Evaluation of Retinal Nerve Fiber Layer using Scanning Laser Polarimetry

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ABSTRACT
Early diagnosis of glaucoma requires evaluation of the retinal nerve fiber layer (RNFL) to pick-up subtle changes before visual field defects. Scanning laser polarimetry using the GDx VCC offers a unique tool for imaging of RNFL changes in glaucoma. It is useful for early diagnosis and also to detect progression of glaucoma. The following review covers the basic principles, interpretation, clinical utility of this technology and reviews the literature on its current applications.

Keywords: Scanning laser polarimetry, RNFL, GDx, Glaucoma.

INTRODUCTION

Even though field defects on full threshold central perimetry are considered the gold standard for the diagnosis of glaucoma, the analysis of RNFL may soon overtake the role of visual fields in the early diagnosis of glaucoma. The retinal nerve fiber layer (RNFL) assessment for glaucoma diagnosis and follow-up has several distinct advantages over current diagnostic approaches as RNFL defects occur prior to visual field loss. As many as half of all ganglion cells can be lost before a defect is detected by the visual field. It has also been documented that RNFL changes can occur prior to optic nerve head (ONH) changes. Also, RNFL evaluation has been found to be more sensitive for predicting future visual field loss compared to ONH evaluation, and is a better predictor of damage than C/D ratio. Red-free RNFL photography has been used to study the RNFL, but the subjective interpretation of the results and the practical problems of the method limit its usefulness.

Principle of Scanning Laser Polarimetry

The retinal nerve fiber layer (RNFL) is made of highly ordered parallel axon bundles which contain microtubules, cylindrical intracellular organelles with diameters smaller than the wavelength of light. The highly ordered (paralleled) structure of the microtubules is the source of RNFL birefringence which is the splitting of a light wave by a polar material into two components. These components travel at different velocities which creates a relative phase shift termed retardation. This retardation is proportional to the thickness of the RNFL. A scanning laser polarimeter is basically a confocal scanning laser ophthalmoscope with an integrated ellipsometer to measure retardation. Retinal scanning laser polarimetry (SLP) determines the RNFL thickness, point by point in the peripapillary region, by measuring the total retardation in the light reflected from the retina. Polarized light passes through the eye and is reflected off the retina. Because the RNFL is birefringent, the two components of the polarized light are phase shifted relative to each other (Fig. 1) and this is captured by a detector, and converted into thickness (in microns).

Anterior Segment Birefringence

In addition to the RNFL, the anterior segment (the cornea and lens) is birefringent. The total retardation of a subject’s eye is the sum of the cornea, lens and RNFL birefringence. Compensation of anterior segment birefringence is necessary to isolate RNFL birefringence. Early scanning laser polarimeters (e.g. the GDx NFA and the GDx access) compensated for anterior segment birefringence based on fixed values for the axis and magnitude of the anterior segment birefringence. This, however, varies for each individual.
Variable Corneal Compensation

The GDx variable corneal compensation (VCC) measures and individually compensates for anterior segment birefringence for each eye (Fig. 2). For this, the specific axis and magnitude of the anterior segment birefringence is determined by first imaging the eye without compensation. The uncompensated image presents total retardation from the eye and includes retardation from the cornea, lens and RNFL. The macular region of this image is then analyzed to determine the axis and magnitude of the anterior segment birefringence. The macular region birefringence is uniform and symmetric due to the radial distribution of Henle’s fiber layer. However, in uncompensated scans, a non-uniform retardation pattern is present in the macula due to the birefringence from the anterior segment. The axis and magnitude values from the anterior segment can be computed by analyzing the non-uniform retardation profile around the macula. The axis of the anterior segment birefringence is determined by the orientation of the ‘bow-tie’ birefringent pattern (Fig. 3) in the macula and the magnitude of the anterior segment birefringence is calculated by analyzing the circular profile of the birefringence in the macula according to standard equations. In cases of macular pathology, an alternative method is available that accurately compensates for the anterior segment birefringence.

