The Relationship between Standard Automated Perimetry and GDx VCC Measurements

Nicolaas J. Reus and Hans G. Lemij

PURPOSE. To investigate the relationship between retinal light sensitivity measured with standard automated perimetry (SAP) and retardation of the peripapillary retinal nerve fiber layer (RNFL) measured with the GDx VCC (Laser Diagnostic Technologies, Inc., San Diego, CA).

METHODS. Forty-seven healthy subjects and 101 patients with glaucoma were examined with SAP and with the commercially available scanning laser polarimeter GDx VCC, with automated individualized compensation of anterior segment birefringence. Individual visual field test points and peripapillary RNFL retardation measurements were grouped into six corresponding sectors. The correlation between perimetry and GDx VCC measurements was determined, and the relationship between RNFL retardation and perimetry, expressed both in the standard decibel scale and in an unlogged scale, was described with linear regression analysis.

RESULTS. A statistically significant correlation was found in most sectors between perimetry and GDx VCC measurements in patients with glaucoma, but not in healthy subjects. A linear relationship was found between the unlogged sensitivities and GDx VCC measurements for the superotemporal and inferotemporal sectors. In the decibel scale, this relationship was curvilinear.

CONCLUSIONS. GDx VCC measurements of the peripapillary RNFL relate well with functional loss in glaucoma. Based on the observed relationships between function and structure, patients with mild to moderate visual field loss in glaucoma may be better monitored with the GDx VCC and patients who have severe loss, with SAP. (Invest Ophthalmol Vis Sci. 2004;45: 840–845) DOI:10.1167/iovs.03-0646

Glaucoma is an optic neuropathy with loss of retinal ganglion cells (RGCs) and their axons.1–3 The loss of RGC axons may be apparent structurally as a local and/or a diffuse thinning of the retinal nerve fiber layer (RNFL)3–6 and of the neuroretinal rim.5 Functionally, RGC atrophy leads to characteristic visual field defects.7 In clinical practice, as well as in clinical trials, both structural and functional losses are assessed for the diagnosis and monitoring of glaucoma.1,8,9

Functional losses by glaucoma are traditionally evaluated with standard automated perimeter (SAP). Perimetry assesses the differential light sensitivity (unlogged-DLS = Ld/Lt – Lb), where Lb is background luminance and Lt the stimulus luminance at threshold)10 at various locations in the central retina which is typically expressed in a decibel scale (decibel-DLS = 10 × log10 Lmax/(Lt – Lb), where Lmax is the perimeter’s maximum stimulus luminance). The relationship between function and structure has been found to be curvilinear for the relationships between decibel-DLS and number of ganglion cells1,12 and neuroretinal rim area.13–15 However, when differential light sensitivity is expressed in the unlogged-DLS scale, function appears to relate linearly to structure, as has been shown by Garway-Heath et al.11,15,16

Structural losses of the RNFL can be evaluated with scanning laser polarimetry (SLP). Instruments featuring this technique, such as the GDx nerve fiber analyzer (NFA) and the GDx VCC (both from Laser Diagnostic Technologies, Inc., San Diego, CA), estimate the thickness of the RNFL by measuring the summed retardation of a polarized scanning laser beam, induced by the form-birefringent microtubules that support the RGC axons.17–19 Retardation in these instruments is usually expressed in micrometers of thickness, based on the relationship between the amount of retardation and the histologically determined RNFL thickness in monkey eyes,19 although this relationship may vary somewhat in each nerve fiber bundle around the optic nerve head (Huang X, et al. IOVS 2003;44: ARVO E-Abstract 3365).

Both the GDx NFA and the GDx VCC are equipped with an anterior segment compensator to cancel the birefringent effects of the cornea and, to a lesser degree, the lens. Whereas the compensator of the GDx NFA is fixed, the GDx VCC is equipped with an automated so-called variable corneal compensator (VCC), allowing eye-specific compensation of anterior segment birefringence. Because of large interindividual and intraregional variability in anterior segment birefringence,20–22 measurements with the GDx NFA do not always accurately reflect the RNFL,24 and have been reported to have only a moderate correlation with perimetry.25–30 Equipped with a VCC, SLP has been shown to allow objective assessment of localized structural RNFL defects.20 In addition, using a modified GDx NFA, Bowd et al.25 have shown that SLP measurements with VCC in patients with predominantly mild glaucomatous damage correlate better with perimetry than those with fixed compensation.

The purpose of the present study was to investigate the functional-structural relationship between standard automated perimetry and measurements of peripapillary RNFL retardation with the commercially available GDx VCC in healthy subjects and patients with glaucoma.

