Structural and Functional Relationships in Glaucoma Using Standard Automated Perimetry and the Humphrey Matrix

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Purpose: To evaluate and compare correlations between structural and functional loss in glaucoma as assessed by optical coherence tomography (OCT), scanning laser polarimetry (GDx VCC, as this was the model used in this study), standard automated perimetry (SAP), and the Humphrey Matrix (Matrix).
Methods: Ninety glaucomatous eyes identified with SAP and 112 eyes diagnosed using Matrix were independently classified into six subgroups, either S1/M1 (MD>-6dB), S2/M2 (-12<MD<-6dB) or S3/M3 (MD<-12dB), according to the mean deviation (MD) of each test. Average and sectoral retinal nerve fiber layer (RNFL) thickness and percentage of abnormal classifications using the internal normative databases of OCT and GDx VCC were compared among the six subgroups.
Results: In the SAP subgroups, RNFL thickness values obtained by OCT in the nasal and temporal quadrants and the inferior averages of GDx VCC did not differ between the S1 and S2 subgroups (*p*=0.137, 0.738 and 0.149, respectively). In the Matrix subgroups, no measurement parameters differed between the M1 and M2 groups except for the overall mean and average inferior RNFL thickness given by OCT and the NFI values of GDx VCC (*p*=0.013, 0.016 and 0.029, respectively). When abnormal classifications were compared, all measurement parameters, without exception, were significantly different in both the SAP and the Matrix subgroups.
Conclusions: SAP subgroups showed a good correlation of structural and functional defects when assessed using OCT and GDx VCC. These correlations were weaker in the Matrix subgroups, especially in the early stages of glaucoma.
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Glaucoma is a progressive optic neuropathy characterized by the loss of retinal ganglion cells (RGCs) and axons. These structural changes are known to presage functional deficits, causing gradual visual field (VF) defects.[1-2] Traditionally, glaucomatous structural changes have been assessed by detailed ophthalmoscopic examination. Recently, objective and analytic approaches to structural assessment have become available with the development of imaging devices, most notably optical coherence tomography (OCT) and scanning laser polarimetry (SLP).

Standard automated perimetry (SAP) (Carl Zeiss Meditec Inc., Dublin, CA, USA) is the gold standard for testing functional changes in glaucoma. This technique measures light sensitivity thresholds at each retinal location. However, the method is not selective for the detection of particular glaucoma-related RGC damage. Therefore, VF defects may be detected by SAP only after the death of some RGCs.[3-4]

Humphrey Matrix Frequency doubling technology perimetry (Matrix) (Carl Zeiss Meditec Inc.) was developed to detect damage to magnocellular ganglion cells, which are preferentially affected in glaucoma patients.[5] In this context, the Matrix has been found to be more sensitive than SAP because it can detect VF loss earlier.[6-9]

Using a variable corneal compensator (VCC) (GDx VCC Carl Zeiss Meditec Inc.), a test of structural change, the GDx VCC can estimate the thickness of the retinal nerve fiber layer (RNFL) by measuring the summed retardation of a polarized scanning laser beam induced by form-birefringent microtubules supporting RGC axons.[10-13]

Stratus OCT (Carl Zeiss Meditec Inc.) is used to obtain data on a cross-section of the retina based on the reflectivity of different retinal layers; the technique can define the thickness of the circumpapillary RNFL.[14-16]

Because the two imaging modalities use different technologies to measure distinct aspects of retinal biology, it is possible that measurements derived from these approaches might show different associations with functional change.

In general, damage to the optic nerve and RNFL may precede VF loss in early glaucoma.[17] However, recent clinical trials,

including the Ocular Hypertension Treatment Study and the European Glaucoma Prevention Study, reported that the earliest damage in glaucoma patients can be either structural or functional in nature.[17-18] Therefore, the relationship between functional and structural damage in glaucoma is a topic of debate.

The purpose of this study was to compare the structural changes in glaucoma assessed by OCT and GDx VCC and also the functional relationships detected by SAP and Matrix. We categorized patients into three groups according to the severity of their VF field injury, and evaluated the structural and functional relationships using two different VF tests.

