EXTENDED REPORT

The correlation between optic nerve head topographic measurements, peripapillary nerve fibre layer thickness, and visual field indices in glaucoma

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Aims: To establish whether the structural parameters provided by the Heidelberg retina tomograph (HRT) and the laser diagnostics glaucoma scanning system (GDx) can be used to reflect functional damage in the visual field.

Methods: 62 patients with primary open angle glaucoma underwent examination with the HRT, GDx, and Humphrey field analyser. The relations between the topographic parameters, retinal nerve fibre parameters, and visual field indices were analysed by scatter plot and linear regression.

Results: Among the topographic parameters generated by the HRT, rim area had the best correlation with visual field indices. The "number," maximum modulation, and ellipse modulation generated by the GDx also had correlations with visual field indices. The correlations were better for the sectoral parameters than the global parameters. However, great interindividual variation was found in the association.

Conclusion: Although relations were found between some topographic parameters, RNFL parameters, and visual field indices, great interindividual variation limits the prediction of one parameter from the other. Therefore, both structural and functional aspects should be evaluated in order to obtain full characterisation of the glaucomatous damage for clinical judgment and treatment.

Glaucoma is a progressive optic neuropathy in which morphological changes that occur at the optic nerve head (ONH) and retinal nerve fibre layer (RNFL) are associated with functional deficit, measurable as visual field (VF) loss. Examining and monitoring the optic nerve head and the RNFL, structurally and functionally, is important for diagnosis and treatment. Functional loss is normally recorded with automated static threshold perimetry which is both sensitive and specific to early loss and provides quantitative data for the monitoring of change. Structural damage is still largely dependent on clinical assessment with an ophthalmoscope and the detection of change relies on professional judgment. Although some quantitative evaluations, based on photographic records of the optic nerve head and the RNFL, have been developed, most of them are complicated and time consuming. Recently, the advent of computerised instruments such as the confocal scanning laser ophthalmoscope (Heidelberg retina tomograph, HRT) and scanning laser polarimeter (laser diagnostics glaucoma scanning system, GDx) have introduced rapid and quantitative three dimensional analysis of the optic nerve head and RNFL.

The HRT is a laser scanning tomograph that measures the topography of the optic nerve head and peripapillary retina. The real time, high contrast, topographical image is obtained by a scanning laser ophthalmoscope which comprises a 670 nm diode laser and a confocal imaging system. Based on this topographical image, HRT software generates several parameters describing the optic nerve head and peripapillary RNFL.

The GDx is a scanning laser ophthalmoscope comprising a 780 nm diode laser, polarisation modulator, fixed corneal compensator, and polarisation detector. It uses the birefringent properties of the RNFL to estimate its thickness. The change in the polarisation (retardation) is linearly correlated with the histopathological measurements of the RNFL thickness in monkey[1] and postmortem human eyes.[2] One degree of retardation corresponds to 7.4 μm of thickness.[1] Based on the retardation measurements, the GDx software provides several parameters on the peripapillary RNFL.

Careful evaluation of the optic nerve head and RNFL is crucial in glaucoma, not only for diagnosis, but also for providing information about the location and severity of visual field damage. Examination of stereoscopic optic disc photographs allows accurate prediction of the location of glaucomatous field loss in the upper and lower hemifields in 83% and 91%[3] of patients. RNFL defects also correlate well with the location and extent of visual field loss.[4–6] Apart from the topographical aspect, the relation between structural damage and functional damage also has a quantitative aspect. Optic nerve head parameters, such as C/D ratio, cup area, cup volume, rim width, and rim area are correlated with visual field indices, especially the index mean deviation (MD).[7–9] The semiquantitative RNFL scores are also highly correlated with visual field indices in glaucoma, especially the MD,[10] with white on white perimetry and also with blue on yellow perimetry[11] and other psychophysical tests.[12 13] The measurements of RNFL height by the Rodenstock optic nerve head analyser also correlates, quantitatively, with measurements of visual function in glaucoma.[14]

