

SCIENTIFIC REPORT

Sensitivity and specificity of scanning laser polarimetry using the GDx

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Background/aims: To determine the sensitivity and the specificity of the GDx in the detection of (1) advanced glaucoma, (2) early glaucoma, and (3) nerve fibre bundle defects (NFBD).

Methods: Group A comprised 20 eyes with reproducible glaucomatous visual field defects confirmed by octopus perimetry, group B consisted of 10 eyes with normal visual fields but either glaucomatous NFBD or deterioration of the disc over time clearly visible upon flicker comparison, and group C included 16 eyes with glaucomatous or non-glaucomatous NFBD clearly visible on red free photographs. Forty four eyes of 22 healthy volunteers served as controls. The GDx printouts of all subjects were evaluated by three independent observers in a masked fashion and without the clinical picture of the optic disc. Two of the three observers (SK, UH) were GDx experts, one (KUL) was an untrained GDx user.

Results: Among the GDx experts, sensitivity/specificity was 100%/100% (SK) and 90%/100% (UH) in detecting advanced glaucoma, and 100%/100% (SK) and 90%/100% (UH) in detecting early glaucoma. The sensitivity in detecting NFBD was only 37.5% (SK and UH). For the untrained GDx user the corresponding values were 50%/100% (group A), 20%/100% (group B), and 12.5%/91% (group C).

Conclusion: Detection of (early) glaucoma damage by the GDx, evaluated by trained experts, can be extremely high. To optimise its benefit in clinical routine training in interpreting GDx printouts is highly recommended. Detection of localised NFBD is crucial, even for experts.

The major threat from glaucoma is blindness, caused by progressive loss of retinal ganglion cell axons. This causes a decrease of the retinal nerve fibre layer (RNFL) thickness.^{1–4} Consequently the measurement of the decreasing RNFL thickness can provide important information for the early diagnosis and follow up of glaucoma. There is need for new diagnostic techniques, because it has been shown that by the time of clinical detection, 50% of the RNFL can already be lost.⁵

The GDx is a third generation nerve fibre analyser (NFA, Laser Diagnostic Technologies, San Diego, CA, USA), a scanning laser polarimeter that measures the phase shifting (retardation) of light that has double passed the birefringent fibres of the retinal nerve fibre layer (RNFL).

For the detection of glaucoma and for clinical usefulness, it is significant which stage of the disease can be detected by the device. Early diagnosis is very important for the treatment and prognosis of progressive neuropathies like glaucoma. Consequently our interest was focused on the results of the early glaucoma group. Improved diagnosis can

help prevent unnecessary prophylactic treatment and so protect the patients from side effects of their therapy. It can also lower medical expenses.

The aim of this study is to evaluate the GDx in the detection of advanced glaucoma, early glaucoma, and nerve fibre bundle defects (NFBD) and to compare the data obtained with normal controls.

METHODS

GDx

The thickness of the peripapillary nerve fibre layer was determined using the GDx Nerve Fiber Analyzer (Software Version 2.0.10). This device uses a diode laser with a wavelength of 780 nm to create the polarised laser beam.^{6–9} The thickness data are transferred into a colour coded image. Thin areas of the RNFL relate to darker colours (blue-black), thicker areas to bright colours (yellow-orange). The operator has to position a blue ellipse around the margin of the optic disc. A second green ellipse with a given magnification factor of 1.75 disk diameters is displayed automatically peripherally to the blue centre ellipse. A so called TSNIT (temporal superior nasal inferior thickness) or double hump graph is calculated from 200 points along the green ellipse (fig 1).

The thickness image is divided into four segments: superior 120° (for 0° at a 12 o'clock position: 295°–55°), nasal 70° (55°–125°), inferior 120° (125–245), and temporal 50° (245°–295°). These segments are used to calculate the different parameters of the nerve fibre analysis.

The right and left eye of each patient and each volunteer was examined six times. The pupils were undilated. The quality of all images as determined by the GDx quality check was consistently 90% or higher. The best three images, where the optic disc was centred in such a way that it could be easily aligned, were chosen to create a mean image. All images were taken by the same operator (SM). He also positioned the ellipse around the margin of the optic disc.

Patients

Eighty three eyes were examined in this study. Forty four were eyes of healthy subjects and 39 were eyes of patients from the university eye clinic. The mean (standard deviation) age of the patients was 56.15 (SD 10.56) years and of the volunteers 23.81 (SD 1.54) years. The classification into the different groups was based on nerve fibre photography, visual field defects, flicker comparison of the optic disc, and intraocular pressure. Three groups of patients were defined.

