MEASUREMENT OF LARGE OPTIC DISCS USING THE NERVE FIBER ANALYZER, GDx

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Abstract

Purpose: To determine whether 'large' optic discs would benefit from a separate normative database when undergoing nerve fiber layer analysis with the scanning laser polarimeter.
Method: Scanning laser polarimetry (GDx, Laser Diagnostic Technologies, San Diego, CA) of the peripapillary retinal nerve fiber layer was used to obtain centered 15° images from 97 'large' optic discs. Discs were considered 'large' when centrally placed GDx images resulted in an error message ('not enough pixels') at the default measurement band setting of 1.75 disc diameter (DD). Other measurement band settings (1.4-1.6 DD) were tested to determine the optimal measurement band for 'large' discs, which proved to be 1.4 DD. Using 95 'normal sized' optic discs, polarimetry at 1.4 and 1.75 DD was compared, and the effect of peripapillary atrophy was assessed, to determine whether data obtained at 1.4 DD were comparable to the normative database obtained at 1.75 DD.
Results: Only at 1.4 DD could all 'large' optic discs be measured with the GDx. Of 56 GDx parameters, 27 were significantly different when 'normal sized' optic discs at 1.4 DD were compared to 1.75 DD. Exclusion of eyes with peripapillary atrophy touching the 1.4 DD measurement band still resulted in significant differences in 17 of the 56 parameters.
Conclusions: All 'large' optic discs could be measured only when the measurement band was reduced to 1.4 DD. Data obtained at 1.4 DD is not comparable to the current normative database obtained at 1.75 DD. Peripapillary atrophy may contribute to this difference, and must be considered when compiling a normative database for 'large' discs at 1.4 DD.

Introduction

In glaucoma, optic nerve fiber layer atrophy occurs concurrently with or preceding visual field loss. At present, visual field testing and clinical evaluation of the optic disc and retinal nerve fiber layer (RNFL) remain the most important tools in glaucoma diagnosis, and in following glaucomatous progression. However, these methods are subjective and qualitative in nature[1,2].

Sommer *et al.*[3] and others have reported that RNFL abnormalities are the first observable changes in patients with glaucoma, and may precede visual damage by as much as five years. Recently, promising techniques have been developed for quantification of RNFL thickness and contour[4].

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The scanning laser polarimeter is a new instrument, increasingly being used by ophthalmologists in the evaluation of glaucoma, that quantitatively estimates the RNFL thickness by measuring the change in the rotational component (retardation) of a polarized beam of laser light reflected from the fundus. The amount of rotation has been found to be proportional to the thickness of the birefringent retinal nerve fiber layer[5]. The most recent version is the GDx (Laser Diagnostic Technologies, San Diego, CA). It analyzes the data from single or averaged images by comparing them to a normative database stored in the computer memory. This data analysis occurs only when using the default measurement band setting at 1.75 disc diameter (DD), since the normative database was established at that measurement band location.

It is well known that there is large variation in human optic disc size[1,4,6]. 'Large' optic discs cannot be analyzed as reliably using the scanning laser polarimeter with the measurement band set at 1.75 DD because, at this diameter, some of the pixels needed for data analysis are missing. Some of the parameters reported by the software utilize data from 1500 pixels located peripherally to the inner edge of the measurement band; if there is insufficient image area from the measurement band to the border of the image for a 1500 pixel sample, the software reports that there are insufficient pixels for analysis. One possible solution is to choose a smaller measurement band diameter, such as 1.4 DD for these 'large' discs. However, it is not known whether this solution would enable analysis of most 'large' discs and whether normative data collected at the usual measurement band diameter of 1.75 DD is applicable to 1.4 DD patient data. We designed a study to determine whether images analyzed with the measurement band located at 1.4 DD were comparable to those with the measurement band located at 1.75 DD.

Subjects and methods

One hundred and thirty-five of the 373 glaucomatous patients and normal subjects in the GDx computer database at the University of Washington Eye Center were found to have 'large' optic discs. Discs were considered 'large' when the GDx displayed the message, 'not enough pixels' (Fig. 1) when attempting analysis using the measurement band of 1.75 DD. The remaining 238 glaucomatous patients and normal subjects had 'normal sized' optic discs, since the GDx did not display 'not enough pixels' when attempting analysis at the same measurement band.