The advent of HRT and GDx technology, with good reproducibility[15–18] as well as high sensitivity and specificity[19–22] in glaucoma diagnosis, provides us with better methods for investigating quantitative associations. VF examination relies upon patient responses and usually takes about 5–20 minutes. The subjectivity and variability of the patient performing the test will affect the results and complicate the interpretation. On the other hand, optic nerve head and RNFL examinations by HRT and GDx are objective and take only a few seconds. If the information provided by HRT and GDx could accurately represent the VF, imaging could be used to replace VF examination. The purpose of this study is to analyse the quantitative relation between the structure of the optic nerve head and retinal nerve fibre layer and the functional damage in the visual field in glaucoma. It also aims to study whether the structural parameters provided by HRT and GDx can reflect functional visual field damage.

PATIENTS AND METHODS

Subjects

Sixty two white patients with primary open angle glaucoma were recruited from the outpatient clinics of Manchester Royal Eye Hospital without knowing the severity of visual field defects and optic nerve head damage. Informed consent was obtained from all patients after the examination procedure was fully explained. All patients underwent evaluations including abbreviated medical history, full ocular history, ophthalmological examination, automated visual field test, optic nerve head tomography, and scanning laser polarimetry. The ophthalmological examinations included logMAR visual acuity, slit lamp biomicroscopy, applanation tonometry, gonioscopy, and dilated indirect ophthalmoscopy for optic disc and nerve fibre layer evaluations. Visual field tests were performed with the Humphrey field analyser (HFA) (Model 740, Humphrey-Zeiss, Dublin, CA, USA) using the full threshold 24-2 program. Optic nerve head tomography was performed using HRT (software version 2.01, Heidelberg Engineering GmbH, Heidelberg, Germany). Scanning laser polarimetry was conducted with the GDx (software version 2.0.09, Laser Diagnostic Technologies, Inc, San Diego, CA, USA). Automated visual field testing, optic nerve head tomography, and scanning laser polarimetry were completed on each patient within 6 months of each other. The inclusion criteria included age $\geqslant$40 years, best corrected visual acuity not worse than logMAR 0.4, spherical refractive errors $\leqslant$+5.00 and $\geqslant$−5.00D and cylinder $\leqslant$3.00D, previous experience of full threshold perimetry, reliable HFA visual fields (fixation losses, false positives, and false negatives $<$25%) and good image quality with the HRT and GDx. The exclusion criteria included neurological disease, history of ocular trauma, intraocular surgery, other intraocular disease except early senile cataract, and generalised depression or an abnormal high sensitivity result with the glaucoma hemifield test (GHT). For the purpose of this study, glaucoma was defined as: (1) glaucomatous optic disc based on either cup/disc asymmetry between two eyes $>$0.2, rim defect, notching, excavation, or nerve fibre layer defect, and (2) two consecutive reliable abnormal HFA visual fields with corrected pattern standard deviation (CPSD) outside 95% normal limit, or GHT outside 99% normal limit, or three or more adjacent points with $p < 5\%$ on the pattern deviation probability plot, and one of which must have $p < 1\%$.[23] The index MD was not used because of the possibility of a reduced value resulting from cataract. If both eyes were eligible only one eye of each patient was chosen randomly.

Humphrey field analyser

The visual field was divided into superior, inferior, nasal, and temporal sectors based on the anatomical relation established by Garway-Heath *et al*.[24] The number of points that represented $p < 1\%$ and $p < 5\%$ on the pattern deviation probability plot were also used as global VF indices. With regard to the sectoral VF index (sectoral mean deviation), this was represented by the mean value of all points for each sector on the total deviation plot of the HFA.