Materials and Methods

Participants

The medical records of all patients examined at the glaucoma clinic from January 2007 to March 2008 by one glaucoma specialist were reviewed, and if patients met the inclusion criteria of this study they were consecutively enrolled. All participants underwent a comprehensive ophthalmic examination, including visual acuity measurement, slit-lamp biomicroscopy, intraocular pressure measurement by Goldmann applanation tonometry, central corneal thickness ultrasound pachymetry measurement, SAP, Matrix, GDx VCC, and OCT. Patients were eligible if they had a best-corrected visual acuity greater than 20/40 and a normal anterior chamber and open-angle on slit-lamp and gonioscopic examinations, respectively. Participants with any other ophthalmic disease that could result in VF defects or who had histories of diabetes mellitus were excluded. A glaucomatous optic disc was defined as a disc showing increased cupping (vertical cup-disc ratio >0.6), asymmetrical cupping (a between-eye difference in the vertical cup-disc ratio of >0.2), diffuse or focal neural rim thinning, hemorrhage, or nerve fiber layer defects. Glaucomatous eyes defined by SAP (SAP group) were those with a glaucomatous optic disc appearance and glaucomatous VF defects defined by the glaucoma hemifield test (GHT) as outside 99% of age-specific normal limits and also with a pattern standard deviation (PSD) outside 95% of the normal limit with the 24-2 full threshold program or the 24-2 Swedish Interactive Threshold Algorithm (SITA) standard programs of the HFA.

The same VF criteria were used to define glaucomatous eyes identified by Matrix. Eyes with a glaucomatous optic disc appearance and a GHT result outside 99% of the age-specific normal limits with a PSD outside 95% of the normal limit with Matrix were categorized by Matrix as suffering from glaucoma (Matrix group). Since there were no generalized criteria in Matrix for diagnosing glaucoma, we arbitrarily applied the same criteria as in SAP to the Matrix results.

We included only those patients who, within one month of the initial evaluation, yielded a reliable VF measurement, defined as a false-positive error <15%, a false-negative error < 15% and a fixation loss <20% in both SAP and Matrix. One eye

was randomly selected if both eyes were found to be eligible. Subsequently, 90 eyes were classified as glaucomatous in the SAP group and 112 eyes were identified in the Matrix group. All procedures conformed to the Declaration of Helsinki, and the study was approved by the Ethics Committee of the Asan medical center. Written informed consent was obtained from all patients.

Optical Coherence Tomography (Stratus OCT)

OCT measures RNFL thickness with a low-coherence light source projected onto the retina. The time delay of the light backscatter from the RNFL compared with light reflected by a reference mirror is then calculated. Circumpapillary RNFL was measured in the fast RNFL mode using three 360-degree circular, high-resolution scans with a diameter of 3.4 mm that were centered on the optic disc. RNFL thicknesses of the collective quadrants (360° measure), as well as the individual temporal (316°-45°), superior (46°-135°), nasal (136°-225°), and inferior (226°-315°) quadrants, were obtained for analysis. Diagnostic categorization by Stratus OCT involves a software-based comparison of thickness parameters with an internal normative database of 328 eyes; we also evaluated these parameters in our study. Parameters on the Stratus OCT printout are annotated to indicate whether they fall outside of the 99% confidence interval (CI), between the 95% and 99% CIs (borderline) or within the 95% CI (normal). In this study, only well-focused and centered scans with signal strengths ≥ seven were included, and a parameter was considered outside the normal limits if CI < 95% and within the normal limits if CI > 95%.