Group A (advanced glaucoma) comprised 20 eyes with reproducible glaucomatous visual field defects confirmed by Octopus perimetry, group B (early glaucoma) consisted of 10 eyes with normal visual fields but either glaucomatous nerve fibre bundle defects or deterioration of the disc over time clearly visible upon flicker comparison, and group C (nerve

Abbreviations: NFBD, nerve fibre bundle defects; RNFL, retinal nerve fibre layer; SLP, scanning laser polarimetry.

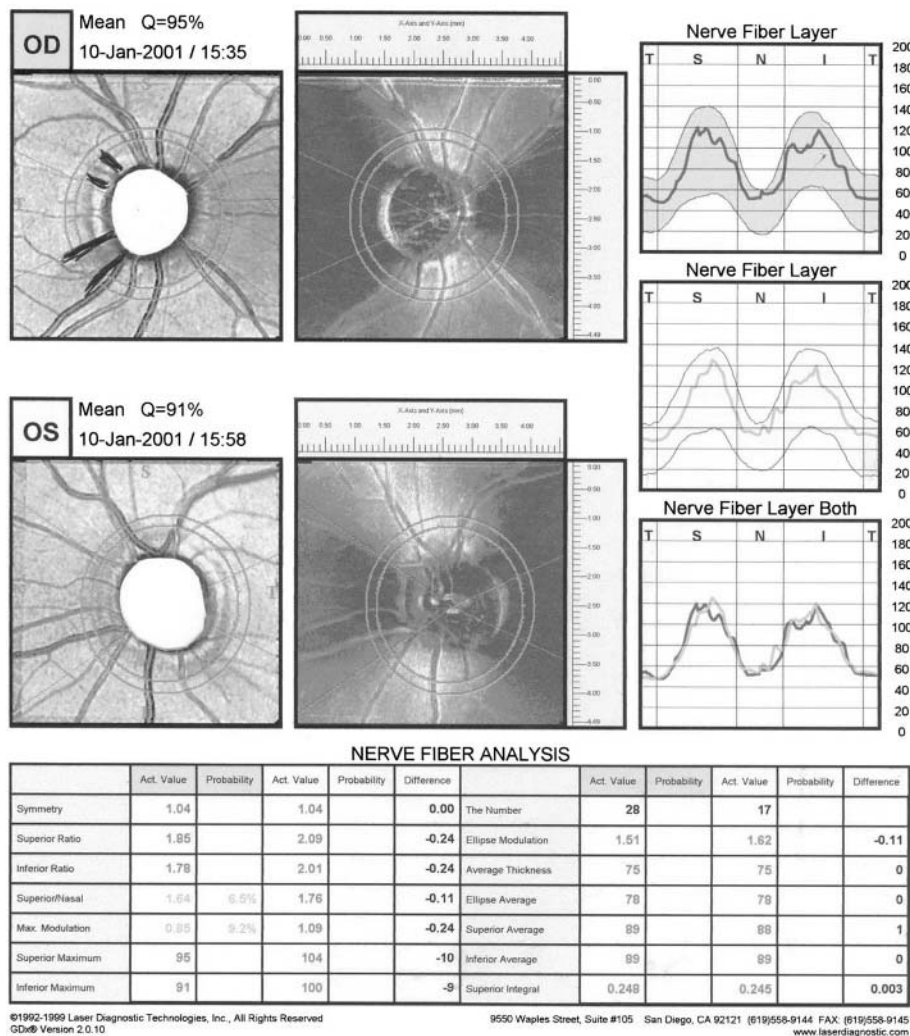


Figure 1 Example of a GDx-printout as it had to be evaluated by the three observers.

fibres bundle defects) included 16 eyes with glaucomatous or non-glaucomatous nerve fibre bundle defects clearly visible on red free photographs (fig 2). Forty four eyes of 22 healthy volunteers served as controls. None of them had visual field defects or ocular diseases.