Confocal scanning laser ophthalmoscope

The optic nerve head tomography was performed by well trained technicians using the Heidelberg retina tomograph (HRT). Magnification error was corrected by keratometry values and refraction results for each individual. Imaging was performed with a 10 × 10° field of view through a $\geqslant$3 mm diameter pupil when the subject viewed at a distant fixation target. Each eye had five scan series recorded at one sitting. The quality of images was assessed with the aid of the HRT software and by the experience of the technician. The best three of these five scan series were used to produce an overall mean topographical image for further analysis. The mean topography had a clear image with a clearly definable disc margin and the mean standard deviation for the height position of each pixel element of the three topographic images was under 40 µm.

The contour line (disc margin) was drawn using a computer mouse system by a trained observer who was masked to the patient diagnosis and characteristics. A series of optic nerve head topographic parameters (optic disc area, cup area, cup/disc area ratio, cup volume, rim area, rim volume, height variation contour, mean cup depth, maximum cup depth, and cup shape measure) and RNFL (mean RNFL thickness and cross section area along the corrected contour line) for the whole disc and predefined sectors were calculated by the software. The sectors used in this study were defined as temporal: −30°–30°, superior: 30°–135°, nasal: 135°–225°, and inferior: 225°–330°.[24] HRT also provides a glaucoma index and a classification of "normal" (positive index) or "glaucoma" (negative index) based on a discriminant function elaborated by Mikelberg *et al*.[25]

Table 1 Global VF indices, topographic parameters by HRT and RNFL parameters by GDx

Visual field	
MD (dB)	−5.77 (4.91)
CPSD (dB)	6.21 (3.29)
No of points p<1%	9.95 (7.63)
No of points p<5%	15.48 (7.48)
GDx	
The number	43.08 (23.62)
Average thickness (µm)	62.47 (11.72)
Ellipse average (µm)	63.09 (12.30)
Total polar integral (µm^2)	0.56 (0.13)
Maximum modulation	1.03 (0.38)
Ellipse modulation	1.74 (0.55)
HRT	
Glaucoma index	−1.84 (1.65)
Disc area (mm^2)	2.01 (0.41)
Cup area (mm^2)	1.07 (0.44)
C/D area ratio	0.52 (0.16)
Rim area (mm^2)	0.94 (0.30)
Cup volume (mm^3)	0.28 (0.20)
Rim volume (mm^3)	0.17 (0.09)
Height variation contour (mm)	0.33 (0.12)
Mean cup depth (mm)	0.27 (0.12)
Maximum cup depth (mm)	0.62 (0.21)
Cup shape measure	−0.05 (0.12)
RNFL thickness (mm)	0.14 (0.06)
RNFL cross section area (mm^2)	0.72 (0.31)

Numbers in parentheses are standard deviations.

Scanning laser polarimeter

RNFL thickness measurement was performed with a laser diagnostics glaucoma scanning system (GDx) by well trained technicians using a 15 × 15° field of view through a $\geqslant$3 mm diameter pupil with the untested eye fixating on a fixation light attached to the GDx. Five high quality images per eye were taken in one sitting. The quality of images was assessed with the aid of the GDx software and by the experience of the technician. The three best images were used to generate an overall mean image. The mean image was clear and had a clearly definable disc margin. On the mean image, the disc margin was established with an ellipse whose parameters were adjusted by an experienced observer who was masked to the patient diagnosis and characteristics. A 10 pixel-wide elliptical band was then automatically positioned concentric with the disc margin outline and 1.75 disc diameters from the centre of the optic disc. A series of RNFL parameters for the whole area, peripapillary ellipse, and predefined sectors were calculated by the software. The default sectors were defined as

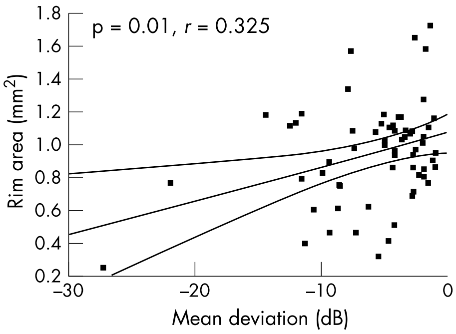

Figure 1 Scatter plot of the relation between rim area by HRT and mean deviation by HFA (linear regression with 95% confidence interval).

temporal: –25°–25°, superior: 25°–145°, nasal: 145°–215°, and inferior: 215°–335°. The "number," average thickness, ellipse average, total polar integral, maximum modulation, and ellipse modulation were regarded as global parameters. Superior (inferior) maximum, superior (inferior) ratio, as well as average, integral, and deviation from normal for four sectors were regarded as sectoral parameters.