A Comparison of VCC Technology with FCC Technology

If the anterior segment birefringence values for a given eye deviate from the assumed values of the fixed compensator, the FCC image will be less comparable. As the VCC individually measures and compensates for the anterior segment birefringence for each eye, discrepancies between scan modes (VCC vs FCC) are the result of incorrect FCC compensation. The VCC scan therefore results in a more accurate RNFL measurement, and is now universally accepted as the standard measurement strategy.

RNFL Measurements

The GDx VCC measurements are taken by scanning the beam of a near-infrared laser (780 nm) in a raster pattern which captures an image with a field 40° horizontally by 20° vertically, and including both the peripapillary and the macular region. Total scan time is 0.8 seconds. For each measurement, the GDx VCC generates two images: A reflectance image and a retardation image. The reflectance image is generated from the light reflected directly back from the surface of the retina, and is displayed as the fundus image on the device screen and printouts. The retardation image is the map of retardation values and is converted into RNFL thickness based on a conversion factor of 0.67 nm/μm. Each image is made up of 256 (horizontal) × 128 (vertical) pixels, or 32,768 total pixels. For an emmetropic eye, 1 pixel is 0.0465 mm in size, and the total scan field is 11.9 mm (horizontal) × 5.9 mm (vertical).
Measurement Technique

Measurement is performed with an undilated pupil of at least 2 mm diameter and takes only about a second to capture the image. Total time for the examination and output is less than 3 minutes for both eyes. The test is totally objective and the reproducibility of images is 5 to 8 micron per measured pixel. A warning is given if image fails to meet requisite criteria. The quality of image is affected by cataracts and poor media clarity. Looking at image allows one to see if the ellipse was placed properly and the ellipse can be manually aligned to conform the disk margin. The diameter of the ellipse is displayed in microns and gives an idea about the actual disk diameter.

Clinical Interpretation of the GDx VCC Printout

For each GDx VCC scan, an age-matched comparison is made to the normative database and any significant deviations from normal limits are flagged as abnormal with a p-value.

Quantitative RNFL evaluation is provided through four key elements of the printout (Fig. 5):
1. Thickness map
2. Deviation map
3. TSNIT graph
4. Parameter table.

The Thickness Map

The thickness map shows the RNFL thickness using a color scale that follows the color spectrum going from blue to red. Thick RNFL values are colored yellow, orange and red while thin RNFL values are colored dark blue, light blue and green. The color scale follows the color spectrum (blue to red) up to 120 microns. Each quadrant is analyzed and actual deviation from normal, in microns, is displayed. Deviations from normal are highlighted in yellow if they are borderline (p < 0.10) or in red if they are outside normal limits (p < 0.05). The normal pattern is a symmetrical hourglass shape of bright colors superior and inferior and dark colors nasal and temporal.

An Abnormal pattern may include any/all of the following:
1. Diffuse loss of RNFL
2. Focal defects are seen as concentrated dark areas (visible on fundus image as well)
3. Asymmetry between superior and inferior quadrants
4. Asymmetry between the two eyes
5. Higher than normal nasal and temporal thickness.

The Deviation Map

The deviation map reveals the location and magnitude of RNFL defects over the entire thickness map. The deviation map analyzes a 128 × 128 pixel region (20° × 20°) centered on the optic disk. To reduce variability due to slight anatomical deviations between individuals, the 128 × 128 pixel thickness map is averaged into a 32 × 32 square grid, where each square is the average of a 4 × 4 pixel region (called super pixels). For each scan, the RNFL thickness at each super pixel is compared to the age-matched normative database, and the super pixels that fall below the normal range are flagged by colored squares based on the probability of normality. Dark blue squares represent areas where the RNFL thickness is below the 5th percentile of the normative database, i.e. there is only 5% probability that the RNFL thickness in this area is within the normal range. Light blue squares represent deviation below the 2% level, yellow represents deviation below 1%, and red represents deviation below 0.5%. The deviation map uses a grayscale fundus image of the eye as a background, and displays abnormal grid values as colored squares over this image (Fig. 6).