All the images in the database had been obtained after patients had given informed consent, and were acquired with the patient sitting in an upright position with undilated pupils in a non-darkened room. The eye was centered on the 15×15° field of view (256×256 pixels) by using the LED fixation device attached to the GDx. Three images were obtained from each eye.

For our study, we chose 97 images from the 'large' optic discs group of 135 glaucomatous patients and normal subjects. Images were chosen only when the optic discs were centrally placed in the image to ensure that 'large' optic discs were chosen due to disc size and not to improper technique. Then, 95 images of 'normal sized' optic discs were chosen from the 238 glaucomatous patients and normal subjects to match the number of 'large' optic discs, again selecting only images with well-centered optic discs.

The 192 images of normal and glaucomatous eyes for our study had been obtained

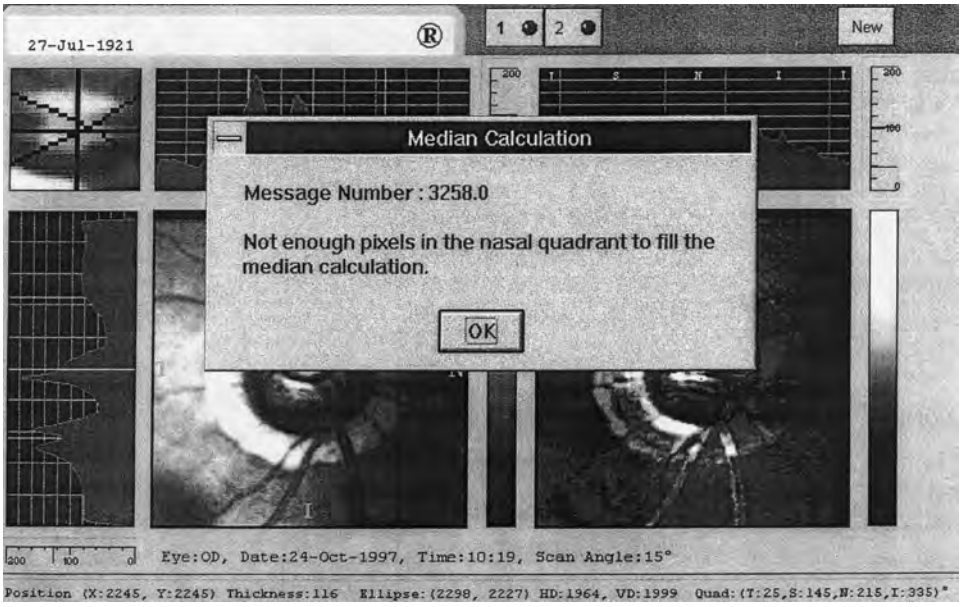

Fig. 1. Error message displayed when attempting analysis of a large disc with insufficient pixels in the nasal quadrant peripheral to the inner edge of the default 1.75 DD measurement band.

from 125 subjects, 59 of whom were normal with a corrected Snellen visual acuity of 20/20, intraocular pressure of less than 21 mmHg, and no history of eye disease. Sixty-six patients had glaucoma diagnosed clinically by glaucomatous optic disc changes and by using the Humphrey Field Analyzer (Humphrey Instruments, Inc.) 24-2 program with glaucomatous field damage and a mean deviation of -6dB or more.

The 97 'large' optic discs (33 females 32 males; age range 25-93 years) were imaged from 32 normal subjects and 33 glaucomatous patients, 43 of whom were white, 16 Asian, three black, and three Hispanic. Measurement bands located at 1.6, 1.5, and 1.4 DD were used on these optic discs to find the optimum location for the measurement band.

The 95 'normal sized' optic discs (31 females, 30 males; age range 25-93 years) were imaged from 27 normal subjects and 33 glaucomatous patients, 27 of whom were white, three Asian, three black, and one Hispanic. Of 95 'normal sized' optic disc images, 54 resulted from an averaging of three images, eight resulted from an averaging of two images, and 33 were single images. As a matter of course during patient imaging, three images adequate for averaging were obtained. However, for the purposes of this study, we discarded all images that were not optimally centered, resulting in some single and some averages of two.