Analysis

Correlations were evaluated by scatter plot and linear regression for a range of global and sectoral parameters with the HRT, GDx, and HFA. A statistically significant association was taken when the p value was $\leqslant 0.05$.

RESULTS

This study enrolled 62 white patients with primary open angle glaucoma. Patients' age ranged from 40 to 81 (mean 65.76 (SD 8.95)) years of age. The R/L ratio was 33/29 and the male/female ratio was 36/26. The global visual field indices, global topographic parameters by HRT, and global RNFL parameters by GDx are shown in Table 1.

The correlations between global topographic parameters by HRT and global VF indices were only found to be significant for rim area and disc area. Rim area was correlated to MD, CPSD, and the number of points with $p < 5\%$. Surprisingly, disc area was related to MD (Table 2). Figure 1 shows the scatter plot of the relation between rim area and mean deviation.

Among the sectoral topographic parameters, correlations were found between the C/D ratio, rim area, rim volume, thickness, and cross sectional area of RNFL and MD for combined superior and inferior sectors and inferior sector (Table 3). There were also correlations between rim area and height variation contour and MD for the superior sector. Although statistics showed associations between some sectoral topographic parameters and MD in nasal and temporal sectors, the scatter plots did not reveal any strong relation. The associations may have been heavily biased by one or two extreme values.

With regard to the RNFL parameters by GDx, the "number," maximum modulation, and ellipse modulation correlated with CPSD, number of points with $p < 1\%$ and 5%, and with MD (correlation coefficient ~ 0.4) (Table 4). The scatter plot of the relation between maximum modulation and mean deviation is shown in Figure 2.

Table 2 Correlation between global topographic parameters by HRT and global VF indices

	MD p value (r)	CPSD p value (r)	No of points p<1% p value (r)	No of points p<5% p value (r)
Glaucoma index	NS	NS	NS	NS
Disc area (mm²)	0.021 (0.294)	NS	NS	NS
Cup area (mm²)	NS	NS	NS	NS
C/D area ratio	NS	NS	NS	NS
Rim area (mm²)	0.01 (0.325)	0.05 (0.25)	NS	0.041 (0.26)
Cup volume (mm³)	NS	NS	NS	NS
Rim volume (mm³)	NS	NS	NS	NS
Height variation contour (mm)	NS	NS	NS	NS
Mean cup depth (mm)	NS	NS	NS	NS
Maximum cup depth (mm)	NS	NS	NS	NS
Cup shape measure	NS	NS	NS	NS
RNFL thickness (mm)	NS	NS	NS	NS
RNFL cross section area (mm²)	NS	NS	NS	NS

Statistics by linear regression.
NS = not significant, *r* = correlation coefficient.

Table 3 Correlation between sectoral topographic parameters by HRT and corresponding sectoral VF mean deviation

	Combined superior and inferior sectors p value (r)	Superior sector p value (r)	Inferior sector p value (r)	Nasal sector p value (r)	Temporal sector p value (r)
Disc area (mm²)	NS	NS	NS	0.019 (0.297)	0.01 (0.325)
Cup area (mm²)	NS	NS	NS	NS	NS
C/D area ratio	0.007 (0.242)	NS	0.05 (0.25)	NS	NS
Rim area (mm²)	0.000 (0.327)	0.021 (0.292)	0.006 (0.344)	NS	0.012 (0.317)
Cup volume (mm³)	NS	NS	NS	NS	NS
Rim volume (mm³)	0.001 (0.290)	NS	0.008 (0.335)	NS	NS
Height variation contour (mm)	NS	0.018 (0.301)	NS	NS	NS
Mean cup depth (mm)	NS	NS	NS	NS	NS
Maximum cup depth (mm)	NS	NS	NS	NS	NS
Cup shape measure	NS	NS	NS	NS	0.018 (0.3)
RNFL thickness (mm)	0.005 (0.249)	NS	0.02 (0.295)	NS	0.034 (0.27)
RNFL cross section area (mm²)	0.003 (0.267)	NS	0.02 (0.294)	NS	0.012 (0.318)

