Relationships between Standard Automated Perimetry, HRT Confocal Scanning Laser Ophthalmoscopy, and GDX VCC Scanning Laser Polarimetry

Nicolaas J. Reus and Hans G. Lemij

PURPOSE. This study was designed to determine and compare the relationships between visual function measured with standard automated perimetry (SAP) and structure, either as neuroretinal rim area measured with confocal scanning laser ophthalmoscopy (CSLO), or as retinal nerve fiber layer thickness determined by scanning laser polarimetry with variable corneal compensation (SLP-VCC).

METHODS. Forty-six healthy subjects and 76 glaucoma patients were examined with SAP, with CSLO by means of the commercially available Heidelberg Retina Tomograph I (HRT), and with SLP-VCC by means of the commercially available GDX VCC. The relationships between SAP, expressed either in the typically used decibel scale or as number of abnormal points in the total deviation probability plot, and CSLO and between SAP and SLP-VCC were described with linear and logarithmic regression analysis for global data and six individual sectors. The relationship between measurements with CSLO and SLP-VCC was fit with linear regression analysis.

RESULTS. The relationships between SAP and CSLO and between SAP and SLP-VCC appeared curvilinear for all sectors except the temporal one between SAP and SLP-VCC. For CSLO, a logarithmic fit was significantly better than a linear one for the global data and in the superotemporal and inferonasal sectors. For SLP-VCC, a curvilinear fit was better for the global data and in the superotemporal, supranasal, and inferonasal sectors. CSLO data correlated linearly with SLP-VCC data in all sectors, except temporally.

CONCLUSIONS. CSLO and SLP-VCC showed a very similar curvilinear relationship with SAP. The observed curvilinear relationships confirm earlier reports that these imaging devices appear to detect glaucomatous loss earlier than SAP. (Invest Ophthalmol Vis Sci. 2005;46:4182–4188) DOI:10.1167/iovs.04-1029

Glaucoma is a progressive optic neuropathy with loss of retinal ganglion cells (RGCs) and their axons, leading to loss of vision. In clinical practice, functional losses are often assessed with standard automated perimetry (SAP). Structural losses may be assessed in a qualitative or semiquantitative way with direct or indirect ophthalmoscopy, stereoscopic optic disc photography, and red-free fundus photography. A more quantitative and objective analysis of structural losses may be performed with confocal scanning laser ophthalmoscopy (CSLO) and scanning laser polarimetry with variable corneal compensation (SLP-VCC).

CSLO, featured in the commercially available Heidelberg Retina Tomograph (HRT; Heidelberg Engineering GmbH, Dossenheim, Germany), assesses the topography of the optic disc. It measures the intensity of light reflected off the retinal surface at subsequent depths of focus. The weighted peak reflectance is thought to represent the interface between the retinal surface and the vitreous. The measured depths of peak reflectance at various points in the optic disc are used to construct a topography map of the optic disc (e.g., Fig. 1, middle panel).

SLP-VCC, featured in the commercially available GDX VCC (Carl Zeiss Meditec AG, Jena, Germany), estimates the thickness of the peripapillary retinal nerve fiber layer (RNFL) by measuring the summed retardation of a polarized scanning laser beam, presumably induced by the form-birefringent microtubules that support the RGC axons. The amount of retardation is proportional to the thickness of the RNFL and is therefore usually expressed in micrometers of thickness. Retardation measurements at various points around the optic disc are used to construct a thickness map of the RNFL (e.g., Fig. 1, right panel). Equipped with VCC, SLP measurements have been shown to accurately assess RNFL morphology.

Recently, we found a curvilinear relationship between function by SAP and structure by SLP-VCC in a large cohort of healthy subjects and glaucoma patients, when function was expressed in the standard, logarithmic, decibel scale. When expressed in an unlogged scale, SAP measurements correlated linearly with SLP-VCC measurements. In the present study, we investigated the relationship between function by SAP and structure by CSLO and compared it to the relationship between SAP and SLP-VCC in a single population of healthy subjects and glaucoma patients. In addition, we compared measurements of neuroretinal rim area by CSLO with measurements of RNFL thickness by SLP-VCC.