METHODS

Forty-seven healthy subjects and 101 patients with glaucoma were examined with SAP ( Humphrey Field Analyzer [HFA] III, 24-2 Full Threshold or Swedish interactive threshold algorithm [SITA] Standard test program; Carl Zeiss Meditec, Dublin, CA) and SLP with individualized compensation of anterior segment birefringence (GDx VCC; Laser Diagnostic Technologies, Inc.) The research adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from the subjects after explanation of the nature and possible conse-

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Automated Perimetry versus GDx VCC Measurements

RESULTS

The relationship between perimetry and GDx VCC measurements can be graphically presented for all sectors in Figure 2. We found statistically significant correlations between standard

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automated perimetry and GDx VCC measurements in patients with glaucoma \((P < 0.001)\), in all sectors except the temporal one \((P = 0.059)\), with \(r_s\) of 0.77, 0.52, 0.46, 0.51, 0.38, and 0.19 for the sectors ST, SN, N, IN, IT, and T, respectively (Fig. 2, Table 1). In healthy subjects, no statistically significant correlations between perimetry and GDx VCC measurements were found in any sector \((P > 0.13)\), except the superonasal one \((P = 0.012; \text{Fig. 2, Table 1})\).

When fit with a least-squares linear regression model, the relationship between decibel-DLS and RNFL retardation in healthy subjects and patients with glaucoma yielded \(R^2\) values of 0.48, 0.42, 0.29, 0.37, and 0.35 for the sectors ST, SN, N, IN, and IT, respectively (for slopes, \(P < 0.001\)). For the unlogged-DLS, the \(R^2\) values of the linear regression models were 0.52, 0.48, 0.26, 0.35, and 0.43, respectively (\(P\) of slopes < 0.001).

**FIGURE 2.** Scatterplots of differential light sensitivity (DLS), expressed as decibel-DLS (left) and unlogged-DLS (right), against peripapillary RNFL retardation measured with the GDx VCC (Laser Diagnostic Technologies, Inc.). (○) Healthy subjects; (■) patients with glaucoma. Sectors: (A) superotemporal; (B) superonasal; (C) nasal; (D) inferonasal; (E) inferotemporal; (F) temporal.
For the sectors ST, SN, and IT, linear regression analysis yielded statistically significant better fits for the unlogged-DLS scale than for the decibel-DLS scale (signed rank test, $P = 0.011$, $P < 0.001$, and $P = 0.011$, respectively). Conversely, for the sectors N and IN, linear regression analysis yielded statistically significant better fits for the decibel-DLS scale (signed rank test, $P < 0.001$ and $P = 0.004$, respectively). We did not fit the relationship between perimetry and GDx VCC measurements for the temporal sector with linear regression analysis, because they did not correlate.

**DISCUSSION**

We have shown a correlation between standard automated perimetry and GDx VCC measurements in patients with glau-
Table 1. Correlation between SAP and GDx VCC Measurements

<table>
<thead>
<tr>
<th>Sector</th>
<th>Glaucoma Patients</th>
<th>Healthy Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( r_s )</td>
<td>( P )</td>
</tr>
<tr>
<td>Superotemporal</td>
<td>0.77</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Superonasal</td>
<td>0.52</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nasal</td>
<td>0.46</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferonasal</td>
<td>0.51</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Inferotemporal</td>
<td>0.38</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Temporal</td>
<td>0.19</td>
<td>0.059</td>
</tr>
</tbody>
</table>

Degrees of association, measured with Spearman’s rank correlation coefficient \( (r_s) \), between SAP differential light sensitivity and GDx VCC measurements in patients with glaucoma (\( n = 100 \)) and healthy subjects (\( n = 47 \)) for the six sectors described in Figure 1.

The linear relationship that we found between function and structure was linear in the unlogged-DLS scale. In the standard decibel-DLS scale, a curvilinear relationship was apparent. Because the sectors ST and IT are reportedly most affected by glaucoma and patients with glaucoma with mild to moderate functional loss, in more advanced functional loss, the opposite may be more useful than SLP for follow-up. Patients with glaucomatous visual field defects of mixed severity may be best monitored with a combination of SLP and SAP.

The relationship was similar in the SN sector (Fig. 2B) but less pronounced in the N sector (Fig. 2C). In the IN sector, however, GDx VCC measurements did not appear to be better at detecting mild glaucomatous loss than perimeter (Fig. 2D). We argue, however, that the IN sector, which relates to the uppermost visual field of the HFA 24-2 program, has poor perimetric reproducibility, which limits its clinical usefulness.

