Specificity and sensitivity of glaucoma detection in the Japanese population using scanning laser polarimetry

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Aims: To investigate the usefulness of the scanning laser polarimeter (GDx; GDx Nerve Fiber Analyzer) for glaucoma detection in the Japanese population, and to investigate the difference in the thickness of retinal nerve fibre layer (RNFL) between normal tension glaucoma (NTG) and primary open angle glaucoma (POAG).

Methods: 69 eyes of 69 normal subjects and 115 eyes of 115 chronic open angle glaucoma patients (60 NTG and 55 POAG patients) were studied. The thickness of RNFL was measured with GDx. An eye was diagnosed as glaucomatous, if at least one original GDx variable showed p < 0.05. The difference in thickness of RNFL between the NTG and POAG groups was then investigated.

Results: 46 normal eyes (66.7%) were diagnosed as not glaucomatous (no variables showing p < 5%), and 93 glaucomatous eyes (46 NTG and 47 POAG eyes) (80.9%) were diagnosed as glaucomatous. Actual values of average thickness, ellipse average, superior average, and superior integral were significantly lower in the POAG group than those in the NTG group.

Conclusions: New variables which elucidate focal RNFL defects or early changes are needed to improve the moderate detection ability found in this present study. The pattern of the change in RNFL may differ in NTG and POAG groups.
normal limits in each eye. \( p \) values for mean deviation and pattern standard deviation were not <0.05. All chronic open angle glaucoma patients had the following characteristics: normal open angle; typical glaucomatous optic disc cupping and visual field defects; no history of retrobulbar optic neuritis, anterior ischaemic optic neuropathy, or intracranial lesion. The intraocular pressure of NTG patients without therapy was below 21 mm Hg on repeated measurements, whereas pretreatment intraocular pressure of POAG patients was 21 mm Hg or above. Patients who had a refractive error (spherical equivalent) that exceeded −5 dioptres (D) were excluded from the study (patients’ average refractive error was −1.07 (2.04) dioptres, with no significant difference in the refractive error between the normal subjects and chronic open angle glaucoma patients). The eyes of glaucoma patients studied had a best corrected visual acuity above 20/25. HFA (central 30-2 program) was performed on each patient. With reliable measurements of visual field (fixation loss <20%, false negative and false positive <15%), the evaluation of glaucomatous visual field defects was made based on a liberal criteria (≥2 adjacent points of ≥5 dB loss each, ≥1 adjacent point of ≥10 dB loss each, or difference of ≥5 dB across nasal horizontal meridian at ≥2 adjacent points) of a previous report. In the present study, the glaucoma patients were divided into the three groups by results obtained from the HFA central 30-2 program as follows: 43 eyes (NTG:POAG = 22:21) in the early stage of the disease (mean deviation (MD) ≥ −5D), 40 eyes (NTG:POAG = 23:17) in the moderately progressed stage (−5 DB > MD > −15 DB), and 32 eyes (NTG:POAG = 15:17) in the progressed stage (MD ≤ −15 DB). The average (SD) value of the MD in all glaucoma patients was −10.47 (8.54) dB. The average (SD) MD value for each stage of the two groups is shown in Table 1. The average (SD) MD in NTG and POAG patients was −9.62 (7.65) dB and −11.38 (9.40) dB, respectively, with no significant difference (\( p = 0.271 \), Student’s \( t \) test). The average (SD) age in NTG and POAG patients was 60.0 (10.3) years and 56.6 (13.6) years, respectively, showing no significant difference (\( p = 0.137 \), Student’s \( t \) test). The average (SD) refractive error in NTG and POAG patients was −1.19 (2.04) dioptres and −0.94 (2.04) dioptres, respectively, also with no significant difference (\( p = 0.513 \), Student’s \( t \) test).

The thickness of the RNFL was measured with a scanning laser polarimeter. Its basic principles and technical characteristics have been described extensively. Briefly, this instrument consists of a confocal scanning laser ophthalmoscope with a polarisation modulator, a cornea polarisation compensator, and a polarisation detection unit. Measurement of RNFL thickness is based on the assumption that the RNFL possesses birefringent properties that change (retard) the state of polarisation of an illuminating laser beam. This change can be measured by determining the phase shift between extraordinary and ordinary beams. The extent of retardation is linearly correlated with the thickness of the RNFL. Approximately one degree of retardation corresponds to 7.4 \( \mu \)m of RNFL thickness as measured histologically after removal of the cornea. The light source of the instrument consists of a near infrared diode laser (wavelength 780 nm) in which the state of polarisation has been modulated. The polarised light penetrates the birefringent RNFL and is partially reflected from the deeper layer of the retina. It is separated from the illuminating light beam by a non-polarising beam splitter. The state of polarisation of the light is analysed by the polarisation detection unit. Then the electrical signal from the detector is digitised and stored in the memory of a personal computer for later analysis. A total of 65 536 retinal locations (256 × 256 pixels) are tested, allowing the examiner to create a retardation map in which the thickness of the RNFL is measured for each retinal location.