Scanning Laser Polarimetry (SLP)

SLP imaging was performed in a standardized fashion (GDx VCC software version 5.5.0) with a circular scan (3.2 mm in diameter) centered on the optic disc. The general principles of SLP with variable corneal polarization compensation (VCC) have been described in detail elsewhere.[19-21] We only analyzed eyes with a scan quality score of eight or better. Images with atypical retardation patterns (ARPs) were excluded from the study. The SLP parameters examined were TSNIT (temporal, superior, nasal, inferior, and temporal) imaging, superior imaging, inferior average imaging, and the nerve fiber indicator (NFI). The GDx VCC printout provides probabilities of abnormality based on a comparison with an internal database containing information on 540 normal eyes. In this study, a parameter was considered outside the normal limits if $p<0.05$ and within the normal limits if $p>0.05$. For the NFI parameter, the manufacturer-suggested cutoff of < 30 was considered as within the normal limits, whereas values of 31-100 were considered abnormal.

Study Group

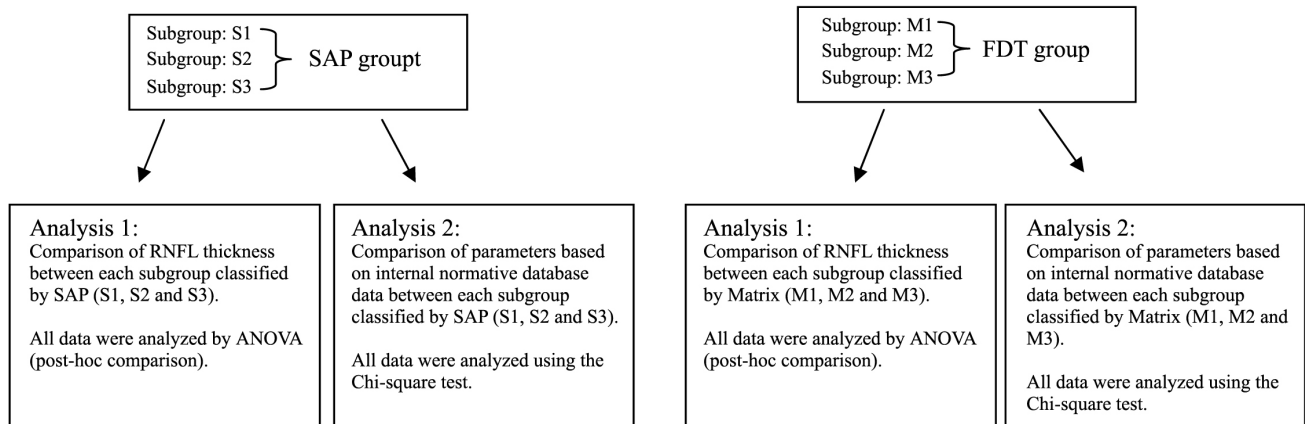Participants were classified based on the severity of their

Fig. 1. Overview of the division of the SAP and Matrix groups and Analyses 1 and 2.

functional damage as assessed by SAP and Matrix. Since no generalized criteria for categorizing glaucoma severity using Matrix exists, we used the same mean deviation (MD) values for both SAP and Matrix. With reference to the mean deviations of SAP and Matrix, each VF defect was classified as early (no worse than -6dB): groups S1 and M1; moderate (worse than -6 dB but not worse than -12dB): groups S2 and M2; and advanced (worse than -12dB): groups S3 and M3.[22] The S1, S2 and S3 subgroups were classified according to SAP severity, whereas subgroups M1, M2 and M3 were determined by Matrix severity scores.

Data analysis

All statistical tests were performed using a statistical soft-

ware package (SPSS 15.0 for Windows; SPSS Inc., Chicago, IL). RNFL thicknesses measured by OCT and GDx VCC were compared among the three groups categorized by MD scores from both SAP and Matrix using a one-way analysis of variance (ANOVA) with pairwise, post-hoc Tukey comparisons. The normative classifications determined by the internal databases of the OCT and GDx VCC instruments were compared among the three subgroups for each of SAP and Matrix using the Chi-square test. Differences with a value of $p<0.05$ were considered statistically significant (Fig.1).