Polarimetric retardation data were analyzed from 'normal sized' optic discs using measurement bands located at 1.4 and 1.75 DD from the disc margin. The 50 parameters (Table 1) comprising the full standard 'glaucoma analysis' printout provided by the GDx were used. Six additional parameters (two ratio, two maximum modulation, and two region modulation parameters) were also calculated in an external computer analysis routine from the average retardation values obtained from sixteen 22.5° sectors of the measurement band. The ratio parameters (Ra) were obtained from the sum

Table 1. Fifty standard analysis parameters automatically calculated by the GDx

Five integral nerve fiber layer thickness values (total polar, superior, temporal, inferior, nasal integral)
Five average values of nerve fiber layer thickness (total polar, superior, temporal, inferior, nasal average)
Five integral nerve fiber layer thickness above blood vessels (total polar, superior, temporal, inferior, nasal integral)
Five average values above blood vessels (total polar, superior, temporal, inferior, nasal integral)
Six integral thickness ratios (superior/nasal, inferior/nasal, temporal/nasal, superior/inferior, superior/temporal, inferior/temporal)
Six average thickness ratios (superior/nasal, inferior/nasal, temporal/nasal, superior/inferior, superior/temporal, inferior/temporal)
Four nasal normalized average thickness ratios (superior, temporal, inferior, nasal)
Four temporal normalized average thickness ratios (superior, temporal, inferior, nasal)
Four maximum/median thicknesses (superior maximum, inferior maximum, temporal maximum, nasal median)
Six maximum/median ratios (superior maximum/inferior maximum, superior maximum/temporal median, inferior maximum/temporal median, superior maximum/nasal median, inferior maximum/nasal median, temporal median/nasal median)

of the five 22.5° sectors in the superior (RaSN) or inferior (RaIN) region divided by the sum of the three 22.5° sectors in the nasal region. The four modulation parameters (Mod) were each derived from the minimum retardation (across a 22.5° sector) in the nasal and temporal regions averaged to create a 'baseline' value. This baseline was then subtracted from the maximum 22.5° sector retardation value in the superior (MxModS) and inferior (MxModI) regions, and five times the 'baseline' value was subtracted from the sum of the five 22.5° sector retardation values in the superior (ReModS) and inferior (ReModI) regions. These six parameters were used by Xu *et al.*[7], except that 10° sector widths were used. We used the default values of 22.5° sectors to simplify the analysis routine.

Data from 95 'normal sized' optic discs obtained at the 1.4 DD measurement band were compared with data obtained from the 1.75 DD measurement band to determine whether data from the 1.4 DD measurement band were comparable with the normative database obtained from the 1.75 DD measurement band. This was repeated after the exclusion of 'normal sized' optic discs in which peripapillary atrophy touched or overlapped the measurement band located at 1.4 DD. The data were analyzed using Student's *t* test.

We also compared 48 'large' optic discs from 32 normal subjects (analyzed in spite of the warning message, 'not enough pixels', at the default measurement band of 1.75 DD, to the normative database to determine whether the parameters would still be normal even with the loss of pixels. We used the 14 parameters from the GDx printout called 'advanced normals analysis' for this comparison (Fig. 2). A parameter was considered abnormal when the GDx displayed the designation 'borderline' or 'outside normal'.

From the 373 subjects in our GDx computer database, we calculated the number of subjects with optic discs in which peripapillary atrophy affected the 1.4 DD measurement band. Also, from the 238 'normal sized' optic disc subjects, we calculated the number of subjects with optic discs affected by peripapillary atrophy at the 1.75 DD measurement band. This was done to see how many subjects could be analyzed at each of the measurement band diameters.