The TSNIT Map

The TSNIT stands for temporal-superior-nasal-inferior-temporal and displays the RNFL thickness values along the calculation circle starting temporally and moving superiorly, nasally, inferiorly and ending temporally. In a normal eye, the TSNIT plot follows the typical ‘double hump’ pattern with thick RNFL measures superiorly and inferiorly and thin RNFL values nasally and temporally. The TSNIT graph shows the curve (or
Fig. 5: Various parameters for quantitative RNFL evaluation
function) of the actual values for that eye along with a shaded area which represents the 95% normal range for that age. In a healthy eye, the TSNIT curve will fall within the shaded area. When there is RNFL loss, the TSNIT curve will fall below this shaded area, especially in the superior and inferior regions. In the center of the printout at the bottom, the TSNIT graphs for both eyes are displayed together. In a healthy eye, there is good symmetry between the TSNIT graphs of the two eyes and the two curves will overlap. However, in glaucoma, one eye often has more advanced RNFL loss and, therefore, the two curves will have less overlap. A dip in the curve of one eye relative to another is indicative of RNFL loss (Fig. 7).

The Parameter Table

The TSNIT parameters are summary measures based on RNFL thickness values within the calculation circle. The calculation circle is a fixed circle (a fixed size band) centered on the optic nerve head (ONH) which is 0.4 mm wide with outer and inner diameters of 3.2 and 2.4 mm respectively (see Fig. 7). These parameters are automatically compared to the normative database and are quantified in terms of probability of normality. Normal parameter values are displayed in white, abnormal values are color-coded based on their probability of normality. The probability levels used are the same as the deviation map: Dark blue represents 5% likelihood of being normal, light blue represents 2% level, yellow 1% and red 0.5%.

The five TSNIT parameters are: TSNIT average, superior average, inferior average, TSNIT standard deviation (TSNIT SD) and intereye symmetry.

a. **TSNIT average**: The average RNFL thickness around the entire calculation circle.

b. **Superior average**: The average RNFL thickness in the superior 120° region of the calculation circle.

c. **Inferior average**: The average RNFL thickness in the inferior 120° region of the calculation circle.

d. **TSNIT SD**: This measure captures the modulation (peak to trough difference) of the double-hump pattern. A normal eye will have high modulation in the double-hump RNFL
pattern, while a glaucoma eye will typically have low modulation in the double-hump pattern (Fig. 8).

e. **Intereye symmetry**: Measures the degree of symmetry between the right and left eyes by correlating the TSNIT functions from the two eyes. Values range from –1 to 1, where values near one represent good symmetry. Normal eyes have good symmetry with values around 0.9.

f. **The nerve fiber indicator (NFI)**: The NFI is a global measure based on the entire RNFL thickness map and is calculated using an advanced form of neural network, called a support vector machine (SVM). It utilizes information from the entire RNFL thickness map to optimize the discrimination between healthy and glaucomatous eyes. The output of the NFI is a single value that ranges from 1 to 100 indicating the overall integrity of the RNFL with classification based on the ranges: 1 to 30 as normal, 31 to 50 as borderline and 51+ as abnormal.

Clinical research has shown that the NFI is the best parameter for discriminating normal from glaucoma with sensitivity and specificity of the NFI reported to be as high as 89% and 98% respectively.

### Abnormal Scan

Although there is no consensus on definition of an abnormal scan, the following guidelines can be used (see Figs 5 to 7).

- **TSNIT average**, superior average, inferior average, TSNIT standard deviation, intereye symmetry or NFI are abnormal at p < 1% level.
- They are considered borderline at p < 5% level (in general if NFI is > 47 at the p < 1% level or >30 at p < 5% level, the scan is abnormal).