In the present study, a 15 degree field size was used and the optic disc was centred in the middle of the image for all image acquisitions. The pupils were not dilated. All measurements were obtained from a mean of three images. The average SD of RNFL thickness in retinal locations (pixels) in the mean of the three images was within 8 \( \mu \)m in each eye. The 10 pixel wide band was located concentric with the optic disc margin at 1.75 disc diameters. The margin of the optic disc was approximated by an ellipse placed around the inner margin of the peripapillary scleral ring. To calculate absolute values in the integral of RNFL thickness, errors in magnification were corrected using Bengtsson’s correction27 with axial length. All analyses at one location were performed by the same operator. Before starting this study, we confirmed that interoperator variation was negligible.

The GDx variables examined in the present study were symmetry, superior ratio, inferior ratio, superior/nasal, max modulation, ellipse modulation, ellipse average, superior average, inferior average, average thickness, and superior integrals (Table 2). GDx number was excluded from the study because it is not indicated with the probability. A total of 1500 pixels per quadrat (120 degrees for superior and inferior quadrants, 50 degrees for the temporal quadrant, and 70 degrees for the nasal quadrant) peripheral to an ellipse 1.75 disc diameters from the centre of the disc was used to calculate symmetry, superior ratio, inferior ratio, superior/nasal, and max modulation. Ellipse modulation, ellipse average, superior average, and inferior average were calculated using pixels within the 10 pixel-wide elliptical band that was automatically positioned concentric with the disc margin outline and 1.75 disc diameters from the centre of the optic disc.

When at least one GDx variable, out of 11 variables described above had a \( p \) value <5%, we defined that eye as glaucomatous by GDx. We studied the specificity and sensitivity of glaucoma diagnosis in Japanese normal subjects and glaucoma patients. We also studied the difference in sensitivity between the NTG and POAG group. Comparisons between groups were done using Student’s \( t \) test and multivariate logistic regression analysis. The thickness of the RNFL may be changed related to not only the visual field change but also age. The relation between visual field change and refractive error has been reported. In the present study, we selected multivariate logistic regression analysis to analyse these complicated correlating factors. Comparisons between the OAG group and normal subjects were done using multivariate logistic regression analysis (\( p \) value calculated by using the OAG group and normal subjects as dependent variables, and

<p>| Table 1 | The average of mean deviation of Humphrey field analysis in each stage of the two glaucoma groups |</p>
<table>
<thead>
<tr>
<th>Stage</th>
<th>NTG group</th>
<th>POAG group</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early stage</td>
<td>−2.42 (1.54) (n=22)</td>
<td>−2.59 (1.39) (n=21)</td>
<td>0.706</td>
</tr>
<tr>
<td>Moderately progressed stage</td>
<td>−9.42 (2.82) (n=23)</td>
<td>−10.02 (3.14) (n=17)</td>
<td>0.530</td>
</tr>
<tr>
<td>Progressed stage</td>
<td>−20.51 (4.72) (n=15)</td>
<td>−23.63 (4.88) (n=17)</td>
<td>0.079</td>
</tr>
<tr>
<td>Total</td>
<td>−9.62 (7.65) (n=60)</td>
<td>−11.38 (9.40) (n=55)</td>
<td>0.271</td>
</tr>
</tbody>
</table>

NTG = normal tension glaucoma, POAG = primary open angle glaucoma.

Comparisons between groups were done using Student’s \( t \) test. Data are reported as mean (SD).
age, refractive error, individual variable GDx p <5% or not as independent variables, and p value calculated by using the OAG group and normal subjects as dependent variables, and age, refractive error, actual value of a GDx variable as independent variables). Also comparisons between NTG and POAG groups were done using multivariate logistic regression analysis (p value calculated by using the NTG and POAG group as dependent variables, and age, refractive error, MD, individual variable GDx p <5% or not as independent variables, and p value calculated by using the NTG and POAG group as dependent variables, and age, refractive error, MD, actual value of a GDx variable as independent variables). Trend by severity was tested by Cochran-Armitage’s test. A level of p <0.05 was accepted as statistically significant. Data were reported as mean (SD).

RESULTS

Forty six of 69 normal eyes (66.7%) were diagnosed as not glaucomatous by GDx. Ninety three of 115 glaucomatous eyes (80.9%) were diagnosed as glaucomatous by GDx. The number of GDx variables with p < 5% in the 23 normal eyes diagnosed as glaucomatous by GDx were from 1 to 4, mean 2.0 (SD 1.1). Superior/nasal showed lowest specificity and highest sensitivity (Tables 3 and 4).