METHODS

Forty-six healthy subjects (46 eyes) and 76 patients with glaucoma (76 eyes) were recruited prospectively for the present study. The research adhered to the tenets of the Declaration of Helsinki. The institutional human experimentation committee approved the research. Informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study.

Healthy Subjects

Healthy subjects of white ethnic origin were recruited either consecutively from an ongoing longitudinal follow-up study (n = 28) or from employees of The Rotterdam Eye Hospital and their spouses and friends (n = 18). All healthy subjects had a glaucoma hemifield test within normal limits and no nerve fiber bundle abnormalities, as described by Keltner et al., in the total and/or pattern deviation probability plots with SAP. In addition, they had healthy-looking optic discs, IOP ≤ 21 mm Hg in both eyes, and open angles on gonioscopy.

From the Glaucoma Service, The Rotterdam Eye Hospital, Rotterdam, The Netherlands.


Supported by The Rotterdam Eye Hospital Research Foundation, Rotterdam, The Netherlands; and Stichting Glaucoma Fonds, Leiden, The Netherlands.

Submitted for publication August 27, 2004; revised December 8, 2004, and June 15, 2005; accepted September 13, 2005.

Disclosures: N.J. Reus, Laser Diagnostic Technologies, Inc. (F); H.G. Lemij, Laser Diagnostic Technologies, Inc. (F, C).

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be marked ‘advertisement’ in accordance with 18 U.S.C. §1734 solely to indicate this fact.

Corresponding author: Nicolaas J. Reus, The Rotterdam Eye Hospital, PO Box 70030, NL-3000 LM Rotterdam, The Netherlands; reus@eyehospital.nl.


Copyright © Association for Research in Vision and Ophthalmology

Downloaded From: https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933437/ on 07/15/2018
Slit-lamp examination was unremarkable in all eyes. All subjects had a best-corrected visual acuity of 20/40 or better. None had any significant history of ocular disease, a history of intraocular surgery (except uncomplicated cataract surgery), relatives in the first and/or second degree with glaucoma, systemic hypertension for which medication was used, diabetes mellitus, or any other systemic disease. One eye was randomly selected for analysis.

**Glaucoma Patients**

Glaucoma patients of white ethnic origin were recruited consecutively from an ongoing longitudinal follow-up study ($n = 75$) or after referral by a glaucoma specialist (HGL) for clinical reasons ($n = 1$). All patients had a glaucomatosus appearance of the optic disc (with notching or thinning of the neuroretinal rim), a corresponding nerve fiber bundle visual field defect, as described by Keltner et al., with SAP, and open angles by gonioscopy. Slit-lamp examination was unremarkable in all eyes. All patients had a best-corrected visual acuity of 20/40 or better. None had any significant history of ocular disease other than glaucoma, a history of intraocular surgery (except any uncomplicated cataract or glaucoma surgery), systemic hypertension for which medication was used, diabetes mellitus, or any other systemic disease. One eye was randomly selected if both were eligible.

**Demographics**

The mean age ($\pm$ SD) of the healthy subjects and the patients with glaucoma was $60 \pm 12$ and $62 \pm 10$ years, respectively, which did not differ significantly ($t$-test, $P = 0.39$). The disc area ($\pm$ SD), derived from the HRT data, was $1.95 \pm 0.35 \text{ mm}^2$ in the healthy subjects and $2.00 \pm 0.41 \text{ mm}^2$ in the glaucoma patients, which did not differ significantly ($t$-test, $P = 0.47$).

In the healthy group, 23 (50%) of the 46 subjects were men. Of the glaucoma patients, 46 (60%) of the 76 were men. Twenty-five (54%) of the 46 randomly selected eyes in the healthy subjects were right eyes; in the glaucoma group, 37 (49%) of the 76 eyes were right eyes.

