each imaging technique. A replicate measurement is defined as two scans acquired in identical condition. The operators (3) obtained each scan without knowledge of the previous values. Consistency of agreement between replicate measurements was analyzed by constructing Bland-Altman plots (difference between observation 1 and observation 2 against the average of observation 1 and observation 2) from each technique.²⁵ Relationship between the difference and magnitude of measurements was evaluated using standard procedures (SD of measures plotted against their mean, and rank correlation coefficient of variability against magnitude).^{26–29} If test-retest variability increased with the magnitude of measurements, then the within-subject standard deviations were not independent of the magnitude, and a natural logarithm transformation of the data resolved this problem. This adjustment is important, because we included a sample of patients with a wider range of visual field and anatomic measurements.

Repeatability was evaluated with the repeatability coefficient ($RC = 1.96 \cdot 2 \cdot S_w$)²⁵ where S_w is the within-subjects SD from one-way analysis of variance (subjects $\times$ imaging parameter).²⁵ For 95% of the subjects, differences of two measurements by an imaging technique will be within the range of $\pm RC$. Thus, RC is indicative of the reproducibility error. The within-subject variances (squared differences of observation 1 and observation 2) were used to compare repeatabilities between the following imaging techniques: GDx-VCC versus StratusOCT for global RNFL, and HRT-II versus StratusOCT for ONH topography. Comparisons were performed by using paired t -tests on natural log-transformed data.³⁰ Results then were anti-logged to indicate the limits around a single measurement, on a numerical scale that is regarded as values for the true clinical measurement. A secondary analysis for RC and comparisons of within-subject variances was also performed, which included the effects from age, and logMAR (logarithm of the minimum angle of resolution)

and LOCS-III scores as regressors in a general linear model. Relationship between visual field mean deviation (MD) and within-subject variances was evaluated with the Pearson correlation coefficient. Statistical analysis was performed with commercial software (JMP software version 5.0.1a; SAS Institute, Cary, NC).

Results

Participant's demographic characteristics are shown in Table 1. The patients with glaucoma were older than the control subjects—particularly those with moderate to severe degrees of field loss. The majority of participants were women. Because the primary analysis consisted of comparisons between two measures within each subject, differences in age, gender, logMAR, and LOCS III scores should not have affected our conclusions. Nevertheless, results obtained after adjusting for age, logMAR and LOCS III scores were comparable to the ones obtained from unadjusted analysis, as shown below.

Bland-Altman plots showed that the agreement of RNFL measurements was consistent in all four stages of visual function for GDx-VCC and StratusOCT (Fig. 1). Similarly, RCs for both imaging techniques were stable through all stages of field loss. Overall, these RCs were within 4 μm for GDx-VCC and 6 μm for StratusOCT (Fig. 2). Repeatability of GDx-VCC was better than StratusOCT because GDx-VCC had consistently lower RCs than StratusOCT at each stages of field loss. Significant differences in variances between GDx-VCC and Stratus-OCT further supports the differences found in repeatabilities between these two techniques (Table 2). The within-subject variance for StratusOCT was 5 to 6.5 times that for GDx-VCC, except in the severe field loss stage in which StratusOCT variance was 1.7 times that for GDx-VCC. Although the NFI show good reproducibility in the control subjects, the RCs for NFI steadily increased with worsening of field loss (Fig. 3). As shown in Figures 2 and 3, RCs were smaller after adjustment for age, logMAR and LOCS III scores but followed similar profiles compared with crude data. The RCs were even lower after nine eyes with ABP were excluded, particularly in severe cases; however, these values followed a similar pattern: NFI variability increased with increasing disease severity, whereas average RNFL remained stable.