The normal values of the GDx VCC parameters in the Indian population (40-70 years) according to our database of 200 subjects (40-60 years) is as follows:

<table>
<thead>
<tr>
<th>TSNIT parameters</th>
<th>OD Actual val.</th>
<th>OS Actual val.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSNIT average</td>
<td>48.08</td>
<td>33.27</td>
</tr>
<tr>
<td>Superior average</td>
<td>54.39</td>
<td>48.23</td>
</tr>
<tr>
<td>Inferior average</td>
<td>62.33</td>
<td>28.06</td>
</tr>
<tr>
<td>TSNIT Std. Dev.</td>
<td>22.36</td>
<td>14.83</td>
</tr>
<tr>
<td>Intereye symmetry</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>NFI</td>
<td>25</td>
<td>63</td>
</tr>
</tbody>
</table>

\[
\text{Inferior average} = 62.1 \pm 6.6 \ (38.9-74.3) \text{ microns} \\
\text{NFI} = 17.2 \pm 6.9 \ (4-35)
\]

### Additional Diagnostic Parameters

For an extended analysis, the following parameters are also available on this machine:

- **Symmetry**—superior quadrant thickness/inferior quadrant thickness
- **Superior ratio**—superior quadrant thickness/temporal quadrant thickness
- **Inferior ratio**—inferior quadrant thickness/temporal quadrant thickness
- **Maximum modulation**—thickest quadrant/thinnest quadrant within image
- **Ellipse modulation**—thickest quadrant/thinnest quadrant within ellipse.

In eyes with advanced chorioretinal degeneration or peripapillary atrophy the GDx VCC image may show very high retardation values (supranormal) with a pink color depicting a thickness > 140 microns. This occurs due to additional birefringence from the sclera and such abnormal scans should not be used for interpretation of the RNFL. In eyes with peripapillary atrophy, the default scan diameter can be manually increased to fall outside the atrophic area around the disk. However, the normative database comparisons are affected, if the calculation circle is reset.

### Detecting Progression of RNFL Loss: Serial Analysis

The serial analysis printout has five key elements that should be considered when assessing RNFL change over time (Fig. 8): Thickness maps, deviation maps, deviation from reference maps, parameters tables and TSNIT graph. A change probability map has also been added in the new software. The serial analysis can compare up to four exams. The first exam is the baseline or reference exam, and all follow-up exams are compared to this. A colored rectangle to the left of the thickness map contains the date and quality score of each exam. The same color is used in the TSNIT graph to indicate which TSNIT curve corresponds to which exam (see Fig. 8).

The deviation from reference map displays the RNFL difference of the follow-up exam compared to the baseline. If the difference exceeds 20 microns at any pixel, it is color coded. The areas of RNFL change shown on the deviation from reference map frequently, but not always correspond to the areas of loss detected by the deviation map, because the deviation map shows loss compared to the normative database while the deviation from reference maps shows RNFL change over time in the same eye. The TSNIT Graph shows the TSNIT curves for all exams, its color corresponding to the color of the vertical rectangle next to each exam. The TSNIT curves are overlaid on the shaded area representing the normal range for that age. RNFL loss results in a lower TSNIT curve on the follow-up exam compared to baseline (Figs 8 and 9).
Fig. 9: GDx VCC scan in advanced glaucoma with diffuse RNFL loss
Thus, progression of the RNFL over a period provides key data regarding:
1. Identification of RNFL defect
2. Rate of progression of RNFL
3. Assessment of treatment effectiveness.

The new software which helps in investigating the progression is GPA™ (progression analysis for GDx) (Figs 9 and 10). Guided progression analysis (GPA) compares measurements over time and determines, if the differences are statistically significant. GDx GPA reports “possible progression” when significant change is detected and “likely progression” when significant change is confirmed. Possible progression requires a minimum of three visits, and likely progression requires a minimum of four. The GDx GPA algorithms are designed to have 95% specificity for likely progression. This means theoretically that GPA will correctly identify 95% of stable eyes as not changing. At this time, there is no quantitative clinical data on the sensitivity of GPA. Progression analysis has two modes: Fast and extended. Fast mode is for analyzing data sets that include single measurements. It compares change to the predetermined average measurement variability derived from a sample population. In contrast, extended mode requires means of three measurements, and GPA calculates the individual measurement variability of each eye for a selected patient. It measures and detects the progression based on three different parts of the analysis:
1. Image change map
2. TSNIT change graph

**Image Change Map**

Image change map recognizes the change in the reflectance image. The minimal cluster size considered is 150 pixels which is 2% of image area. Any significant change in the image is depicted on the progression map. “Possible progression” areas are shown in yellow, “likely progression” areas in red, and “possible increase” areas in purple.