Statistics by linear regression.
NS = not significant, *r* = correlation coefficient.

Table 4 Correlation between global RNFL parameters by GDx and global VF indices

	MD p value (*r*)	CPSD p value (*r*)	No of points p<1% p value (*r*)	No of points p<5% p value (*r*)
The number	0.003 (0.366)	0.018 (0.3)	0.005 (0.354)	0.019 (0.298)
Average thickness (μm)	NS	NS	NS	NS
Ellipse average (μm)	NS	NS	NS	NS
Total polar integral (μm^2)	NS	NS	NS	NS
Maximum modulation	0.001 (0.402)	0.018 (0.299)	0.007 (0.340)	0.034 (0.269)
Ellipse modulation	0.001 (0.402)	0.033 (0.272)	0.028 (0.279)	0.034 (0.269)

Statistics by linear regression.
NS = not significant, *r* = correlation coefficient.

Table 5 Correlation between sectoral RNFL parameters by GDx and corresponding sectoral VF mean deviation

	Combined superior and inferior sectors p value (*r*)	Superior sector p value (*r*)	Inferior sector p value (*r*)	Nasal sector p value (*r*)	Temporal sector p value (*r*)
Maximum (μm)	0.008 (0.236)	NS	0.013 (0.313)	NA	NA
Average (μm)	0.03 (0.195)	NS	0.006 (0.346)	NS	NS
Integral (μm^2)	0.005 (0.253)	NS	0.003 (0.377)	NS	NS
Ratio	0.005 (0.250)	NS	0.03 (0.277)	NA	NA
Deviation from normal (μm)	0.007 (0.242)	NS	0.014 (0.311)	NS	NS

Statistics by linear regression.
NS = not significant, *r* = correlation coefficient.
NA = sectoral RNFL parameters not available.

All the sectoral RNFL parameters including maximum, average, integral, ratio and deviation from normal showed correlation with MD for combined and inferior sectors. None of these sectoral RNFL parameters demonstrated correlation with MD for other sectors (Table 5).

Unexpectedly, the RNFL parameters, including average thickness, ellipse average, and total polar integral by GDx and RNFL parameters, including thickness and cross section area by HRT, had no correlation. As for the correlation among the topographic parameters of the HRT, many optic nerve head parameters correlated with RNFL parameters. C/D area ratio, rim area, rim volume, and maximum cup depth correlated with both RNFL thickness and cross section area (correlation coefficient: 0.273–0.695). Rim volume had the highest correlation coefficient, nearly 0.7. There were also correlations between cup area and height variation contour and RNFL thickness (correlation coefficient: 0.344, 0.251) as well as disc area and RNFL cross section area (correlation coefficient: 0.299). RNFL thickness and RNFL cross section area were also correlated with a correlation coefficient of 0.965.

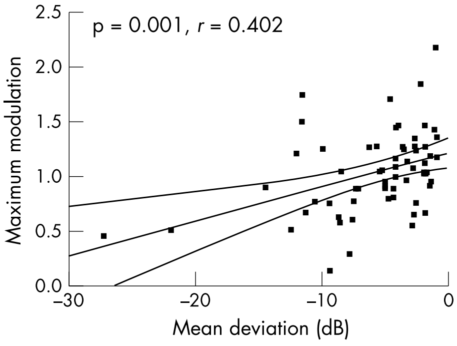

Figure 2 Scatter plot of the relation between maximum modulation by GDx and mean deviation by HFA (linear regression with 95% confidence interval).

