Scanning laser polarimetry in glaucomatous and nonglaucomatous Brazilian subjects

Polarimetria de varredura a laser em grupos de brasileiros glaucomatosos e não glaucomatosos

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ABSTRACT

Purpose: To compare the results of scanning laser polarimetry of the retinal nerve fiber layer obtained by using the GDx Scanning Laser System® in primary open angle glaucoma (POAG) and nonglaucomatous Brazilian subjects over 40 years, also analyzing the differences between the data obtained from right and left eyes. **Methods:** Forty-six POAG patients and 44 normal subjects were enrolled in this study. Retardation data were assessed by the GDx Scanning Laser System®. The medians of the parameters printed in the result were compared in these two groups, separately in the right and left eyes, using Mann-Whitney's test. Also the frequencies of outside normal parameters and quadrants of deviation from normal graph were compared in these two groups, using chi-square or Fisher's exact test. **Results:** All parameters obtained by GDx differed in a statistically significant way between the two groups, except symmetry for left eyes. The frequency of inferior quadrant with $p<5\%$ regarding deviation from normal graph was higher in the glaucomatous group. The most frequent outside normal limits parameters in the glaucomatous group were: maximal modulation, ellipse modulation, superior average and inferior average. All parameters except symmetry and superior/nasal differed between right and left eyes in the nonglaucomatous group. **Conclusion:** The parameters obtained by GDx are different in normal and glaucomatous subjects of that population. There are some parameters that deviate from normal values with a greater frequency in glaucomatous patients. An evident difference between the data of right and left eyes of normal subjects in this group was also observed.

Keywords: Glaucoma; Nerve fibers; Retina/pathology; Ophthalmological diagnostic technics; Perimetry

INTRODUCTION

Retinal nerve fiber layer (RNLF) analysis has been investigated for early glaucoma diagnosis[1]. Some studies suggest that RNFL loss precedes visual field defects by years[2-3] and showed that RNFL defects could be detected in fundus photography five to ten years before visual field abnormalities[3]. However fundus photography used for RNFL analysis has some technical limitations such as subjectivity of the examiner and difficulties caused by medium opacities[4].

In this regard some devices have been developed in order to detect and quantify early RNFL loss[5]. One of them is based on RNFL birefringence. This technique uses a polarized light with confocal laser technology that

passes through the nerve fiber layer (retardation) and is called polarimetry[5]. This retardation has been correlated with RNFL thickness in histopathologic studies[6].

The GDx Scanning Laser System®, Laser Technologies, San Diego, CA, USA is a scanning laser polarimeter that comprises a software, which is based on data obtained in previous studies. It provides parameters which are indicated as normal, borderline or outside normal, when the software compares the database with the data obtained from a suspect patient[7]. The actual value of the parameters provided by this software in detecting glaucoma and whether the results are similar in different populations are questions still under investigation.

Weinreb et al., in1998, observed that by adding outside normal parameters, the sensitivity and specificity of the glaucoma diagnosis test are increased, and the most important parameters in a study were ellipse modulation, average thickness and ellipse average[8].

The aim of this study was to analyze the results obtained by the software that comprises the GDx Scanning Laser System®, in a group of primary open angle glaucoma patients and nonglaucomatous subjects of a Brazilian population over 40 years, and also to compare the results obtained on right and left eyes.

METHODS

The study protocol was approved by the Ethics Committee of the Hospital São Paulo and an informed consent was obtained from all participants after the nature of the study had been explained (#181/98).

Nonglaucomatous subjects

Forty-four volunteers were enrolled in this study. Inclusion criteria were: age of 40 years or over, no history of eye disease, except refractive error (eyes with spherical equivalent exceeding +6.00 or –6.00 D were excluded[9-10], intraocular pressure (IOP) of 20 mmHg or less on three different occasions, no prior eye surgery, open angle, no abnormalities on biomicroscopy and dilated fundus examination, cup to disc ratio of 0.4 or less and normal visual fields.

The visual field was tested with a Humphrey® Field Analyzer (HFA), Zeiss Humphrey System, Dublin, CA, USA using a full-threshold 24-2 examination, and was considered normal when it included acceptable reliability, GHT and CPSD within normal limits and not more than two contiguous depressed points in the pattern deviation graph (p<5%).

Glaucomatous patients

Forty-six primary open angle glaucoma patients were recruited from the Glaucoma Section of the Department of Ophthalmology of the Universidade Federal de São Paulo. Inclusion criteria were: age of 40 years or over, IOP greater than 20 mmHg, cup to disc ratio 0.5 or more, no prior eye surgery, open angle, no other abnomalities at biomicroscopy nor dilated fundus examination and abnormal visual field (acceptable reliability, three or more depressed contiguous nonperipheral points in the pattern deviation graph (p<5%), GHT outside normal limits and CPSD with p<0.5%).