The mean deviation ($\pm$ SD; range) of the visual field was $0.38 \pm 0.09$ dB ($-1.55$ to $2.75$) in the healthy group and $-9.52 \pm 8.43$ dB ($-30.39$ to $-1.25$) in the glaucoma group. The pattern standard deviation ($\pm$ SD; range) of the visual field was $1.63 \pm 0.26$ dB (1.13 to 2.30) in the healthy eyes and $8.55 \pm 4.32$ dB (1.99 to 15.92) in the glaucomatosus eyes.

The mean period ($\pm$ SD; range) of the visual field was $3.41 \pm 0.26$ months in healthy subjects and $0 \pm 1$ month in glaucoma patients.

**Visual Field Testing**

Visual field testing was performed with a commercially available analyzer (Humphrey Field Analyzer II [HFA]; Carl Zeiss Meditec AG, Jena, Germany) by means of the 24-2 Full-Threshold (FT) or Swedish Interactive Threshold Algorithm (SITA)-Standard test program. Twenty-nine (65%) of the 46 healthy subjects and 73 (96%) of the 76 glaucoma patients were tested with the FT paradigm. Visual fields had to be reproducible as well as reliable. Reliability criteria applied were as follows: fixation losses < 25%; and false-positive and false-negative response rates $\leq 20\%$ for the FT test paradigm and $\leq 7\%$ for the SITA-Standard test program. In glaucomatosus eyes with advanced field loss, higher false-negative response rates were accepted: up to $33\%$ for the FT paradigm and up to $12\%$ for the SITA-Standard paradigm. The two visual field test points nearest to the blind spot were excluded from analysis. The 52 remaining test points were grouped into 6 sectors based on the relationship between visual field test points and regions of the optic disc, as described by Garway-Heath et al. (Fig. 1). For each sector, the arithmetic mean differential light sensitivity (DLS) was calculated. DLS was expressed in the typically used decibel scale ($\text{DLS} = 10 \cdot \log_{10} \frac{L_{\text{max}}}{L_{\text{st}}}$, where $L_{\text{max}}$ is the perimeter’s maximum stimulus luminance, $L_{\text{st}}$ is the stimulus luminance at threshold, and $L_{\text{st}}$ is background luminance). For the HFA, $L_{\text{st}} = 31.6$ apostilb (ash) and $L_{\text{max}} = 10,000$ asb. Because various large clinical trials, such as the Collaborative Initial Glaucoma Treatment Study (CIGTS) and the Early Manifest Glaucoma Trial, analyze probability plots instead of raw DLS values for evaluating progression of visual field loss, we also calculated a weighted score of the number of abnormal points in the total deviation probability plot with a sensitivity below the fifth percentile for each sector. To this end, we awarded points with a sensitivity at $P < 0.05$ a score of 1, points at $P < 0.02$ a score of 2, points at $P < 0.01$ a score of 3, and points at $P < 0.005$ a score of 4. We then calculated the sum of scores of all points within a sector. For example, the superotemporal sector with 14 test points could have a minimum score of 0 and a maximum score of 56 (i.e., $4 \times 14$).

**CSLO Measurements**

CSLO measurements were performed with the HRT by three trained and experienced operators. Pupils of subjects were undilated and the room lights were left on. Before each measurement, the subject’s corneal curvature radius was entered into the software. The patient’s face was then gently placed onto the head-and-chin rest of the HRT, and imaging was performed at the 1.5-cm imaging head-eye distance recommended in the instruction manual, as the subject viewed a distant fixation target. Three high-quality images at a $15^\circ \times 15^\circ$ scanning angle were recorded for each subject. The quality of the images was judged by the technician with the aid of the HRT software. All images were of high quality, i.e., with a centered optic disc, with a clear light-dark-light pattern over the 52 consecutive images, even and just illuminated throughout the individual images, and without any motion artifacts. A mean topography image, computed from the three scans, was used for subsequent analysis with the HRT software (version 1.4.0.0). Mean images with a mean SD of the height measurements $>50$ $\mu$m were excluded from analysis. The optic disc margin was manually marked at the inner edge of Eslching’s ring by one of the authors (NJH). When in doubt about the position of the optic disc margin, stereoscopic optic disc photographs were examined to assist accurate positioning. The standard reference plane was used for calculations of optic disc topography, with the relative and tilted coordinate system turned on. The software calculated the rim area ($\text{mm}^2$) for the whole disc (global) and for six individual sectors: superotemporal (ST; extending from 45°–90°, relative to the temporal meridian), supranasal (SN; 90°–135°), nasal (N; 135°–225°), inferonasal (IN; 225°–270°), inferotemporal (IT; 270°–315°), and temporal (T; 315°–45°).
SLP Measurements