It can detect narrower and deeper defects. This design has specificity of 95%.

**TSNIT Progression Graph**

The ring around the optic nerve is divided into 64 equal segments and compared on follow-up. If three adjacent segments show significant change on follow-up, the progression is indicated. Areas between the current baseline set and the current exam that report significant change are displayed with likely
progression shown in red, possible progression shown in yellow, and possible increase shown in purple.

This design also has 95% specificity to detect the defects. It can detect shallower and broader defect better as compared to other parameters.

**Parameter Progression Chart**

TSNIT average, superior average and inferior average are compared. On the chart regression line is drawn to show likely progression and \( p < 5\% \) (Fig. 11). This design also has 95% specificity. This can detect diffuse changes in the RNFL better.

This parameter can also compare the rate of progression before and after treatment, thus helpful in guiding the treatment line.

GDx GPA uses two different algorithms to determine significant change, based on GPA mode.

- **CFB (Change from baseline)**: Based on changes from two baseline exams compared to measurement variability. It is most sensitive when there is little variability between baselines. Mean readings are treated as single data points.

- **SIM (statistical image mapping)**: Based on trend analysis. All visits contribute to change detection, as opposed to CFB in which the data from the first two and last two visits are used to determine, if change occurred. Therefore, SIM is able to detect progression between the first two visits better than CFB.
Advantages of GDx VCC

- Easy to operate
- Does not require pupillary dilatation
- Good reproducibility
- Does not require a reference plane
- Can detect glaucoma on the first exam
- Early detection before standard visual field
- Comparison with age-matched normative database
- It is independent of the optical resolution of the human eye.

Limitations

- Does not measure actual RNFL thickness (inferred value)
- Measures RNFL at different locations for each patient
- Does not differentiate true biological change from variability
- Limited use in moderate/advanced glaucoma
- Requires a wider database from the Indian population
- Fourth machine prototype (cannot update earlier versions)
- Affected by anterior and posterior segment pathology like:
  - Anterior segment disease (e.g., ocular hypertension, neovascularization)
  - Posterior segment disease (e.g., macular degeneration, retinal detachments)
- Collection of images is poor (resulting in discarding the data)

PRACTICAL TIPS

- Verify image quality. In case image is of poor quality, a flag is displayed at the top of the page. Discard images with poor registration, Q < 7, or TSS < 40 whenever possible or interpret with caution.
- Review the summary box. A possible progression flag indicates additional follow-up visits are recommended to confirm change. A likely progression flag indicates statistically significant change is detected in GDx measurements. A possible increase flag could indicate high measurement variability, especially when increase and progression are flagged simultaneously.
- Correlate GDx results with other clinical tests to detect glaucomatous progression. Rate of progression, locations of the detected progression, age of the patient, stage of the disease and other clinical factors should be considered before taking a clinical decision.
- Instrument or calibration change is indicated in the summary parameter charts by a blue asterisk at the top of the charts where a GDx instrument has changed.
- Typical scan score (TSS) provides a measure of the “typicality” of the RNFL image. In an atypical scan, the retardance profile does not match the known anatomical RNFL distribution and can be characterized by a variable retardance pattern. Atypical scans are more common in pale fundi, high myopes and elderly eyes. TSS ranges from 0 (very atypical) to 100 (very typical). Exams with TSS < 40 should be interpreted with caution.