There was no statistically significant difference between the mean age of normal and glaucomatous subjects. Demographic data are summarized in table 1. Table 2 shows that there was a statistically significant difference between visual field parameters and cup/disc ratio of the two groups.

Thirty-four right eyes and 32 left eyes from the glaucomatous group met the inclusion criteria, while 42 right eyes and

Table 1. Patient demographic data		
	Glaucomatous	**Nonglaucomatous**
Age (years)	61	59
(± SD; range)	(±11,6; 41 to 90)	(±12,1; 40 to 87)
Sex	27 (59%) F	36 (82%) F
	19 (41%) M	8 (18%) M
Race	19 (41%) W	29 (66%) W
	24 (52%) B	15 (34%) B
	3 (7%) Y	0 Y
F= female; M= male; W= white; B= black; Y= Asian		

Table 2. Visual field parameters and cup/disk ratios				
	Glaucomatous		**Nonglaucomatous**	
	OD	**OS**	**OD**	**OS**
MD (dB)	-12.10	-13.00	-2.60	-3.00
(± SD)	(± 8.50)*	(± 8.20)*	(± 2.40)*	(± 2.30)*
CPDS	5.80	6.30	1.00	1.40
(± SD)	(± 3.20)*	(± 3.00)*	(±0.70)*	(±1.10)*
Cup-to-Disc Ratio: Vertical				
0.1 – 0.4	0 (0)*	0 (0)*	39 (93%)*	37 (95%)*
0.5 – 0.7	13 (36%)*	13 (38%)*	3 (7%)*	2 (5%)*
0.8 – 1.0	23 (64%)*	21 (62%)*	0*	0*
Total	36 (100%)	34 (100%)	42 (100%)	39 (100%)
Mean Cup-to-Disc: Vertical (± SD)	0.79 (±0.14)*	0.78 (±0.14)*	0.31 (±0.12)*	0.30 (±0.11)*
*Statistically significant difference between glaucomatous and nonglaucomatous subjects				

39 left eyes from nonglaucomatous group were included. The more important eye exclusion reasons were: presence of absolute glaucoma or phthisis, cataracts and pseudophakia. These reasons are listed in Table 3 for the glaucomatous and nonglaucomatous groups.

Nerve fiber layer data

The retardation data were obtained by the GDx Scanning Laser System®, Laser Diagnostic Technologies, Inc., San Diego, CA, USA in a room with constant illumination, before pupil dilation and all measurements were performed by the same trained examiner. Three images were obtained from each eye to create a mean image, as follows: the examiner traced an ellipse around the scleral limit of the disc and then the program performed the analysis. In accordance with the manual published by the manufacturer, the polarimetric data were obtained from a scanned area of 256 X 256 pixels and each pixel correlated with a value by the software. The software also creates an ellipse that comprises 1.75 diameter of the initial ellipse traced by the examiner and the data obtained in the scanned area are divided into superior, inferior, temporal and nasal quadrants to perform the calculation of the parameters. The parameters used in the current analyses were those shown in the printed result, that are: symmetry, superior ratio, inferior ratio, superior/nasal, maximal modulation, ellipse modulation, average thickness, ellipse average, superior average, inferior average, superior integral, deviation from normal graph[7]. The number was not used in this analysis.

Statistical Analysis

Mann-Whitney's test was used to test the homogeneity of the two groups in regard to age. The Wilcoxon test was used to compare RNFL measurements of right and left eyes in both groups. Mann-Whitney's test was applied in order to compare the obtained values of the parameters of the two groups. The frequency of outside normal parameters and quadrants of the deviation from normal graph, as determined by the software, in both groups was also analyzed by chi-square or Fisher's exact test.

RESULTS

Almost all parameters included in the result of GDx showed a statistically significant difference between glaucomatous and nonglaucomatous subjects in this study, except the symmetry parameter for left eyes (Table 4).

Table 5 shows that the frequency of parameters outside normal was significantly higher in the glaucomatous group regarding these parameters for both eyes: maximal modulation (for right eyes 30% of this parameter was shown as outside normal in the glaucomatous group and 9% in the nonglaucomatous, 35% and 5% in the glaucomatous and the nonglaucomatous groups respectively for left eyes), ellipse modulation (19% and 2% for right eyes, 12% and 0 for left eyes), superior average (11% and 0 for right eyes, 15% and 0 for left eyes) and inferior average (22% and 0 for right eyes, 23% and 0 for left ones).