SLP measurements were performed with the GDx VCC by three trained and experienced technicians. Pupils of subjects were undilated and the room lights were left on. The spherical equivalent refractive error of each eye was entered into the software to allow the GDx VCC to focus on the retina. If necessary, the focus was adjusted manually in 0.25-diopter steps. The patient’s face was gently placed into the face mask of the GDx VCC. To maintain the same orientation of the slow axes of the birefringent structures in the eye to that of the instrument’s compensator, the operator saw to it that the patient’s head was as vertical as possible during all measurements. For each scan, the operator aligned the instrument with the cornea and the sclera of the measured eye. Anterior segment birefringence was assessed\(^1\) for each eye individually, after which the eye was scanned with individualized compensation, as has been described previously.\(^8\) The quality of each scanned image was judged by the technician with the aid of the GDx VCC software (version 5.4). All images were of high quality, i.e.,, with a centered optic disc, well-focused, even and just illuminated throughout the image, and without any motion artifacts. The margin of the optic disc was manually marked with an ellipse on a reflection image of the fundus. The GDx VCC software positioned a circle, 8 pixels wide (~0.4 mm in an emmetropic eye) and with an inner diameter of 54 pixels (~2.5 mm in an emmetropic eye), centered on the center of the ellipse. The instrument processed the retardation values within this band to give 256 values evenly distributed along the circle, after which they were grouped into 64 sectors and exported by the software. These values were subsequently grouped into six sectors with the same dimensions and orientation as for the HRT data (Fig. 1).

Data Analysis

To determine any correlation between function and structure, the degree of association between SAP (expressed as DLS and as abnormal number of points) and CSLO measurements and SAP (expressed as DLS and as abnormal number of points) and SLP-VCC measurements was determined with Spearman’s rank correlation coefficient (\(r_s\)) for the global data and for each sector individually.

Then, the relationship between SAP and CSLO measurements and SAP and SLPVCC measurements was described with a least-squares linear (\(y = a + b \cdot x\)) and logarithmic (\(y = a + b \cdot \log_{10} x\)) regression analysis. We determined this relationship for the healthy subjects who were tested with either the SITA or FT paradigm (\(n = 46\)) and the glaucoma patients who were tested with the FT paradigm (\(n = 73\)). In addition, we investigated the relationships in two other groups separately: healthy subjects (\(n = 28\); 1 subject was excluded for age-matching) and glaucoma patients (\(n = 66\); 7 subjects were excluded for age-matching) who were tested with the FT paradigm, and glaucoma patients who were tested with the FT paradigm (\(n = 73\)).

For comparison with a recent study by Schlottmann et al.,\(^15\) we used a paired \(t\)-test to evaluate the null hypothesis that the absolute prediction errors (absolute values of the residuals) had the same mean for both models (logarithmic and linear regression). Significance was assumed at \(P < 0.05\). For comparison, we plotted neuroretinal rim area measured with CSLO against RNFL thickness measured with SLP-VCC for the global data and also for the individual sectors and described their relationship with linear regression analysis.

RESULTS

The relationships between SAP and CSLO measurements and between SAP and SLPVCC measurements are graphically presented in Figure 2. SAP measurements, expressed either as DLS

---

**FIGURE 2.** Scatterplots of DLS, expressed in the standard decibel scale, against CSLO measurements (left panels) and against SLP-VCC measurements (right panels) for global data and 6 individual sectors. ● Healthy eyes tested with the FT paradigm; ○ healthy eyes tested with the SITA paradigm; ■ glaucomatous eyes tested with the FT paradigm; □ glaucomatous eyes tested with the SITA paradigm.