DISCUSSION

Previous reports have described the topographic and quantitative relation between the optic nerve head, RNFL, and visual field defects. The introduction of the HRT and GDx is helpful for investigating quantitative associations. Many global or sectoral topographic parameters measured with the HRT have been found to be correlated with global or sectoral visual field indices. They included cup area, cup/disc area ratio, rim area, rim volume, cup shape measure, RNFL thickness, and RNFL cross section area. Different studies revealed different parameters as having the strongest correlation with the visual field. Most of the studies emphasised the importance of cup/disc ratio,[26] rim area,[27] cup shape measure,[27–30] RNFL thickness,[26 31–33] and RNFL cross section area.[26 30] These correlations were stronger in the group combining healthy and glaucoma subjects than in the glaucoma subjects alone.[26 27 33] In addition, the correlations were better for MD than for CPSD.[27 30] With regard to the correlations for sectors, some studies showed less association for inferior RNFL measurements and the corresponding VF,[26] but some demonstrated less association for superior RNFL measurements.[33 34] However, most of the studies agreed that the temporal sector had the poorest association.[30 31] This is explained by the temporal sector usually remaining unaffected until a late stage of the disease.

In our study, correlations between HRT parameters and VF indices were only found between rim area and MD, CPSD and the number of points for p <5% on pattern deviation probability plot. There are several reasons why this study did not find as many significant correlations as reported in previous studies. Firstly, the sample size may not have been large enough. Tole *et al*[30] found all the significant correlations disappeared when analysis was confined to the glaucoma patients with MDs of <-10 dB. They supposed it reflected the statistical effect of reducing the numbers from 106 eyes to 61 eyes. However, relations between topographic parameters and MD were found with smaller sample sizes (47) in other studies.[27] Secondly, our study only included glaucoma patients. As mentioned above, the correlations were better for combined groups owing to the larger range of values. Thirdly, the visual field defects in our study were less severe compared with other studies. Mean MD in our study was −5.77 (SD 4.91) dB. Only two (3.2%) patients had an MD worse than −20 dB. In other studies, the mean MD ranged from −6.38 to −10.12 dB[26 27 30 32] with a higher percentage of glaucoma patients with the MD worse than −20 dB (11.5%,[26] 7.5%[30]). The mean CPSD in our study was 6.21 (SD 3.29) dB with 83.9% of them having a CPSD of <10 dB. The mean CPSD for other studies ranged from 5.16 to 9.16 dB[27 32] with a higher percentage of glaucoma patients with CPSD >10 dB (28.3%[30]). From the scatter plots, we noticed that advanced glaucoma cases had a large influence on the relation between topographic parameters and VF indices. Since our study included less advanced glaucoma cases, it could be expected that it would not reveal such high associations. This finding is supported by the research of Teesalu *et al*.[29 34] Their scatter plots also demonstrated that the advanced glaucoma patients played an important part in establishing an association. When the advanced glaucoma patients, with an MD worse than −10 dB, were excluded from the data set, the associations were considerably weakened. Fourthly, from our scatter plots, for a specific VF index, the value of the corresponding topographic parameters had a large range. The large intersubject variability weakens any relation between topographic parameters and VF indices. Based on the 95th percentile of the standardised rim/disc area ratio, Bartz-Schmidt *et al*[35] calculated the relative rim area loss and correlated this with the visual field index MD. The scatter plot showed an exponential change with 40% of the neuroretinal rim area lost before the appearance of the first VF defect. Half of the neuroretinal tissue had been lost when a 6 dB decrease in the MD occurred. In the early stage of glaucoma, a small change in MD was accompanied by a large amount of rim loss. While in the later stages of glaucoma, a large change in MD was only accompanied by a small amount of change in rim loss. Their scatter plot also demonstrated great interindividual variation among glaucoma patients. The variation was greater for early glaucoma than for advanced glaucoma. For MD between 0 to −6 dB, the relative rim loss can range from 0% to 70%. On the other hand, for MD between −6 dB and−12 dB, the relative rim loss only ranged from 40% to 80%. Hence, greater interindividual variation in early glaucoma further hampered the relation, especially when most of the subjects had only mild VF loss.