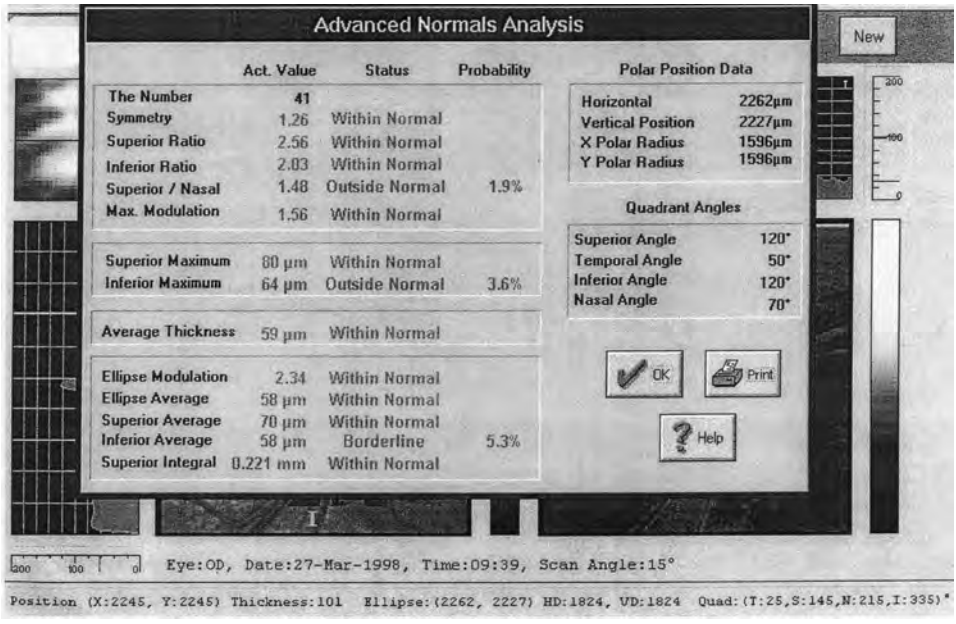

Fig. 2. Printout entitled 'advanced normals analysis' with 14 calculated parameters used to compare large discs from normal patients against the normative database at the default 1.75 DD measurement band setting. A parameter was considered abnormal if it displayed either 'outside normal' or 'borderline' in the status column.

Results

We tried to find a measurement band that could be used to reliably measure 'large' optic discs without encountering the warning message, 'not enough pixels'. When measurement bands of 1.6, 1.5, 1.4 DD were used, 31, 61 and 97 of the 97 optic discs, respectively, could be measured without the error message, showing the variation in the size of optic discs in the 'large' optic disc group (Table 2).

At the 1.4 DD measurement band setting, all 'large' optic discs could be measured without encountering the warning message 'not enough pixels'. Therefore, we obtained data from 'normal sized' optic discs at the 1.4 DD measurement band and compared them with the data from the same group obtained at the default measurement band of 1.75 DD, to see if they were comparable. We found that 21 the 50 standard GDx parameters and six externally calculated parameters separately analyzed were significantly different ($p<0.05$). When the analysis was repeated with the exclusion of the 53 optic discs (20 normal, 33 glaucomatous) with peripapillary atrophy that were touching or within the measurement band located at 1.4 DD, 11 of the 50 standard GDx parameters and all the six externally calculated parameters were significantly different.

When the 48 'large' optic discs from 32 normal subjects were compared to the normative database at the default measurement band of 1.75 DD, 38 'large' optic discs from 29 normal subjects were found to have at least one of the 14 'advanced normals analysis' parameters showing an abnormal result.

Table 2. Behavior of different measurement band diameters on images of large optic discs that do not have sufficient pixels peripheral to the inner edge of the measurement band for optimal analysis at the default setting of 1.75 DD

Disc diameter	*Number of large discs (n=97) with sufficient pixels for analysis peripheral to inner edge of the measurement band*	*Large discs (n=97) with peripapillary atrophy touching or overlapping the measurement band*
1.6	31	1
1.5	61	18
1.4	97	43

Of the 373 subjects in our GDx computer database, 135 had 'large' optic discs and 51 of the remaining 283 subjects had peripapillary atrophy affecting the 1.75 DD measurement band. At the 1.4 DD measurement band setting, we found 183 of the 373 subjects had peripapillary atrophy touching or within the measurement band.

Discussion

The images for our study were chosen only when the optic discs were optimally centered. Therefore, it was not possible for all analyzed images to be an average of three separate images since, in some patients, some of the images in a group of three were not well centered. Data from an average of three images have been found in previous studies to reduce interoperator and intraoperator variability in serial image sessions[8]. The inclusion of some single and some two-image averages should be of minor importance since our analysis of the normal discs made comparisons of different measurement band sizes within a single image.

At present, the GDx nerve fiber analyzer software reports difficulty analyzing patients with 'large' optic discs since, at the default measurement band setting of 1.75 DD, insufficient pixels are located peripherally to the inner border of the measurement band. This results in an error message which, if ignored, causes most of the normal subjects with 'large' optic discs to be flagged as abnormal on the resulting analysis. Of the 48 normal discs classified as 'large', 38 were statistically abnormal on one or more of the analysis parameters. Therefore, to be able to analyze all 'large' optic discs with GDx software, a smaller measurement band has to be used.