Results

The mean age of the 90 participants in the SAP group was 56.9 ± 13.4 years, and the mean age of the 112 participants in

Table 1. Patient Characteristics

	SAP group (n=90)	Matrix group (n=112)	p-value
Age (years) (mean±SD)	56.9±13.4	54.4±12.6	0.674
Sex			
Male (n and %)	45 (50.0%)	57 (50.9%)	
Female (n and %)	45 (50.0%)	55 (49.1%)	
Refraction (D) (Mean±SD)	-0.56±2.04	-0.69±1.91	0.527
MD (Mean±SD)	-7.63±6.17	-8.10±5.90	0.872
PSD (Mean±SD)	6.97±4.26	5.22±1.88	0.000[*]
Vision (Log mar scale)	-0.82±0.17	-0.82±1.6	0.831
Tested eye			
Right (n and %)	52 (57.8%)	73 (65.2%)	
Left (n and %)	38 (42.2%)	39 (34.8%)	
Type of glaucoma			
POAG (n and %)	17 (18.9%)	19 (17.0%)	
NTG (n and %)	65 (72.2%)	82 (73.2%)	
SOAG (n and %)	5 (5.6%)	6 (5.4%)	
PACG (n and %)	3 (3.3%)	5 (4.4%)	

D=diopters; SAP=standard automated perimetry; Matrix=frequency doubling technology perimetry 24-2 performed with the Humphrey Matrix; SD=standard deviation; MD=mean deviation;PSD=pattern standard deviation; SAP group=laucoma group diagnosed by standard automated perimetry; Matrix group=laucoma group diagnosed by Humphrey Matrix perimetry; POAG=rimary open angle glaucoma; NTG= normal tension glaucoma; SOAG=econdary open angle glaucoma; PACG=rimary angle closure glaucoma.
[*] statistically signifilcant ($p<0.05$).

Table 2. Subgroups divided by mean deviations of SAP and Matrix

Grade	SAP group				Matrix group			
	Subgroup	No.	MD (Mean±SD)	PSD (Mean±SD)	Subgroup	No.	MD (Mean±SD)	PSD (Mean±SD)
Early (-6dB<MD)	S1	21	-1.43±1.04	2.78±0.79	M1	47	-2.65±2.00	4.19±1.28
Moderate (-12dB<MD<-6dB)	S2	50	-6.51±2.59	6.69±3.45	M2	39	-8.53±1.67	5.38±1.67
Severe (MD<-12dB)	S3	19	-17.41±4.41	12.34±2.38	M3	26	-16.8±3.21	9.36±3.53

MD=mean deviation; PSD=pattern standard deviation; No.=number of patients; SAP group: glaucoma group diagnosed using standard automated perimetry; S1, S2, S3=subgroups divided by mean deviation of standard automated perimetry; Matrix group=glaucoma group diagnosed using Humphrey Matrix perimetry; M1, M2, M3=subgroups divided by mean deviation of Humphrey Matrix perimetry.

Table 3. Comparison of OCT and GDx VCC parameters between the SAP group and the Matrix group

Instrument	Parameter	SAP group	Matrix group	p-value
Stratus OCT	Superior thickness	94.64±28.66	104.21±27.61	0.402
	Nasal thickness	64.79±17.81	68.42±18.44	0.764
	Inferior thickness	94.04±32.87	106.09±31.45	0.378
	Temporal thickness	61.97±19.64	65.18±18.08	0.438
	Average thickness	79.66±19.58	86.77±18.55	0.409
GDx VCC	TSNIT average	41.36±8.19	43.91±7.94	0.634
	Superior average	48.76±11.36	52.35±10.97	0.675
	Inferior average	44.23±11.25	47.88±11.50	0.894
	TSNIT SD	14.40±4.95	15.86±5.10	0.833
	NFI	54.91±23.26	46.04±22.37	0.673

NFI=nerve fiber indicator; SAP group=glaucoma group diagnosed using standard automated perimetry; Matrix group=glaucoma group diagnosed using Humphrey Matrix perimetry; TSNIT=temporal-superior-nasal-inferior-temporal; SD=standard deviation.