The quantitative relation between RNFL and established VF defects can also be analysed with the GDx. Global RNFL parameters, including the "number," average thickness, ellipse average, total polar integral, maximum modulation, and ellipse modulation have all been reported to correlate with the MD for populations including normal and glaucoma subjects. The sectoral parameters, such as superior and inferior average thickness, superior/temporal and inferior/temporal ratios, and the deviation from normal for superior and inferior sectors, have also been found to correlate with MD.[36] The "number," maximum modulation, and ellipse modulation have also been found to be correlated with CPSD. But the correlation coefficients were not as high as that for MD. However, when analysing a population of glaucoma patients, correlations were only found between the "number" and mean deviation and between maximum modulation and mean deviation.[37] Generally speaking, the "number," maximum modulation, and ellipse modulation had a better relation with MD and CPSD than other RNFL parameters.

In this study, we found that the "number," maximum modulation, and ellipse modulation correlated well with the global visual field indices, including MD, CPSD, and the number of points missed on pattern deviation probability plot at the 5% and 1% levels. The importance of modulation parameters was emphasised by the study in which modulation parameters correlated more strongly with MD than summed or ratio based parameters. However, no strong correlation was found between any parameter and PSD.[38] Our scatter plots demonstrated that the advanced cases have greater influence on the relation between RNFL parameters and visual field indices. Moreover, for a specific value of VF index, there was a larger degree of variability in the RNFL parameters. Thus it is very difficult to accurately predict RNFL measurements or VF from each other. The study of Kwon *et al*[39] also mentioned this problem. The VF mean sensitivity and deviation showed a bilinear correlation with peripapillary nerve fibre layer thickness. This bilinear correlation made the accurate predictions of one from the other difficult and made it difficult to establish a critical RNFL thickness. A normal VF can be associated with a wide range of RNFL thicknesses. When the RNFL thickness was greater than 70 μm, the VF mean sensitivity was nearly normal and changed little. When RNFL thickness was below this level, it was associated with a rapid decrease in the VF sensitivity. The precise correlation between VF and GDx was further hampered by a large individual variability around the bilinear fit.

For both HRT and GDx, the relations were better and more parameters were found to have correlation with VF indices for sectors than for the whole area. A certain amount of ONH or RNFL damage must occur before the global parameters showed significant changes. Thus, interpretation of the global parameters may overlook focal damage of ONH or RNFL. This may be the reason why sectoral parameters and sectoral VF indices had a better association than the global parameters and global VF indices.

It is hard to explain why the relations between the RNFL parameters, by either HRT or GDx, and VF were better in the inferior hemiretina than in the superior hemiretina. One explanation for this may be related to different amounts of damage in the inferior and superior hemiretinas. The inferior sector is usually the first to be damaged,[40] and in our study there were more cases with advanced VF damage in the superior field. Nevertheless, we did not find significant differences between the MD of superior and inferior hemifields although there were significant differences for the RNFL parameters. Surprisingly, different results were obtained from these two instruments. HRT revealed that the RNFL thickness was greater in the superior sector while the GDx found that the RNFL thickness was greater in the inferior sector. Furthermore, no correlation was found between GDx and HRT in RNFL parameters. The discrepancy and lack of any relation between these two instruments may derive from different principles of RNFL measurements. The HRT does not measure the RNFL directly, rather it measures the distance between a defined reference plane and the vitreal surface of the retina. Thus, the RNFL thickness reflects not only the RNFL, but also the supporting glial tissue including astrocytes and Müller cell axons. In contrast, the GDx is independent of a reference plane or magnification.