Using a 1.4 DD measurement band, all 'large' optic discs can be measured, but data obtained with a 1.4 DD measurement band are not comparable with the normative database obtained at the 1.75 DD measurement band. Many parameters (21 of the 50 standard GDx and the six externally calculated parameters) were significantly different ($p<0.05$). There are several reasons why so many parameters may have been significantly different:

1. With increasing radius from the optic disc, there is an increase in total cross-section of the retinal nerve fiber layer in histological specimens[3]. This would result in an increase in the integral parameters[7], and could explain why four of the five integral parameters used in our study were significantly different between 1.4 DD and 1.75 DD measurement bands. The increase in the total cross-section of the retinal nerve fiber

layer with increasing radius may not be proportionate in different quadrants because five of the six integral ratio parameters (superior/nasal, inferior/nasal, temporal/nasal, superior/temporal, inferior/temporal) were significantly different.

2. Retinal nerve fiber layer thickness and mean retardation decrease with increasing radial distance from the optic disc area, and this is especially evident in the superior and inferior quadrants[2,9-11]. We found that only one of the five mean sector value parameters (temporal) was significantly different. However, five of the six mean ratio parameters (superior/nasal, inferior/nasal, temporal/nasal, superior/temporal, inferior/temporal) were significantly different, similar to the findings with the integral ratios.

3. Studies have shown that the optic nerve fiber count is directly proportional to the optic disc size[8,12]. This may mean that 'large' optic discs may have more nerve fibers than 'normal sized' discs and are therefore not comparable. This would mean that these two groups should not use the same normative database. However, Anton *et al.*[6] found no association between retardation and optic disc area when they analyzed 62 subjects (24 normal subjects and 38 patients with ocular hypertension), although the study does not describe the range of the optic disc sizes measured.

4. The measurement band located at 1.4 DD may not be uniformly useful because retardation artifacts are more common immediately adjacent to the disc margin, which causes reflected light to be scattered away from the incident beam, and the polarization effect may not be as strong.

5. Peripapillary retinal atrophy was found to be present in some of the normal subjects and glaucomatous patients in our study. Fifty-three of the 95 'normal sized' optic discs had peripapillary atrophy touching or located within the measurement band located at 1.4 DD. Studies show high retardation measurements occurring in these areas[9,11] because of high scleral reflectivity[13], causing increasing variability.

When we repeated our data analysis (data from the 1.75 DD measurement band versus data from the 1.4 DD measurement band), after the exclusion of 'normal sized' optic discs with peripapillary atrophy affecting the 1.4 DD measurement band, 17 parameters (11 of the 50 standard GDx and six externally calculated parameters) were significantly different. This compares to 27 (21 of the 50 standard GDx and six externally calculated parameters) if discs with peripapillary atrophy were not excluded, showing that while peripapillary atrophy may have had some deleterious effect there are other factors that still need to be considered.

Using the default measurement band of 1.75 DD for analysis on the 373 subjects in our GDx computer database, 186 (50%) had mean images which were not optimal for analysis (135 subjects with 'large' optic discs and 51 of the remaining 238 subjects affected by peripapillary atrophy). If the current measurement band of 1.75 DD were changed to 1.4 DD for all subjects, all the 'large' optic discs would have sufficient pixels for analysis. However, the number of subjects with optic discs affected by peripapillary atrophy would increase to 183. Therefore, at the 1.4 DD measurement band setting, 49% (183 of the 373) of the glaucomatous patients and normal subjects would not be optimal for analysis.

When we used two different measurement bands, 1.75 DD for the 'normal sized' optic disc subjects and 1.4 DD for the 'large' optic disc subjects, 51 of the 135 and 62 of the 238 subjects, respectively, had peripapillary atrophy affected at each of the measurement bands. Therefore, only 113 of the 373 subjects (30%) would not be optimal for analysis. This would mean that we could analyze 20% more patients than by using the current method with a single measurement band diameter.

The nerve fiber analyzer has been found to be reliable in providing quantitative measurements that correspond to known properties of the RNFL in normal and glaucomatous eyes[9]. It is a promising new instrument that will be in routine clinical use in the near future. From our study, we conclude that, by establishing another normative database at the 1.4 DD measurement band, in addition to the current 1.75 DD measurement band, for use in the 'large' optic disc patients, we could increase the patient population that can be optimally analyzed from 50% to 70%.

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