Table 4. Analysis 1: Comparison of RNFL thickness between each subgroup classified by SAP (S1, S2 and S3) and Matrix (M1, M2 and M3)

Instrument	Parameter	SAP group			Matrix group		
		S1-S2	S1-S3	S2-S3	M1-M2	M1-M3	M2-M3
Stratus OCT	Superior thickness	0.011[*]	<0.001[*]	0.003[*]	0.206	<0.001[*]	<0.001[*]
	Nasal thickness	0.137	0.020[*]	0.036[*]	0.966	0.005[*]	0.003[*]
	Inferior thickness	<0.001[*]	<0.001[*]	<0.001[*]	0.013[*]	<0.001[*]	<0.001[*]
	Temporal thickness	0.738	0.001[*]	0.001[*]	0.697	<0.001[*]	0.001[*]
	Average thickness	0.001[*]	<0.001[*]	<0.001[*]	0.016[*]	<0.001[*]	<0.001[*]
GDx VCC	TSNIT average	0.015[*]	<0.001[*]	0.002[*]	0.110	<0.001[*]	<0.001[*]
	Superior average	0.024[*]	<0.001[*]	0.002[*]	0.396	<0.001[*]	<0.001[*]
	Inferior average	0.149	0.001[*]	0.020[*]	0.089	0.015[*]	<0.001[*]
	TSNIT SD	0.049[*]	0.001[*]	0.003[*]	0.858	<0.001[*]	0.001[*]
	NFI	0.002[*]	<0.001[*]	<0.001[*]	0.029[*]	<0.001[*]	<0.001[*]

SAP group: glaucoma group diagnosed using standard automated perimetry; S1, S2, S3=subgroups divided according to the mean deviation of standard automated perimetry; Matrix group=glaucoma group diagnosed using Humphrey Matrix perimetry; M1, M2, M3=subgroups divided according to the mean deviation of Humphrey Matrix perimetry; NFI=nerve fiber indicator; TSNIT=temporal-superior-nasal-inferior-temporal; SD=standard deviation; All data were analyzed by ANOVA (post-hoc comparison).
[*] statistically significant ($p<0.05$).

the Matrix group was 54.4±12.6 years. Table 1 summarizes the demographics and clinical characteristics of both groups. In the SAP group, 21 eyes were classified as S1, 50 eyes as S2, and 19 as S3, according to MD criteria. In the Matrix group, 47 eyes were classified as M1, 39 eyes as M2, and 26 eyes as M3 (Table 2).

Analysis 1: SAP subgroups vs. Matrix subgroups with reference

to RNFL thicknesses assessed by OCT and GDx VCC

Structural parameters assessed by OCT and GDx VCC were compared in the SAP subgroups and the Matrix subgroups (Table 3). Average RNFL thickness measured by OCT was 79.7±19.5 μm in the SAP group and 86.8±18.6 μm in the Matrix group (p= 0.41). The average NFI determined by GDx VCC was 54.9± 23.3 in the SAP group and 46.0±22.4 in the Matrix group (p=

Table 5. Comparison of observed parameters with data in internal normative databases between each subgroup classified by SAP (S1, S2 and S3) and Matrix (M1, M2 and M3)