Table 6 shows that the frequency of quadrants outside normal ($p<5\%$) in the glaucomatous group was significantly higher in the inferior quadrant for both eyes (30% of the inferior

Table 3. Excluded eyes in glaucomatous and nonglaucomatous group

	Glaucomatous n=46		Nonglaucomatous n=44	
	OD n=36	OS n=34	OD n=42	OS n=39
Absolute glaucoma or Phthisis	3	6	0	0
Cataracts	3	2	1	1
Visual field did not match the inclusion criteria	0	2	0	0
Fundus venous occlusion	2	1	0	0
Previous trabeculectomy	1	1	0	0
Pseudophakia	1	0	1	4
Total	10	12	2	5

Table 4. Medians of the parameters of GDx: statistical significance of observed differences

	Gl OD (n= 36)	NonGl OD (n=42)	P* (OD)	Gl OS (n=34)	NonGl OS (n=39)	P* (OS)
Symmetry	1.18	1.06	0.019**	1.02	1.00	1.000
Superior ratio	1.94	2.62	0.014*	1.50	2.13	0.000*
Inferior ratio	1.70	2.55	0.000*	1.51	2.12	0.000*
Superior/nasal	1.54	1.91	0.000*	1.65	2.19	0.000*
Maximal modulation	1.07	1.37	0.000*	0.93	1.37	0.000*
Ellipse modulation	1.90	2.80	0.000*	1.76	2.41	0.000*
Average thickness	64.50	68.00	0.014*	61.00	66.00	0.015*
Ellipse average	63.00	71.50	0.000*	60.00	70.00	0.000*
Superior average	68.00	80.00	0.000*	64.50	74.00	0.000*
Inferior average	63.50	83.50	0.000*	66.50	80.00	0.000*
Superior integral	0.19	0.22	0.020*	0.18	0.21	0.012*

* Statistically significantly higher in nonglaucomatous eye; **Statistically significantly higher in glaucomatous eye; Gl= Glaucomatous; NonGl= Nonglaucomatous

quadrants were outside normal in the glaucomatous group and 2% in the nonglaucomatous for right eyes, 20% in the glaucomatous and 3% in the nonglaucomatous for left eyes).

Table 7 shows that the values of the parameters differ in a statistically significantly way between right and left eyes in the nonglaucomatous group, except symmetry and superior/nasal. This difference was not detected in the glaucomatous group, except for the superior ratio. The glaucomatous paired eyes were also stratified for initial, moderate and severe glaucomatous visual field loss (MD ≤ -10 dβ, n=3; -10 dβ < MD ≤ -20 dβ, n=4 e MD ≥ -20 d≤, n=3 respectively) and still no difference between the parameters of right and left eyes was observed.

DISCUSSION

It is well documented that racial differences exist in the appearance of the normal optic nerve[9,11-13]. Using prior versions of polarimeters it was also observed that racial differences are seen in the retardation data from RNFL[14-15].

The GDx software contains a database developed in an American population. The software has the aim to differentiate glaucomatous from normal subjects, but it is based on a specific population.

In urban Americans, Germans and Japanese the retardation data differ between normal and glaucomatous subjects[16-20].

Table 5. Frequency of outside normal parameters

	GI OD	%	NonGI OD	%	GI OS	%	NonGI OS	%
Symmetry	13*	36	3*	7	9	26	6	15
Superior ratio	4	11	2	5	17**	50	4**	10
Inferior ratio	6	17	2	5	20**	59	7**	18
Superior/nasal	20*	55	8*	19	6	18	2	5
Maximal modulation	11*	30	4*	9	12**	35	2**	5
Ellipse modulation	7*	19	1*	2	4**	12	0**	0
Average thickness	0	0	0	0	0	0	0	0
Ellipse average	3*	8	0*	0	2	6	0	0
Superior average	4*	11	0*	0	5**	15	0**	0
Inferior average	8*	22	0*	0	8**	23	0**	0
Superior integral	0	0	0	0	3	9	2	5

*Statistically significantly more frequent in glaucomatous right eyes; **Statistically significantly more frequent in glaucomatous left eyes; GI= Glaucomatous; NonGI= Nonglaucomatous

Table 6. Frequency of quadrants outside normal in the "deviation from normal graph"