Table 3 shows the sensitivity and specificity of each GDx variable in all glaucomatous eyes and normal subjects. It also shows the average of each GDx variable within each group, as well as the difference between the glaucoma group and normal subjects (multivariate logistic regression analysis). The specificity of each GDx variable was symmetry: 90.0%, superior ratio: 92.8%, inferior ratio: 92.8%, superior/nasal: 87.0% max modulation: 91.3%, ellipse modulation: 91.3%, average thickness: 98.6%, ellipse average: 97.1%, superior average: 95.7%, inferior average: 98.6%, and superior integral: 100%. In average thickness, ellipse average, superior average, inferior average, and superior integral, there was no significant difference between the OAG group and normal subjects in p <5% or not (multivariate logistic regression analysis). Actual values of symmetry, average thickness, ellipse average, superior average, and superior integral showed no significant difference between normal subjects and the glaucoma group (multivariate logistic regression analysis).

Table 4 shows the sensitivity of each GDx variable in the NTG and the POAG groups. The sensitivity of superior/nasal, max modulation, ellipse modulation, and superior average was significantly lower in the NTG group than in the POAG group (multivariate logistic regression analysis). Table 3 also shows the average of each GDx variable within each group, as well as the difference between the two groups (multivariate logistic regression analysis).
logistic regression analysis). The values of average thickness, ellipse average, superior average, and superior integral were significantly lower in the POAG group than those in the NTG group.

Sensitivity for each stage of the two groups is shown in Table 5. Sensitivity of all glaucomatous eyes in early, moderately progressed, and progressed stages was 67.4%, 80.0%, and 100%, respectively with sensitivity increasing gradually with progressives stages of the disease (Cochran-Armitage’s test; p < 0.001).

**DISCUSSION**

In the present study, GDx proved moderately useful for glaucoma detection with an overall specificity of 66.7% and sensitivity of 80.9%. Because glaucomatous eyes in the present study had abnormal appearing optic discs and because abnormal appearing discs are correlated with abnormal RNFL, sensitivities might be artificially high in the present study. Actual values of symmetry, average thickness, ellipse average, superior average, and superior integral did not show a significant difference between normal subjects and the glaucoma group (multivariate logistic regression analysis). However, the overlap in RNFL thickness between normal eyes and glaucomatous eyes has been reported.7 There is also wide variation among normal individuals in the thickness of the RNFL as measured by scanning laser polarimetry,8 9–13 which may be due to differences in prenatal regression of retinal ganglion cells in individuals.14 15 In the present study, this wide variation might be the cause of the lack of significant difference between normal subjects and glaucoma patients in five of the GDx variables. Weinreb et al16 reported that using three variables of GDx (average thickness, ellipse modulation, and average ellipse thickness) resulted in sensitivity and specificity of 74% and 92%, respectively. The difference between the study of Weinreb et al16 and the present study may be because the methods of calculating sensitivity and specificity were different. Although the studies concerned with glaucoma diagnosis using scanning laser polarimeter have been reported,14 15 16–18 this is the first trial to investigate the usefulness of each original GDx variable. We arbitrarily defined the parameters for diagnosis of glaucoma in the present study; choosing the simplest application of GDx which would be most practical in non-specialty clinics. In the present study, GDx variables using an absolute value showed lower sensitivity than those using a ratio, and this was also consistent with the study of Kubota et al21 which was in Japanese glaucoma patients. These results may be due to the wide distribution of RNFL thickness data generated by the GDx for which the linear relation between corneal polarisation axis and posterior segment retardation parameters is partly responsible.21 In average thickness, ellipse average, superior average, inferior average, and superior integral there was no significant difference in p < 5% between the OAG group and normal subjects in the present study. Moreover, sensitivity of average thickness and ellipse average was 0.9% and 3.5%, respectively. Although this may be due to the overlap in RNFL thickness between normal and glaucomatous eyes, the difference in the usefulness of these two parameters in the study of Weinreb et al16 and the present study is still unclear. Differences due to race and the percentage of NTG patients might have influenced these results.

We previously reported that the relation between values for RNFL thickness obtained by scanning laser polarimetry and the visual field indices was different in NTG and POAG eyes.22 23 In the present study, the sensitivity of superior/nasal, max modulation, ellipse modulation, and superior average was significantly lower in the NTG group than in the POAG group. Also, the actual values of average thickness, ellipse

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**Table 4** Specificity, sensitivity of GDx variables in normal tension glaucoma and primary open angle glaucoma, and the difference between the two groups. Average of each GDx variable in each group and the difference between the two groups.