Instrument	Parameter	Chi-square test		Number of abnormal parameters					
		SAP group	Matrix group	S1 (n=21)	S2 (n=50)	S3 (n=19)	M1 (n=47)	M2 (n=39)	M3 (n=26)
Stratus OCT	Superior thickness	0.001*	<0.001*	3 (14.3%)	25 (50.0%)	15 (78.9%)	8 (17.0%)	11 (28.2%)	38 (33.9%)
	Nasal thickness	0.026*	0.007*	1 (4.8%)	12 (24.0%)	6 (31.6%)	4 (8.5%)	4 (10.3%)	10 (38.5%)
	Inferior thickness	<0.001*	<0.001*	3 (14.3%)	23 (46.0%)	18 (94.7%)	7 (14.9%)	12 (30.8%)	19 (73.1%)
	Temporal thickness	<0.001*	<0.001*	1 (4.8%)	11 (22.0%)	12 (63.2%)	4 (8.5%)	4 (10.3%)	10 (38.5%)
	Average thickness	<0.001*	<0.001*	3 (14.3%)	21 (42.0%)	18 (94.7%)	7 (14.9%)	8 (20.6%)	20 (76.9%)
GDx VCC	TSNIT average	0.003*	0.001*	12 (57.1%)	36 (72.0%)	17 (89.5%)	22 (46.8%)	26 (66.7%)	22 (84.6%)
	Superior average	0.030*	0.001*	12 (57.1%)	35 (70.0%)	19 (100.0%)	21 (44.7%)	23 (59.0%)	24 (92.3%)
	Inferior average	0.002*	0.013*	10 (47.6%)	33 (66.0%)	17 (89.5%)	21 (44.7%)	22 (56.4%)	20 (76.9%)
	TSNIT SD	0.006*	0.014*	8 (38.1%)	23 (46.0%)	16 (84.2%)	18 (38.3%)	13 (33.3%)	18 (69.1%)
	NFI (>30)	0.013*	0.004*	13 (61.9%)	39 (78.0%)	19 (100%)	24 (51.1%)	28 (71.8%)	23 (88.5%)

SAP group=glaucoma group diagnosed using standard automated perimetry; S1, S2, S3=subgroups divided by mean deviation of standard automated perimetry; Matrix group=glaucoma group diagnosed using Humphrey Matrix perimetry; M1, M2, M3=subgroups divided by mean deviation of Humphrey Matrix perimetry; NFI=nerve fiber indicator; TSNIT=temporal-superior-nasal-inferior-temporal; SD=standard deviation; All data were analyzed using the Chi-square test.
* statistically significant ($p<0.05$).

0.67). Overall, no RNFL thickness parameter measured using either OCT or GDx VCC differed, with statistical significance, between the SAP and Matrix groups.

In the SAP group, average, superior and inferior RNFL thicknesses measured by OCT were significantly different between the S1 and S2 groups (p=0.001, 0.011 and 0.000, respectively), whereas the average and inferior RNFL thicknesses were significantly different in the M1 and M2 groups (p=0.016 and 0.013, respectively). Nasal and temporal RNFL thicknesses did not differ when the S1 and S2 or the M1 and M2 subgroups were compared. TSNIT values, superior averages, TSNIT SDs, and NFIs assessed by GDx VCC were significantly different between the S1 and S2 subgroups, but only NFIs were significantly different between the M1 and M2 subgroups. All parameters of OCT and GDx VCC were significantly different between the S2 and S3 subgroups and also between the S1 and S3 subgroups. Matrix subgroup analysis also revealed significant differences between groups M2 and M3, and M1 and M3 (Table 4).

Analysis 2: SAP group vs. Matrix group with reference to normative classifications assessed by OCT and GDx VCC

We used the Chi-square test to compare structural parameters interpreted with the internal normative databases. Compared to abnormal classifications, percentages of such classifications among the subgroups were significantly different in all parameters in both the SAP and Matrix subgroups (Table 5).

Discussion

SAP is considered to be a standard approach for detecting VF loss in glaucoma.[1] However, SAP may not be able to detect early functional changes because of redundancies in RGCs and optic nerve fibers, which can mask damage.[23,24]

As a screening device, Humphrey Matrix Frequency doubling technology perimetry (Matrix) is known to be similar to or better than the Humphrey field analyzer.[25-28] Frequency doubling technology (FDT) perimetry was developed as a method to detect early glaucoma by attempting to functionally isolate "My" cells, which may be selectively damaged in the early stages of glaucoma.[1,25,29] My cells are not functionally redundant (making up 3-5% of all ganglion cells); the FDT technique thus has the theoretical potential to identify early VF loss.[30,31]

Matrix perimetry is an updated version of FDT perimetry, employing a larger number of stimulus locations and smaller targets than those used in FDT perimetry. Matrix also provides the global indices of SAP, such as MD, PSD and GHT classification, in a standard printout.[32-35] Comparison of Matrix and SAP threshold sensitivities is not appropriate because the two technologies measure different aspects of retinal sensitivity SAP assesses differential light sensitivity, and Matrix obtains data on contrast sensitivity. Although global indices were reported to be significantly correlated between SAP and Matrix,[36,37] there is no consensus for the definition of glaucomatous VF defects as determined by Matrix. Therefore, we used the same criteria (PSD < 5% and abnormal GHT) to define glaucoma identified by both SAP and Matrix, and we divided patients into three groups according to the severity of the MD.