Bland-Altman plots for ONH parameters showed that agreement for the following parameters of HRT-II and StratusOCT were less consistent with advancing disease severity: rim area, cup area, and cup-to-disc area ratio (Fig. 1). These parameters also showed increasing RCs with worsening of visual field loss (Fig. 2, unadjusted and adjusted models). Meanwhile, repeatability was stable for vertical cup-to-disc ratio with HRT-II and for horizontal cup-to-disc ratio with StratusOCT (Fig. 2). However, repeatability of HRT-II was superior to that of StratusOCT, with the HRT-II yielding smaller RCs than StratusOCT and significant differences were found between the repeatabilities of these two techniques (Table 3). Overall, the within-subject variance for StratusOCT was two to eight times that for HRT-II. Rim area presented the highest differences in variances between these two devices. As shown in Figure 2, RCs were smaller after adjusting for age, and logMAR and LOCS III scores; however, these RC followed similar patterns as with RC from crude data: increase variability with increasing disease severity for rim and cup area, and cup-to-disc area ratio. Most of the comparisons remain significant with the adjusted model. In addition, increasing field loss was significantly related to increased variability for the following parameters: NFI, cup area, cup-to disc area ratio, and vertical cup-to-disc ratio (StratusOCT); and rim area and cup area (HRT-II), as shown in Table 4.

Discussion

In prior studies evaluating the reproducibility of GDx-VCC, HRT-II, and StratusOCT, it was assumed that the reproducibility of measures with each device would be the same across all stages of visual function.^{1–5} Such uniformity has certainly not been the case with visual field testing, in which threshold variability increases with advancing disease impairing the ability of visual field test to detect progression.⁹ Most of these prior reproducibility studies in which these techniques have been used included patients with glaucoma who had predominantly early field loss or subjects with healthy eyes. The present study showed that the general assumption of uniform repeatability across stages of disease severity is not true of several disc topographic measurements, showing an increase in test–retest variability with increasing field loss.

The repeatability of GDx-VCC and StratusOCT for global RNFL was stable through stages of field loss; but the repeatability of GDx-VCC was better than that of StratusOCT. It is unclear why GDx-VCC showed better RCs than StratusOCT. A possible explanation is that the two measurements obtained with GDx-VCC are related because they sharing the same corneal compensation adjustment, which was obtained before the RNFL measurements and used on all subsequent RNFL measures. It is likely that this shared corneal compensation introduced a bias of the second measurement to the first one; thus, reducing the measuring error on GDx-VCC. Alternatively, the landmark feature of the StratusOCT could yield greater variance because of positioning errors. Regardless of this superiority, RCs for both instruments were within the theoretical resolution specified for each device.^{31,32} Although GDx-VCC was better than StratusOCT, NFI from GDx-VCC would not be useful for longitudinal evaluation and follow-up of patients with glaucoma because of the poor repeatability—particularly with increasing disease severity. In addition, excluding eyes with ABP from the analysis improved repeatability; however, variability across disease stages remained comparable as before. Thus, ABP was evident in less than 7% of the population studied and was not responsible for the variations in test–retest results observed with GDx-VCC.

In agreement with a previous study that evaluated HRT-II repeatability of rim area,² we found that test–retest repeatability of rim area was good in controls and in patients with early field loss. However, our findings showed a dramatic decrease in repeatability of rim area in patients with more advanced field loss, even after taking into account the effects from age, visual acuity and lens status.

Jampel et al.³³ evaluated the reproducibility of two HRT-II measures of rim area in patients with various degrees of glaucomatous damage including advanced stage. The authors found no association between the reproducibility of rim area with the degree of field loss. However, there are three issues with the methodology of this study. First, the authors evaluated repeatability of two measurements, but these measurements were not replicates because there was an interval of 6 months between the first and second measurements. Second, the authors failed to control for the well-described effect from fluctuations of the IOP on topographical measurements.^{34–36} Third, a 6-month interval between measurements is probably a short time to develop progressive changes in patients with early glaucoma, but it may not be the case in patients in far advanced disease stages. Thus, the effect of order of measurements, interval between measurements, and fluctuations in IOP between measurements could have affected their results. This prior study reported the within-subject SD (S_w); the present study used RC calculated from S_w . Nevertheless, Jampel et al. reported S_w values that varied across stages of field loss and were higher than the ones we found in the present study suggesting greater variability in their results at any stage of field loss than in ours. In the present study, we used data from replicate measurements (i.e., after quick

successions and without previous knowledge of results), and the order effect of testing and fluctuations in IOP should not have influenced our results.