The linear relationship that we found between function (unlogged-DLS) and structure was similar to those reported by Garway-Heath et al. \( ^{11} \) between unlogged-DLS and the number of RGCs and neuroretinal rim area, and to the theoretically modeled one by Swanson et al. (Swanson WH, et al. J OVS 2003;44:ARVO E-Abstract 57) between unlogged-DLS and the number of RGCs. In addition, our finding of a curvilinear functional-structural relationship between decibel-DLS and RNFL retardation corresponds with the reported relationships between decibel-DLS and number of RGCs and between decibel-DLS and neuroretinal rim area. \( ^{1,4,15} \)

Several investigators also studied the relationship between SAP and SLP measurements and reported no correlation or only a mild one in healthy and glaucomatous eyes. \( ^{24,50} \) Their poor correlation may be attributable to differences in study populations and the use of different parameters. More important, they used SLP with a fixed compensator of anterior segment birefringence, instead of a variable one. Knighton et al. \( ^{35} \) reasoned that an individualized anterior segment compensation of birefringence would be necessary for accurate measurement of RNFL retardation. \( ^{20,22} \) Our results support those of Bowd et al., \( ^{24} \) who compared a variable with a fixed anterior segment compensator and found an improved relationship between visual function and structure with VCC. Of interest, Bowd et al. \( ^{32} \) found that the relationship between decibel-DLS and GDx measurements with VCC was better described by a linear model than by a curvilinear one in all sectors. However, their data related to predominantly mild glaucomatous damage (mean MD: \(-2.7 \pm 3.74 \text{ dB} \) [SD]), whereas we used a much larger range of glaucomatous eyes and also many healthy eyes. Their smaller range may have precluded the detection of curvilinearity in the relationship between function and structure.

In the sectors ST and IT, the \( R^2 \) values of the linear regression models describing the relationship between unlogged-DLS and RNFL retardation were 0.52 and 0.43, respectively. Therefore, 48% to 57% of the variation in unlogged-DLS was not explained by RNFL retardation alone. In the other sectors, 52% to 95% of the variation in this relationship was unexplained. Some of this scatter may be due to retardation originating from axons that had their origin outside the points tested by the HFA. Such axons may relate to areas either between the tested points or outside the entire test area displayed in Figure 1. In addition, mismatching of the six optic nerve head (ONH) sectors and the visual field test points in the map constructed by Garway-Heath et al. \( ^{52} \) may have added to the variation in the correlation between perimetry and GDx VCC measurements. Garway-Heath et al. \( ^{52} \) have reported that the range of possible positions at the ONH of RGC axons originating from each visual field test point location covers almost 30°. Factors that contributed to the variation in that study were the intereye variability in the position of the ONH in relation to the fovea, intereye variability in retinal magnification, and variations in shape, rotation, and tilt of the ONH. \( ^{52} \) Apart from these variations, our data may also have been influenced by variation in the positioning of the head during SLP. Some of the unexplained variation in the relationship between DLS and RNFL retardation may also be attributable to the reproducibility of measurements with SAP and SLP. For example, the variability in DLS within subjects has been shown to be substantial. \( ^{54,56,57} \) Therefore, combining the results of several subsequent visual field tests may improve the relationship between DLS and RNFL retardation. To what extent the variability of GDx VCC measurements has influenced our results is unclear, because its reproducibility of measurements has not yet been assessed. Some variation in DLS may also have been due to age-related changes in the ocular media as well as age-related changes of the retina, \( ^{58} \) other than loss of RGCs, and changes in the central nervous system.

For DLS values near zero, we still measured retardation equivalent to approximately 20 μm or more (Fig. 2). A possible explanation for this is that some RGCs had stopped functioning, but their axons were still present, thus exhibiting birefringence. Axons have been identified in the RNFL that have no demonstrable visual function. \( ^{59} \) Another explanation is that we measured residual retardation from incomplete compensation of anterior segment birefringence or that we measured retardation induced by birefringent structures in the eye other than the RGC axons or anterior segment, as has been suggested by measurements with polarization sensitive optical coherence tomography (De Boer JF, et al. J OVS 2003;44:ARVO E-Abstract 3388). It is unclear whether an offset may have been present in the instrument itself. The offset may also have been caused by the retardation originating from axons that had their origin outside the tested points of the HFA 24-2 program (i.e., either between the testing points or outside the tested central 24° area).

In the present study, we found a linear relationship between unlogged-DLS and RNFL retardation and a curvilinear relationship between decibel-DLS and RNFL retardation. This suggests that the unlogged-DLS scale may be more appropriate...
for comparing structural and functional measurements than the standard dB scale, as suggested earlier by Garway-Heath et al.\textsuperscript{13} Clinically, however, the standard decibel scale may be more appropriate, because the variability of perimetric measurements between healthy subjects appears to be less when expressed in the decibel-DLS scale than in the unlogged-DLS scale (cf. Figs. 2A–F; right and left images). This apparent improved variability may, however, lower its sensitivity to detecting change, notably at the higher end of the decibel-DLS scale. Such change might, as stated earlier, be better monitored with SLP than with SAP.

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References