---
or as abnormal number of points, were significantly correlated with both CSLO and SLP-VCC measurements for the global data as well as for most individual sectors (Fig. 2, Tables 1 and 2). In the temporal sector, however, SAP measurements were not significantly correlated with SLP-VCC measurements \( (r_s = 0.003, P = 0.98) \) and \( r_s = 0.03, P = 0.74 \), for SAP expressed as DLS and abnormal number of points, respectively) (Fig. 2, Tables 1 and 2).

The significant relationships between function and structure were curvilinear in appearance (Fig. 2). Healthy eyes had high DLS values with large rim areas and high retardation values. However, glaucomatous eyes had lower DLS values with smaller rim areas and lower retardation values. However, there was considerable overlap in measurements between the groups.

With regard to the relationships between SAP and CSLO data with both healthy subjects and glaucoma patients included, logarithmic regression analysis yielded higher coefficients of determination \( (R^2) \) than linear regression analysis both for the pooled data and for the ST, SN, and IT sectors (Table 3). For the other sectors, logarithmic regression analysis was not significantly different from linear regression analysis (Table 3). When only healthy subjects and patients with glaucoma who were tested with the FT paradigm were analyzed, logarithmic regression analysis yielded significantly higher \( R^2 \) values than linear regression analysis for the pooled data and for the ST sector (Table 3). When only the glaucoma patients tested with the FT paradigm were analyzed, logarithmic regression analysis appeared to yield higher \( R^2 \) values than linear regression analysis for the global data as well as for most sectors (Table 3). However, this difference was significant only for the ST sector (Table 3).

In the comparisons between SAP and SLP-VCC data with both healthy subjects and glaucoma patients included, we found significantly higher \( R^2 \) values with logarithmic regression analysis than with linear regression analysis for the global data and in the ST, SN, and IN sectors (Table 4). When only healthy subjects and patients with glaucoma who were tested with the FT paradigm were included, logarithmic regression analysis yielded significantly higher \( R^2 \) values than linear regression analysis for the ST and SN sectors (Table 4). When only glaucoma patients tested with the FT paradigm were included, logarithmic regression analysis appeared to yield higher \( R^2 \) values than linear regression analysis for the global data as well as for the individual sectors (Table 4). However, this difference was significant only for the ST and SN sectors (Table 4).

The relationships between SAP and CSLO and between SAP and SLP-VCC appeared very similar (Fig. 2, left and right panels, respectively). Moreover, logarithmic regression analysis of the relationships between SAP and CSLO measurements and between SAP and SLP-VCC measurements did not yield significantly different fits (\( P \)-values for global data and the ST, SN, N, IN, IT, and T sectors: 0.20, 0.64, 0.26, 0.73, 0.31, 0.09, and 0.15, respectively).

With regard to healthy subjects, at the higher end of the DLS values in Figure 2, visual function data obtained with the SITA paradigm appeared to be consistently higher than data obtained with the FT paradigm (Fig. 2). Statistically, DLS values obtained with SITA were significantly higher than DLS values obtained with FT for the pooled data and for the sectors ST, SN, N, IN, and IT (\( P \)-values 0.003, < 0.001, 0.011, 0.004, 0.034, and 0.011, respectively). For the T sector, this difference was not significant (\( P = 0.11 \)).

The CSLO data correlated well with the SLP-VCC data, both for the pooled (global) data (Table 5, Fig. 3) and for the individual sectors (Table 5).