The GDx printouts of all patients and controls were evaluated by three independent observers in a masked

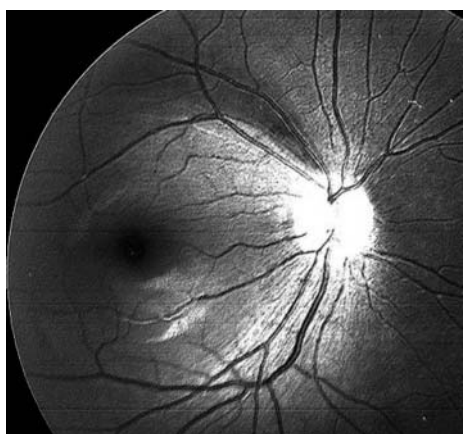


Figure 2 Example of a nerve fibre bundle defect clearly visible on red free photograph.

fashion without any personal information (for example, age, sex, race, name) and without the clinical picture of the optic disc (fig 1), in order to base the decision on the RNFL only and to make detection more difficult. The observers had to decide via a questionnaire whether or not glaucoma and/or NFBFD could be detected. If the observers could not make a diagnosis, they had the option to mark “not definable”. The printouts of the patients and controls were in random order. Two of the three observers (SK, UH) were GDx experts. Observer SK has been working for more than nine years with scanning laser polarimetry and observer UH for more than 12 years. One (KUL) was an untrained, novice GDx user with only half a year’s experience in using the GDx. This was to determine the influence of experience on the sensitivity and specificity of the GDx.

RESULTS

Expert 1’s results showed a high sensitivity and specificity of 100% among the advanced glaucoma and early glaucoma group. All of the 20 advanced and 10 early glaucomatous eyes were detected. All controls were defined as healthy. The specificity changed to 84.6%, when the eight partner eyes from the glaucoma patients were included and presumed to be normal. These eyes showed no signs of glaucomatous damage when conventional diagnostic techniques (octopus perimetry, nerve fibre photography, and flicker comparison of the optic disc) were applied.

The results of expert 2 in detecting glaucoma were similarly high: 90% sensitivity in detecting advanced and early glaucoma and 100% specificity, respectively. Eighteen of the 20 advanced and nine of the 10 early glaucomatous eyes were correctly classified, as well as all the healthy controls. On inclusion of the eight partner eyes, the specificity dropped to 86.5%.

The corresponding values for the untrained GDx user were 50% sensitivity and 100% specificity for the advanced glaucoma. For the early glaucoma 20% sensitivity and 100% specificity were found. Ten of the 20 advanced and only two of the 10 early glaucomatous eyes could be detected. The eight partner eyes were mostly considered as not glaucomatous, so the specificity including these eyes was 96.2%.

The sensitivity as far as the detection of NFBF was concerned was clearly worse. For experts 1 and 2 the sensitivity was 37.5%. Only six of the 16 NFBF were identified. Furthermore expert 1 marked three eyes and expert 2 marked 14 eyes of the patients' group as "not definable". The untrained GDx user could only find two of the 16 NFBF clearly visible on red free photographs. This corresponds to a sensitivity of 12.5%. Eleven eyes of the patients' group and three of the control group could not be defined.

DISCUSSION

This study evaluated the sensitivity and the specificity of the GDx in discriminating between advanced glaucoma, early glaucoma and normal controls, as well as its ability to detect NFBF.

Experts 1 and 2 show very good results with a 90% and 100% sensitivity and a 100% specificity in detecting early and advanced glaucoma. The high results achieved with the early glaucoma group are especially promising. Early diagnosis is the most decisive factor in reducing or preventing glaucomatous damage. It is interesting to note that most of the eight clinically healthy seeming partner eyes of the glaucoma group were considered glaucomatous by the experts. This could either indicate that the sensitivity of the GDx is higher than that of common diagnostic methods or show a high "false positive" result of the expert group.

Table 1 Glaucoma detection by the three observers (actual situation: 20 advanced glaucoma patients, 10 early glaucoma patients, 44 controls, and in parentheses the eight partner eyes without detectable glaucomatous disease from the glaucoma patients)

n = 74 (82)	Advanced glaucoma	Early glaucoma	No glaucoma
Expert 1 (SK)			
Advanced glaucoma	20	0	0 (8)
Early glaucoma	0	10	0 (0)
No glaucoma	0	0	44 (44)
Sensitivity	100%	100%	
Specificity			100% (84.6%)
Expert 2 (UH)*			
Advanced glaucoma	18	0	0 (7)
Early glaucoma	0	9	0 (0)
No glaucoma	2	1	44 (45)
Sensitivity	90%	90%	
Specificity			100% (86.5%)
Untrained GDx user (KUL)			
Advanced glaucoma	10	0	0 (2)
Early glaucoma	0	2	0 (0)
No glaucoma	10	8	44 (50)
Sensitivity	50%	20%	
Specificity			100% (96.2%)

*Two glaucomatous eyes could not be diagnosed by expert 2 and were considered as "no glaucoma".