The correlation between structural damage and functional damage depends on two aspects. From a statistical point of view, the sample size and the characteristics of subjects have a great influence on the result. Larger sample sizes and a larger range of values all contribute to a better correlation. Thus, different studies may get different results because of different sample sizes and different inclusion criteria. From a clinical aspect, the large interindividual variation is the main reason for the poor correlation. It prevents us from predicting accurately the structural damage and functional damage. In an unselected clinical population, the interindividual variation will be even greater than the study results. The larger variation in early glaucoma than advanced glaucoma makes the prediction even more difficult during the early stages of the disease. Moreover, the temporal lag between changes in structure and function may also hamper the prediction. However, a reliable structural or functional estimate is very important clinically, especially for early glaucoma, because it will influence our decision about diagnosis and treatment. In this study, the associations were better between the GDx results and the visual field than between the HRT results and the visual field. GDx has modulation parameters that correct for individual variation by using the patient's own temporal and nasal RNFL thickness as a baseline, which may account for the better correlation. Another reason may be that the RNFL is responsible for the visual function, while the optic nerve head changes such as cup enlargement and deepening are the consequence of RNFL loss.

There are two explanations for the large individual variation in the relations between topographic and RNFL parameters and visual field indices. One is the large variation of these parameters within the normal population. The other is individual differences in the amount of RNFL damage necessary for visual field loss to occur. The study of Bartz-Schmidt *et al*[35] revealed that the amount of rim area loss for certain degree of visual field loss is different for each individual. Evaluating the correlation between ONH or RNFL changes and visual field changes by longitudinal study, instead of looking at the cross sectional data, could, therefore, be of value. Longitudinal analysis is also a good method of removing the influence of the individual variations. Poinoosawmy *et al*[41] investigated longitudinal RNFL thickness change in patients with normal tension glaucoma. Patients with initially better visual fields had a greater reduction in RNFL thickness than did those with initially more advanced visual field defect. Significant correlations between change in RNFL thickness and change in MD over the same period were found.

The HRT and GDx instruments provide quantitative measurements of ONH and RNFL suitable for accurate comparison and the monitoring of change.[42] The examination procedures are simple and fast with fewer restrictions with regard to pupil size and cataract status than standard fundus imaging. However, global or sectoral measurements might overlook focal damage. Since focal damage of ONH or RNFL is a very important and specific sign of glaucoma, we need better parameters to reveal focal damage. The ranked segment distribution (RSD) curve technique[43] in HRT was designed for this purpose. Although the GDx does not have this kind of analysis, it does compare the patient's data with an ethnic specific normal database. The ratio and modulation parameters of the GDx corrected for individual variation have been found to be more suitable for discriminating normal from abnormal.[21 38]

Some important information about the configuration of optic nerve head, such as rim pallor, ISNT rule of rim width, vertical elongation of cup, disc haemorrhage, as well as alterations of lamina cribrosa and vessels, are difficult to obtain from the HRT measurements. Therefore, professional judgments, considering different aspects of information, are essential. Nevertheless, the quantitative measurements from HRT and GDx can assist the clinical judgment for early diagnosis and detection of progression. It is especially helpful for detecting diffuse RNFL damage.

The visual field test depends upon the patient's responses and is more time consuming than HRT and GDx examinations. It would, therefore, be convenient if we could predict visual function from the ONH and RNFL morphology. Unfortunately, the correlation between structure and visual function is not good enough. More appropriate parameters are required to overcome the problem of individual variation. Furthermore, longitudinal studies that establish the value of HRT and GDx in detecting progression, and the correlation between structural changes and functional changes are essential for early diagnosis. At present, visual field examination can't be replaced by imaging of the optic nerve head. Structural information provided by HRT and GDx and functional information provided by VF are both important and are complementary to each other. To obtain a full characterisation of glaucomatous damage, both structural and functional measurements are necessary and should be considered for clinical judgment and treatment.

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