### Table 1. Association between SAP DLS and CSLO or SLP-VCC*

<table>
<thead>
<tr>
<th>Sector</th>
<th>( r_s )</th>
<th>( P )</th>
<th>( r_s )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>0.70</td>
<td>&lt;0.001</td>
<td>0.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST</td>
<td>0.75</td>
<td>&lt;0.001</td>
<td>0.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SN</td>
<td>0.56</td>
<td>&lt;0.001</td>
<td>0.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>N</td>
<td>0.44</td>
<td>&lt;0.001</td>
<td>0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IN</td>
<td>0.64</td>
<td>&lt;0.001</td>
<td>0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IT</td>
<td>0.67</td>
<td>&lt;0.001</td>
<td>0.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T</td>
<td>0.50</td>
<td>&lt;0.001</td>
<td>0.03</td>
<td>0.78</td>
</tr>
</tbody>
</table>

*Values are Spearman’s rank correlations of data for patients with glaucoma (\( n = 75 \)) and healthy subjects (\( n = 46 \)).

### Table 2. Association between SAP Abnormal Number of Points in the Total Deviation Probability Plot and CSLO or SLP-VCC*

<table>
<thead>
<tr>
<th>Sector</th>
<th>( r_s )</th>
<th>( P )</th>
<th>( r_s )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>0.74</td>
<td>&lt;0.001</td>
<td>0.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST</td>
<td>0.71</td>
<td>&lt;0.001</td>
<td>0.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SN</td>
<td>0.53</td>
<td>&lt;0.001</td>
<td>0.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>N</td>
<td>0.42</td>
<td>&lt;0.001</td>
<td>0.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IN</td>
<td>0.59</td>
<td>&lt;0.001</td>
<td>0.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IT</td>
<td>0.68</td>
<td>&lt;0.001</td>
<td>0.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T</td>
<td>0.56</td>
<td>&lt;0.001</td>
<td>0.05</td>
<td>0.59</td>
</tr>
</tbody>
</table>

*Values are Spearman’s rank correlations of data for patients with glaucoma (\( n = 75 \)) and healthy subjects (\( n = 46 \)).

### Discussion

We showed in the present study that measurements of neuroretinal rim area assessed with CSLO correlate well with measurements of function by SAP. Their relationship was very similar to the relationship between SAP and measurements of RNFL thickness with SLP-VCC. In addition, we found for both techniques that the relationship between function and structure was curvilinear when function was expressed in the clinically used decibel scale. These findings compare well with other studies on the relationship between perimetry and measurements of neuroretinal rim area by CSLO\(^{16,17} \) and RNFL thickness by SLP-VCC.\(^{5,15} \) Furthermore, we found that neuroretinal rim area measured with CSLO correlates linearly with RNFL thickness measured with SLP-VCC.

In clinical practice, differential light sensitivity is expressed in a decibel scale. In this scale, higher values are relatively compressed, as lower values are stretched. As a result, functional damage at higher sensitivities will appear relatively small, whereas progressive damage at lower sensitivities will appear relatively large. In eyes with no or only mild to moderate glaucomatous functional loss, clinically relevant changes in neuroretinal rim area and RNFL thickness, which are expressed in a linear scale, might then occur with only small changes in retinal light sensitivity (e.g., see Fig. 2). This suggests that a small neuroretinal rim area or a thin RNFL may be detected in eyes with normal visual fields by SAP. In fact, we have recently reported that perimetrical unaffected eyes of glaucoma patients with unilateral field loss on average have a thinner RNFL with smaller rim areas than the other and smaller areas and lower retardation values. However, there was considerable overlap in measurements between the groups.

With regard to healthy subjects, at the higher end of the DLS values in Figure 2, visual function data obtained with the SITA paradigm appeared to be consistently higher than data obtained with the FT paradigm (Fig. 2). Statistically, DLS values obtained with SITA were significantly higher than DLS values obtained with FT for the pooled data and for the sectors ST, SN, N, IN, and IT (\( P \)-values 0.003, < 0.001, 0.011, 0.004, 0.034, and 0.011, respectively). For the T sector, this difference was not significant (\( P = 0.11 \)).
For the HRT, Wollstein et al.\textsuperscript{20} have found that thinning of the neuroretinal rim may occur in perimetrically unaffected eyes of unilateral normal-pressure glaucoma patients with visual field loss in the other eye. For all three techniques, follow-up of these patients with so-called preperimetric glaucoma is indicated to determine whether these eyes will indeed develop glaucomatous visual field loss with SAP. We would like to stress that these results do not indicate that structural losses occur before functional losses per se. In theory, changes in RGC function might even precede structural changes. However, current techniques for assessing structure, such as SLP-VCC and CSLO, appear to be more sensitive for detecting glaucomatous damage than the routinely used SAP. Whether other psychophysical tests, such as frequency-doubling technology and short-wavelength automated perimetry, may detect functional changes at an earlier stage needs to be explored.