CLINICAL STUDIES USING GDx VCC TECHNOLOGY

The diagnostic accuracy of the GDx VCC for identification of eyes with glaucoma has also been shown to be quite good in various studies.15-17 Weinreb et al15 found that significantly higher sensitivity and specificity with GDx VCC compared to the GDx FCC. RNFL thickness measures from the GDx VCC also have an improved correlation with visual fields.18-20

In an animal model with the lens and cornea removed, Weinreb showed that the retardation is linearly related to the thickness of the RNFL with excellent correlation (r = 0.83) between retardation and the histopathologic measurement of RNFL thickness. The resolution of measurements in vitro was estimated to be 13 m.12

Reus et al determined the diagnostic accuracy of the GDx VCC in the diagnosis of glaucoma in a prospective case series.21 and found that NFI was the best discriminating parameter with a sensitivity and specificity of 89.0 and 95.9% respectively. At the cut-off level of > 40, the sensitivities of the NFI for correctly identifying glaucoma patients with mild, moderate and severe damage were 83.8, 92.9 and 90.1% respectively. Reus et al also compared scanning laser polarimetry (SLP) measurements of retinal nerve fiber layer (RNFL) thickness in perimetrically unaffected eyes of glaucoma patients with those in their fellow eyes with field loss and eyes of healthy subjects.22 They found that GDx VCC measurements showed more RNFL thinning in the perimetrically unaffected eyes of glaucoma patients than in the healthy control eyes. The RNFL in the perimetrically unaffected eyes of glaucoma patients was thicker than that in their fellow eyes with field loss.

Henderson et al studied the relationship between central corneal thickness and retinal nerve fiber layer thickness in ocular hypertensive patients (OHP)23 and found that ocular hypertensive patients with thinner corneas had significantly thinner RNFL values than OHT patients with thicker corneas and healthy control subjects. RNFL defects as assessed by the GDx VCC may therefore represent early glaucomatous damage in OHT eyes.

Reus et al24 found a statistically significant correlation in most sectors between standard automated perimetry and GDx VCC measurements in patients with glaucoma. Based on the observed relationships between function and structure, the authors concluded that 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 perimetry.

Medeiros et al25 compared the ability of scanning laser polarimetry with variable corneal compensation (GDx VCC), confocal scanning laser ophthalmoscopy [HRT II (Heidelberg Retina Tomograph)] and optical coherence tomography (Stratus OCT) to discriminate between healthy eyes and eyes with glaucomatous visual field loss. No statistically significant difference was found between the areas under the receiver operating characteristic curves (AUCs) for the best parameters from the GDx VCC (nerve fiber indicator, AUC = 0.91), Stratus OCT (retinal nerve fiber layer inferior thickness, AUC = 0.92), and HRT II (linear discriminant function, AUC = 0.86). Abnormal results for each of the instruments, after comparison with their normative databases, were associated with strong
positive likelihood ratios. The AUCs and the sensitivities at high specificities were similar among the best parameters from each instrument. Abnormal results (as compared with each instrument’s normative database) were associated with high likelihood ratios and large effects on post-test probabilities of having glaucomatous visual field loss. The authors concluded that calculation of likelihood ratios may provide additional information to assist the clinician in diagnosing glaucoma with these instruments.

Aung et al evaluated the changes in retinal nerve fiber layer (RNFL) thickness in the first 16 weeks after acute primary angle closure (APAC) and found that after an episode of APAC, superior and inferior average RNFL thickness decreases significantly from week 2 to 16.

We evaluated the retinal nerve fiber layer (RNFL) thickness parameters with optical coherence tomography (OCT) using four scan diameters to study the effect of radius of measurement on the RNFL values and then correlated with scanning laser polarimetry (GDx VCC) in 74 eyes. The three measured parameters (superior RNFL, inferior RNFL and average RNFL thickness) showed a significant positive correlation when measurements of OCT3 and GDx VCC were compared. Highest degree of correlation for all 3 parameters was observed with a circular scan radius of 1.73 on OCT3 and Gdx VCC. The following regression equation was obtained:

\[ \text{OCT fast RNFL thickness} = 56.17 + 0.613 \times \text{GDx TSNIT thickness} \]

All the RNFL thickness parameters on OCT showed a decrease in magnitude with an increase in the size of scan radius. Since scan diameters are fixed for both instruments irrespective of the disk diameter, measurements closer to the disk margin in large sized disks will give higher thickness values as compared to measurements at the same radius (but further away from disk margin) in small sized disks. This is one important drawback of the current imaging technologies and normative databases for RNFL thickness on OCT and GDx VCC should take the disk size into account.