Although HRT-II was superior to StratusOCT, this superiority may be related to the fact that, when using HRT-II, an operator defines the contour of the optic disc that is used in the analysis of subsequent scans. In contrast, StratusOCT using an edge-detection algorithm, independently analyzes every repeated scan by automatically identifying reference points and surfaces at the RPE and vitreous–retinal interface, respectively, which could increase the intratest variance. Furthermore, although pupil dilation is often not required for HRT-II, all subjects were imaged after full dilation. Small pupil size (in particular in older subjects) may have an impact on the quality of scans such as framing or poor illumination. Poor quality because of these factors was avoided by imaging after full dilation in all subjects and should not have affected our results.

In conclusion, GDx-VCC and HRT-II showed better repeatability than StratusOCT through all stages of field loss for global nerve fiber layer and optic disc topography measurements, respectively. Repeatability was stable for RNFL measurements across the strata of disease severity. However, for most optic disc topographic parameters, repeatability decreased with increasing glaucomatous damage, particularly for rim area. Although it appears that these imaging techniques have the ability to obtain reproducible measurements in patients with early glaucomatous damage, the decrease in repeatability observed in patients with more advanced damage is likely to compromise the use of NFI by GDx-VCC, rim area, cup area, and cup-to-disc area ratio from both HRT-II and StratusOCT in patients with advanced glaucoma. These findings of increased test–retest variability associated with the degree of glaucomatous damage were evident even after taking into account effects from age, visual acuity and lens media, and such increased test–retest variability should be taken into consideration when designing methods for detecting progressive changes in patients with glaucoma. We suggest interpreting with caution the longitudinal information provided by these parameters in patients with more advanced field loss. Because of their low test–retest variability, the vertical cup-to-disc ratio by HRT-II and global RNFL by GDx-VCC parameters are likely to be useful when evaluating for progressive changes in patients with more advanced glaucomatous damage.

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Figure 1.

Bland-Altman plots constructed for the RNFL (**A**) and for the ONH replicated measurements (**B**), stratified by status of visual field loss. *Solid lines*: fixed bias; *dotted lines*: range of limits of agreement. Contrary to RNFL measurements, the range of limits of agreement for ONH measurements increased with increased severity of field loss.

Figure 2.

RCs displayed for nerve fiber layer and optic disc topographic measurements, across stages of field loss. A low RC is indicative of low test–retest variability. Dimensions of RCs for the nerve fiber layer are in micrometers (except for NFI), and for rim and cup area are in square millimeters. Ratios are dimensionless. Results from analyses with crude data and from analyses that included the effect of age, logMAR score, and LOCS III score are shown. Error bars, SE.

Figure 3.

RCs displayed for GDx-VCC parameters of NFI and average RNFL thickness (TSNIT), across stages of field loss. Results from analysis with crude data and results from analysis that included the effect of age, logMAR score, and LOCS III score are shown, including and excluding atypical scans. Error bars, SE. NBP, normal birefringence pattern.

Table 1

Demographics

	Controls	Glaucoma Patients			P
		Early	Moderate	Severe	
Number of subjects	41	37	29	32	NA
Age (y)	42.1 ± 10.1	54.3 ± 10.5 ^{*,†}	63.1 ± 13.7 [*]	62.7 ± 13.9 [*]	<0.0001
Self-reported race (AA, %)	46	73	66	56	0.094
Sex (female, %)	73	76	62	63	0.496
LogMAR VA	-0.06 ± 0.1	-0.01 ± 0.1	0.04 ± 0.1	0.14 ± 0.5 [*]	0.018
Sphere (D)	0.35 ± 1.6	-0.67 ± 1.8	0.35 ± 1.6	-0.64 ± 1.7	0.002
IOP (mm Hg)	15.2 ± 2.6	15.8 ± 3.4	14.6 ± 3.3	14.3 ± 3.5	0.218
LOCS III scale [‡]					
Nuclear opalescence	1.9 ± 0.7	2.6 ± 0.9	2.5 ± 1.3	2.3 ± 1.5	0.023
Nuclear color	1.9 ± 0.7	2.6 ± 0.9	2.5 ± 1.3	2.3 ± 1.5	0.021
Cortical cataract	0.2 ± 0.3	0.5 ± 1.2	1.2 ± 1.4	0.6 ± 0.9	0.002
Posterior subcapsular opacification	0.1 ± 0.0	0.2 ± 0.5	0.4 ± 0.6	0.2 ± 0.4	0.168

Data are expressed as the mean ± SD for continuous variables and as a percentage for categorical variables. ANOVA was used for comparison of continuous variables and χ^2 for comparison of categorical variables. Significant probabilities are in bold.