<table>
<thead>
<tr>
<th>Specity</th>
<th>Sensitivity in NTG</th>
<th>Sensitivity in POAG</th>
<th>Average value in NTG patients</th>
<th>Average value in POAG patients</th>
<th>p*</th>
<th>p**</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>90.0%</td>
<td>33.3%</td>
<td>25.5%</td>
<td>1.11 (0.23)</td>
<td>1.05 (0.21)</td>
<td>0.348</td>
</tr>
<tr>
<td>SR</td>
<td>92.8%</td>
<td>27.1%</td>
<td>38.2%</td>
<td>1.72 (0.34)</td>
<td>1.66 (0.41)</td>
<td>0.067</td>
</tr>
<tr>
<td>IR</td>
<td>92.8%</td>
<td>30.0%</td>
<td>41.8%</td>
<td>1.59 (0.31)</td>
<td>1.63 (0.45)</td>
<td>0.214</td>
</tr>
<tr>
<td>S/N</td>
<td>87.0%</td>
<td>48.3%</td>
<td>67.3%</td>
<td>1.54 (0.26)</td>
<td>1.45 (0.27)</td>
<td>0.043</td>
</tr>
<tr>
<td>MM</td>
<td>91.3%</td>
<td>35.0%</td>
<td>56.4%</td>
<td>0.99 (0.98)</td>
<td>0.85 (0.40)</td>
<td>0.031</td>
</tr>
<tr>
<td>EM</td>
<td>91.3%</td>
<td>35.0%</td>
<td>54.5%</td>
<td>1.39 (0.49)</td>
<td>1.39 (0.72)</td>
<td>0.027</td>
</tr>
<tr>
<td>AT</td>
<td>98.6%</td>
<td>6%</td>
<td>1.8%</td>
<td>71.3 (13.5)</td>
<td>65.6 (11.8)</td>
<td>0.755</td>
</tr>
<tr>
<td>EA</td>
<td>97.1%</td>
<td>1.7%</td>
<td>5.5%</td>
<td>71.5 (14.3)</td>
<td>66.7 (12.7)</td>
<td>0.126</td>
</tr>
<tr>
<td>SA</td>
<td>95.7%</td>
<td>3.3%</td>
<td>16.4%</td>
<td>80.1 (17.7)</td>
<td>72.2 (16.6)</td>
<td>0.018</td>
</tr>
<tr>
<td>IA</td>
<td>98.6%</td>
<td>6.7%</td>
<td>16.4%</td>
<td>75.7 (17.0)</td>
<td>71.8 (15.4)</td>
<td>0.139</td>
</tr>
<tr>
<td>SI</td>
<td>100%</td>
<td>3.3%</td>
<td>3.6%</td>
<td>0.26 (0.11)</td>
<td>0.22 (0.06)</td>
<td>0.691</td>
</tr>
</tbody>
</table>

**Table 5** Sensitivity using GDx at each stage of all glaucomatous eyes and the two glaucoma groups.

<table>
<thead>
<tr>
<th>Stage</th>
<th>All glaucomatous eyes</th>
<th>NTG group</th>
<th>POAG group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early stage</td>
<td>29/43 (67.4%)</td>
<td>14/22 (63.6%)</td>
<td>15/21 (71.4%)</td>
</tr>
<tr>
<td>Moderately progressed stage</td>
<td>32/40 (80.0%)</td>
<td>17/23 (73.9%)</td>
<td>15/17 (88.2%)</td>
</tr>
<tr>
<td>Progressed stage</td>
<td>32/32 (100%)</td>
<td>15/15 (100%)</td>
<td>17/17 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>93/115 (80.9%)</td>
<td>46/60 (76.7%)</td>
<td>47/55 (85.5%)</td>
</tr>
</tbody>
</table>

NTG = normal tension glaucoma, POAG = primary open angle glaucoma.
average, superior average, and superior integral were significantly lower in the POAG group than in the NTG group. High tension glaucomatous eyes had significantly more diffuse visual field damage than NTG eyes. The present result might indicate that diffuse RNFL loss in the POAG eyes was more easily detected in GDx, because the minimum unit calculated in most GDx variables is a quadrant and this may cause the software to fail to reflect a focal RNFL defect. Others reported that there actually is a difference in visual field defects between normal tension glaucoma and high tension glaucoma; previous reports and the present study might indicate the difference in RNFL and the different pathogenesis between the two groups. Because the number of patients diagnosed as being NTG might vary depending on race, there may be inherent error in glaucoma detection by GDx.

The GDx software has been tested in many clinical trials. GDx variables are calculated by two methods—using a total of 1500 pixels per quadrant peripheral to the ellipse 1.75 disc diameters will be calculated from a smaller pixel population. of 1500 pixels per quadrant peripheral to the ellipse 1.75 disc antigravity axis on assessment of retinal nerve fiber layer thickness by scanning laser polarimetry. Am J Ophthalmol 1999;127:305–16.


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References


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The authors have no proprietary interest in any of the equipment or materials used in this study.

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