Parravano et al reported that average peripapillary RNFL thickness was reduced in patients of diabetes mellitus type 1. Matrix MD, HFA MD, PSD, average peripapillary and superior retinal nerve fiber layer (RNFL) were significantly reduced in patients of diabetes mellitus type 1. The authors concluded that functional and structural retinal testing by Humphrey-Matrix and GDx VCC could be useful for the identification of early retinal impairment in DM1 patients with no sign of retinal vasculopathy.

Martinez et al compared scanning laser polarimetry measurements of RNFL thickness in eyes of migraine patients with those in eyes of age-matched, healthy subject, and reported that the mean RNFL average thickness parameter was found to be thinner in migraine patients. In addition, there was a strong correlation between migraine severity and RNFL average thickness parameters.

Grabska-Liberek evaluated the applicability of selected methods in glaucoma diagnosis in a patient with optic disk drusen. The scanning laser polarimetry showed extensive losses in nerve fiber layer of retina and the retinal thickness analysis showed a reduction of the retina thickness in the posterior pole.

Jankowska-Lech et al reported that evaluation with scanning polarimetry laser might be precious method in discovering retinal nerves fiber layer damage in the course of multiple sclerosis. Presence of defects in retinal nerves fiber layer in patients suffering from multiple sclerosis with no history of retrobulbar neuritis may suggest subclinical damage of optic nerve.

Zaveri et al also concluded that scanning laser polarimetry with variable corneal compensation measurements of RNFL thickness corroborates OCT evidence of visual pathway axonal loss in MS and provides new insight into structural aspects of axonal loss that relate to RNFL birefringence (microtubule integrity). These results support validity for RNFL thickness as a marker for axonal degeneration and support use of these techniques in clinical trials that examine neuroprotective and other disease-modifying therapies.

Garcia-Medina concluded that serial analyses with GDx VCC may be used as objective and quantitative tests to assess the progression of chorioretinal dystrophies like chorioderemia. The groningen longitudinal glaucoma study II. A prospective comparison of frequency doubling perimetry, the GDx nerve fiber analyzer and standard automated perimetry in glaucoma suspect patients concluded that the most frequent finding after a 4-year follow-up of a cohort of glaucoma suspects was conversion on GDx.

Hlavakova et al found a statistically significant decrease of RNFL thickness after LASIK in every single quadrant (Fig. 12). Clinically, the differences in RNFL thickness before and after LASIK were minimal. They proposed that the measurements by means of GDx are influenced by changes in the polarization features of the cornea caused by LASIK procedure.

Iester et al reported that the VCC algorithm is able to compensate for most of the changes in corneal birefringence induced by corneal refractive surgery if the polarization has been recalculated. Because mild changes in GDx parameters could affect the interpretation of the results in some patients, a new postoperative baseline macular image should be acquired.

Arraes et al reported that moderate degrees of PCO and/or acceptable images in pseudophakic patients do not alter the analysis of nerve fiber layer by GDx. Only intense degrees of PCO that hinder analyzable images make the examination impracticable.

Chen et al found that there was no significant difference between the HT-POAG and PACG eyes as far as the various parameters were concerned. GDx VCC shows fair discriminating ability in distinguishing normal from POAG and PACG eyes in Taiwan Chinese population.
GDx -Enhanced Corneal Compensation (GDx-ECC)