At the other end of the spectrum, SAP may be more sensitive in detecting changes in patients with severe glaucomatous functional loss, as functional changes in this part of the decibel scale are maximized. However, the reproducibility of measurements with SAP has been shown to be fairly poor,\textsuperscript{21,22} which may limit its sensitivity for detecting more subtle changes. The reproducibility of the HRT\textsuperscript{23,24} as well as of the GDx VCC (Bagga H, et al. \textit{IOVS} 2004;45:ARVO E-Abstract 5503) appears to be reasonably good over short periods of time. In the long term, however, the reproducibility of the HRT was reported to be only slightly better than that of SAP by means of the Octopus perimeter.\textsuperscript{25} In addition, the dynamic range in these eyes with severe glaucomatous loss is smaller for measurements with CSLO and SLP-VCC than with SAP (e.g., see Fig. 2), which may limit the number of significant changes that can be detected with CSLO and SLP-VCC. Therefore, whether the HRT and GDx VCC may be better able to detect subtle changes than SAP in these eyes remains to be investigated.

We showed in the present study that the relationship between SAP and either CSLO or SLP-VCC was very similar when SAP was expressed as either DLS (dB) or as the number of abnormal points in the total deviation probability plot. These data suggest that analyses for detecting progressive visual field loss based on changes in probability plots, such as used in CIGTS, may yield similar results as analyses based on raw DLS values. However, a limitation of using the number of abnormal points analysis may be that when a point has reached a sensitivity below $P < 0.005$, the depth of the defect is not reflected in this parameter anymore, and data will be censored. Therefore, further research is needed to evaluate these two expressions of visual function in detecting progressive visual field loss in long-term follow-up studies.

Looking at the data of healthy subjects and patients with glaucoma in Figure 2, a curvilinear relationship between function and structure is apparent in most sectors. This was also true when the relationship between function and structure was analyzed in patients with glaucoma only, indicated by the higher $R^2$ values found with logarithmic regression analysis.
We did not find a significant relationship between SAP and SLP-VCC in the temporal sector, which is similar to our previous findings. Conversely, a curvilinear relationship was apparent between SAP and CSLO. In the temporal sector, SLP-VCC measured low amounts of retardation in comparison to the amount of retardation measured in other sectors. This may have yielded a low signal-to-noise ratio that possibly obscured a correlation. In addition, the form-birefringence of the axons in this sector may have been different from that in other sectors (Huang X, et al. IOVS 2003;44:ARVO E-Abstract 363), with a different relationship between the amount of retardation and thickness of the RNFL and a different relationship with SAP.

In conclusion, we showed in the present study that measurements of neuroretinal rim area using CSLO compare well with measurements of RNFL thickness using SLP-VCC. In addition, measurements with these two distinct techniques relate moderately well with RGC function assessed using standard automated perimetry. We think that the curvilinearity of the relationship between function and structure is mainly due to the standard decibel scale in SAP. This scale will probably lead to underestimating early glaucomatous damage by SAP. SLP-VCC and CSLO may better reflect this early damage. In more advanced glaucoma, the standard decibel scale in SAP is likely to overestimate progressive damage. Again, structural assessment with these imaging techniques may then better reflect any truly progressive damage.

The implications of the present findings for clinical glaucoma management, as well as the limitations of the imaging devices, need to be further explored. Furthermore, comparisons between functional measurements with psychophysical tests other than SAP and structural measurements with CSLO and SLP-VCC may be of interest to further explore the relationship between function and structure.
References