Table 2 NFBF detection by the three observers (actual situation: 16 eyes with NFBF, 44 controls, and in parentheses 23 eyes from the glaucoma patients without detectable NFBF on red free photography)

n = 60 (83)	NFBF: yes	NFBF: no
Expert 1 (SK)		
NFBF: yes	6	0 (5)
NFBF: no	10	44 (62)
Sensitivity	37.5%	
Specificity		100% (92.5%)
Expert 2 (UH)		
NFBF: yes	6	0 (8)
NFBF: no	10	44 (59)
Sensitivity	37.5%	
Specificity		100% (88.1%)
Untrained GDx user (KUL)		
NFBF: yes	2	4 (8)
NFBF: no	14	40 (59)
Sensitivity	12.5%	
Specificity		90.9% (88.1%)

More sensitive procedures to detect deterioration over time could help to find a better and more individual therapy for ocular hypertension and early glaucoma patients. It would also allow a better prediction of the moment when they are going to convert into an advanced glaucomatous stage. Follow up studies and further clinical experience with the GDx will be necessary to find out whether it fulfils these requirements.

The results of the untrained clinical user in detecting early and advanced glaucoma were clearly worse, with 20% and 50% sensitivity.

The detection of NFBF, identified clearly on red free photographs, was very difficult for all three observers. The sensitivities of 37.5% (six of 16 NFBF, both experts) and 12.5% (two of 16 NFBF, untrained clinical user) show that the GDx is not suitable for the detection of localised NFBF.

Several studies have been published to determine the sensitivity and the specificity of scanning laser polarimetry (SLP).¹⁰⁻¹⁴ It is difficult to compare them because they used different parameters for analysis, different versions of the NFA/GDx, and different stages of glaucoma damage. One of the first studies about SLP was made with the NFA I, a predecessor of the GDx.¹¹ The authors found a sensitivity of 96% and a specificity of 93%. There were no early glaucoma patients included in the study. All the glaucoma patients had typical glaucomatous visual field defects and were scored "outside normal limits" on the glaucoma hemifield test. The calculation of the sensitivity and the specificity was performed by an objective analysis of different parameters and cut off values. Some studies also evaluated the GDx printouts in a subjective manner by using trained experts.¹⁵⁻¹⁷ The results of the expert group in our study were better than the sensitivity and specificity reported in these studies.

Nicolela *et al*¹⁶ discriminated between three different groups of glaucoma patients (advanced, localised, mixed group) and normal controls. All three groups showed visual field defects. By means of subjective evaluation 93%, 70%, and 47% of the glaucomas from the advanced, localised, and mixed groups respectively were found, and 97% of the controls were correctly identified. The best objective discrimination (different combinations of GDx parameters) identified the localised and mixed glaucoma group better, but showed a specificity of only 69%. The high degree of sensitivity by our two experts in the detection of early glaucoma confirms that the GDx is highly sensitive even for early to moderate glaucoma. Colen *et al*¹⁸ showed that a subjective clinical judgment leads to better discrimination

than the number as a standard parameter of the GDx, especially in the group with mild glaucoma.

Our study confirms that a subjective evaluation of GDx measurements performed by experienced observers can show very good results. The mean age of the control group (23.81 (SD 1.54) years) was significantly lower than the age of the patients' group (56.15 (SD 10.56) years). It is possible that the higher RNFL measurements of the control group led to the assumption that the subject was healthy and this might have positively biased the specificity. On the other hand the great interindividual variability of the RNFL that has been reported in histological measurements¹⁹ and the large overlap in RNFL measurements with SLP between normal and glaucomatous eyes²⁰ might neutralise this effect.

In other studies, one eye per subject is often randomly selected; this was not the case in our study. The comparison of both eyes (asymmetries) could have facilitated the decision of the observers. However, the fact that the age and the optic disc were masked made it more difficult to make a diagnosis.

The GDx can be a valuable additional tool in detecting glaucoma damage even at an early stage. Sensitivity and specificity in interpreting the GDx measurements can be extremely high when the evaluation is performed by trained experts, but among untrained clinical users sensitivity is poor. From these findings we conclude that training in interpreting GDx printouts can greatly improve the sensitivity and is highly recommended in order to optimise its benefits in clinical routine. However, for the detection of localised nerve fibre bundle defects the GDx is not suitable.

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