Scanning laser polarimetry measures the strength of the retinal birefringence measurement relative to optical and digital noise. Its sensitivity can be enhanced using a software algorithm (ECC) which measures the birefringence of the cornea and retina concurrently, as opposed to canceling out the corneal measurement with variable corneal compensation (VCC). This alternate method results in high-quality scans of all subjects. A baseline image, which consists of the mean of three scans, is analyzed. The computerized export of the temporal-superior-nasal-inferior-temporal (TSNIT) plots on the GDx-ECC printout includes the mean RNFL thickness from 64 polar sectors (5.625°/arc). The mean for each of these sectors is computed along a 2.6 mm diameter measurement circle surrounding the optic nerve head. The mean RNFL thickness for the superior (0-180°) and inferior (181-360°) retinal region is computed separately by averaging the corresponding mean sectors. Retinal nerve fiber layer images obtained using enhanced corneal compensation show a stronger structure-function relationship with standard automated perimetry, thereby demonstrating a higher visual field sensitivity compared with variable corneal compensation. Madieros et al concluded that GDx-ECC performed significantly better than GDx VCC in glaucoma detection in patients with more severe atypical retardation patterns. For lower values of TSS and lower AGIS scores, GDx-ECC performed significantly better than GDx VCC and at earlier stages of disease.39

Mai et al reported that RNFL measurements by SLP ECC had, in general, a good measurement repeatability, although some parameters seemed to be less stable in glaucomatous eyes than in healthy eyes and eyes with OHT. SLP ECC may therefore probably be employed for the detection of glaucomatous progression.40

They also reported that structure-function relationship between RNFL retardation and SAP VF sensitivity was stronger in images obtained with the GDx-ECC than with the GDx VCC. ABPs, which appeared more markedly with VCC than with ECC, weakened the structure-function relationship. When eyes with marked ABP images were removed from the analysis, the structure-function relationship with VCC improved, and no statistically significantly differences were found in the relationships between VCC and ECC.41

Morishita et al compared the results of scanning laser polarimetry (GDx) with variable corneal compensation (VCC) and enhanced corneal compensation (ECC) when applied to myopic glaucomatous eyes. They reported that mean typical scan score is significantly lower (p < 0.0001) and the prevalence
of atypical retardance pattern is significantly higher ($p < 0.0001$) by VCC scans than by ECC scans. TSNIT average and temporal average thickness show significantly higher values ($p < 0.001$) by VCC than by ECC. A statistically significant association was observed between TSNIT average and mean deviation of SAP by ECC scan. They therefore concluded that ECC scans showed a better retardation pattern and structure-function relationship than did VCC, and ECC appears to be more suitable for RNFL assessment in glaucomatous eyes that are moderately to highly myopic.$^{42}$

Toth et al found that the intervisit standard deviation, ISD of GDx-ECC NFI but not GDx VCC NFI, was significantly higher in progression than in the stable glaucoma group.$^{33}$ Also, several other ISD values tended to increase in the progressing group. Inferior average, and average thickness along the measuring ellipse (OR = 2.00, $p = 0.042$), as determined with Gdx-ECC (but not with GDx VCC), were associated with visual field progression, independently of patient age. They concluded that with GDx-ECC, increase of ISD is an early sign of glaucoma progression, precedes the development of detectable parameter changes and is associated with visual field progression.

**CONCLUSIONS**

The use of GDx VCC for RNFL assessment in glaucoma enables the clinician to pick-up preperimetric glaucoma and provides objective and quantitative information of the RNFL that is highly reproducible. It can discriminate normal from glaucoma with a high degree of accuracy. The procedure is easy to perform does not need pupillary dilatation, and clinical interpretation of the results is simple and direct.

The quantitative RNFL assessment aids the clinician in the diagnosis and management of glaucoma, and should be used in conjunction with other diagnostic information when making clinical decisions. Treatment should not be started based on GDx VCC parameters alone and the results of other anatomical and functional investigations must be taken into account. An abnormality on the GDx VCC implies that the patients require a closer follow-up to detect progression and confirmation of glaucomatous damage. Nonglaucomatous causes for optic neuropathy must be ruled out by a thorough clinical examination and appropriate investigation.

Further long-term studies are required before the GDx VCC technology becomes accepted as the gold standard for making a diagnosis of glaucomatous optic neuropathy and detecting progression.

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