Stratus OCT and GDx VCC are the two most recent commercial instruments available to analyze peripapillary RNFL thickness. In many studies, both GDx VCC and OCT showed relatively high diagnostic accuracies in glaucoma detection.[38-41] Average RNFL thickness by OCT demonstrated a strong correlation with VF defects.[42] The NFI data from GDx VCC also revealed a strong correlation with VF defects. However, RNFL thicknesses determined by OCT in the nasal and temporal quadrants have been reported to show high measurement varia-

bilities.[43-46]

Reus and Lemij suggested that glaucoma patients with mild-to-moderate VF loss might be better monitored with the GDx VCC.[47] Kim and Kook reported that abnormal scores obtained on FDT perimetry screening programs correlated negatively with RNFL retardation values, as measured in glaucomatous changes seen by SLP.[48] However, to our knowledge, no data confirming a relationship between VF loss and GDx and OCT Matrix data has been published.

In this study, we divided patients into subgroups using MD values from both SAP and Matrix. Our results showed that all structural parameters except nasal and temporal RNFL thicknesses obtained by OCT were significantly different among cases in the three different stages of glaucoma. These findings suggest good correlations between RNFL thickness parameters assessed by OCT and GDx VCC on the one hand, and SAP defects on the other, in patients in different stages of glaucoma. Only nasal and temporal quadrant data of OCT, and the inferior average of GDx VCC, showed no meaningful correlations between early (S1) and moderate (S2) glaucoma stages as assessed by SAP. This might be explained by high measurement variability.[43-45] The fact that nasal and temporal quadrants are relatively more resistant to glaucomatous damage may also partly explain these findings.

However, not all structural parameters showed significant differences between early (M1) and moderate (M2) stages of glaucoma as assessed by Matrix. Average and inferior RNFL thicknesses by OCT and NFI by GDx VCC were significantly different between the M1 and M2 subgroups, but there were no differences in any other parameters. Although some parameters did not differ between the M1 and M2 subgroups, all parameters assessed by GDx VCC and OCT showed significant differences between the moderate (subgroup M2) and advanced (subgroup M3) patients.

Matrix is known to be superior to SAP for detecting the early stages of glaucoma. In this study, we observed that although the Matrix subgroups showed definite structural differences between cases of moderate and severe glaucoma as assessed by GDx and OCT parameters, not all parameters differed between patients with early and moderate glaucoma. This could indicate that Matrix can be an excellent screening device to detect early glaucoma, especially in the preperimetric stage, but it has difficulty in discriminating between the early and moderate stages of glaucoma. The other possible explanation for the poor correlation of structural damage with functional deficits as determined by Matrix in early-to-moderate glaucoma stages is related to the reliability of Matrix itself. Most enrolled participants were tested only once for each Matrix and SAP. The learning effect of Matrix may improve VF outcome in repeat tests. We acknowledge that this is a limitation of our study. Because the study design was retrospective, all participants underwent a comprehensive ophthalmic examination at the initial visit, including SAP, FDT, OCT, and GDx VCC. If reliability indices were poor during testing, the operator stopped the test, explained the process thoroughly, and then restarted the test. To maximize reliability and to minimize learning effect-related issues, we adopted strict VF inclusion criteria.

To our knowledge, this is the first study to examine the relationship between functional and structural damage in glaucoma subgroups of different severities using both SAP and Matrix global indices. We concluded that glaucoma status as defined by both SAP and Matrix correlates with structural loss as assessed by OCT and GDx VCC, but that such correlations are slightly weaker in the early-to-moderate glaucoma stages as defined by Matrix.

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