^{*} Significantly different from the control group; Tukey HSD test, $\alpha = 0.05$.

[†] Significantly different from the severe cohort; Tukey HSD test, $\alpha = 0.05$.

[‡] Three eyes in the severe and in the moderate cohort were pseudophakic.

Table 2

Crude and Age-, LogMAR VA-, and Lens-Adjusted Comparisons of Variances between Matched-Samples of Global (Average) Nerve Fiber Layer Thickness

Visual Field Loss	Mean Difference in Variances of GDx-VCC vs. StratusOCT	<i>P</i> [*]	<i>P</i> [†]
No loss (controls)			
<i>n</i> = 41	6.17	0.007	0.006
Early loss			
<i>n</i> = 37	4.59	0.005	0.006
Moderate loss			
<i>n</i> = 29	6.47	0.006	0.005
Severe loss			
<i>n</i> = 32	1.65	0.408	0.328

* Paired *t*-test. Significant probabilities are in bold.

† Adjusted for age, LogMAR VA score, and LOCS score.

Table 3

Crude and Age-, LogMAR VA-, and Lens-Adjusted Comparisons of Variances between Matched-Samples of Optic Disc Topography

Visual Field Loss	Optic Nerve Head Parameter	Mean Difference in Variances of HRT II vs. Stratus OCT	<i>P</i> [*]	<i>P</i> [†]
No loss (controls)				
<i>n</i> = 41	Rim area	38.86	<0.0001	0.0001
	Cup area	3.72	0.010	0.002
	H C/D	2.21	0.070	0.893
	V C/D	4.03	0.001	0.018
	C/D area	2.17	0.043	0.002
Early loss				
<i>n</i> = 37	Rim area	25.03	<0.0001	<0.0001
	Cup area	4.17	0.0002	0.0003
	H C/D	1.62	0.313	0.036
	V C/D	3.62	0.002	0.003
	C/D area	2.51	0.022	<0.0001
Moderate loss				
<i>n</i> = 29	Rim area	9.87	0.0012	0.037
	Cup area	4.66	0.0121	0.332
	H C/D	2.22	0.109	0.092
	V C/D	2.64	0.031	0.137
	C/D area	0.87	0.815	0.563
Severe loss				
<i>n</i> = 32	Rim area	15.03	<0.0001	0.011
	Cup area	7.23	0.0026	0.110
	H C/D	1.17	0.772	0.191
	V C/D	5.48	0.0006	0.012
	C/D area	6.21	<0.0001	0.015

H C/D, horizontal cup-to-disc ratio; V C/D, vertical cup-to-disc ratio; C/D area, cup-to-disc area ratio.

* Paired *t*-test. Significant probabilities are in bold.

† Adjusted for age, logMAR score, and LOCS III score.

Table 4

Correlations between Visual Field MD and Variances in Imaging Parameters in 139 Eyes

Variance of Imaging Parameter (Observation 1 Minus Observation 2) ²	Pearson Correlation (r)	P
NFI	-0.42	<0.0001
Cup-to-disc area ratio (Stratus OCT)	-0.38	<0.0001
Cup area (Stratus OCT)	-0.25	0.0031
Vertical cup-to-disc ratio (Stratus OCT)	-0.23	0.0065
Average RNFL (Stratus OCT)	0.20	0.0203
Rim area (HRT II)*	-0.19	0.0259
Average RNFL (GDx-VCC)	-0.18	0.0369
Cup area (HRT II)*	-0.17	0.0460
Cup-to-disc area ratio (HRT II)*	-0.16	0.0662
Rim area (StratusOCT)	-0.07	0.4404
Vertical cup-to-disc ratio (HRT II)*	0.06	0.4540
Horizontal cup-to-disc ratio (StratusOCT)	0.06	0.4612
Horizontal cup-to-disc ratio (HRT II)*	-0.03	0.7329

Significant probabilities are in bold.

* Two outliers were excluded.