	GI OD	%	NonGI OD	%	GI OS	%	NonGI OS	%
Superior quadrant	3	8	0	0	8**	20	0**	0
Nasal quadrant	0	0	0	0	0	0	0	0
Inferior quadrant	11*	30	1*	2	8**	20	1**	3
Temporal quadrant	0	0	0	0	0	0	0	0

*Statistically significantly more frequent in glaucomatous right eyes; **Statistically significantly more frequent in glaucomatous left eyes; GI= Glaucomatous; NonGI= Nonglaucomatous

Table 7. Medians of the parameters of GDx. Comparison between right and left eyes by Wilcoxon's test

	GI OD (n= 23)	GI OS (n=23)	P	NonGI OD (n=37)	NonGI OS (n=37)	P
Symmetry	1.18	1.02	0.153	1.06	1.00	0.688
Superior ratio	1.94	1.50	0.002*	2.62	2.13	0.000*
Inferior ratio	1.70	1.51	0.200	2.55	2.12	0.005*
Superior/nasal	1.54	1.65	0.256	1.91	2.19	0.154
Maximal modulation	1.07	0.93	0.135	1.37	1.37	0.002*
Ellipse modulation	1.90	1.76	0.649	2.80	2.41	0.006*
Average thickness	64.50	61.00	0.398	68.00	66.00	0.000*
Ellipse average	63.00	60.00	0.869	71.50	70.00	0.000*
Superior average	68.00	64.50	0.554	80.00	74.00	0.003*
Inferior average	63.50	66.50	0.269	83.50	80.00	0.007*
Superior integral	0.19	0.18	0.230	0.22	0.21	0.000*

* Statistical significance P<0.005. Paired eyes: Glaucomatous n=23; nonglaucomatous n=37. GI= Glaucomatous; NonGI= Nonglaucomatous

Also these differences were previously described in a Brazilian population[21-22]. In agreement with those prior studies all parameters calculated based on the polarimetric data obtained by GDx differ between normal and glaucomatous eyes of individuals from the analyzed population, except the symmetry parameter for left eyes.

The fact that symmetry did not differ between glaucomatous and nonglaucomatous subjects was in agreement with other authors' findings[17,22-23]. In agreement with our result, it was also observed that all the variables provided by the software differ significantly between eyes of patients with glaucomatous perimetric abnormalities and control subjects, except the "superior/inferior" ratio[24].

In this study the parameters that are more frequently shown as outside normal in both eyes of glaucomatous subjects are maximal modulation, ellipse modulation, superior average and inferior average.

The presence of inferior quadrant in the deviation from normal graph suggests glaucomatous loss. Temporal and nasal quadrants do not seem to play an important role in differentiating glaucomatous from normal subjects in this population. This finding is consistent with the results of a previous study[24]. It was also seen that superior and inferior quadrants did correlate with results of psychophysical tests in glaucomatous subjects. This result was not observed in nasal and temporal quadrants[24].

A statistically significant difference between the data obtained from right and left eyes of nonglaucomatous subjects was observed. This difference was not expected to be significant, because it is well known that fellow eyes have some degree of correlation. However this finding is consistent with those previously reported in studies performed with other methods of RNFL analysis[25].

It was also observed that intraindividual differences between the nerve fiber layer are not uncommon, maybe due to nonconnection of some ganglion cells to the respective cerebral nuclei during the early period of life[26].

On the other hand, it was shown that in normal subjects, retardation data obtained with GDx in fellow eyes are highly correlated, but data obtained from some specific NFL regions differ between right and left eyes. The authors attribute these findings to artifacts in the measurements[27].

This is a real possibility because it is well documented that inter- and intraindividual variations in the corneal axis polarization could influence in the RNFL polarization data aquisition by the polarimeter[28,29].

In glaucomatous eyes no differences were observed between the majority of measurements obtained from right and left eyes, probably due to some advanced cases (52,86% of the glaucomatous eyes had moderate to severe visual field loss), which could have masked some possible existing difference observed in the nonglaucomatosous eyes. On the other hand, the difference was not seen also in the group of paired eyes with initial visual field loss, but we should consider that this sample was limited (n=3). Further studies are necessary to elucidate if differences between right and left eyes are seen in glaucomatous patients.

CONCLUSIONS

In conclusion, in a Brazilian population over 40 years the parameters obtained by the GDx differ between normal and glaucomatous eyes and this finding is in agreement with other studies. The presence of some parameters, such as maximal modulation, ellipse modulation, superior average, inferior average or inferior quadrant of the deviation from normal graph, assigned as outside normal, may suggest glaucomatous damage. Some asymmetry between right and left eyes in normal subjects was observed by the GDx results. These asymmetries, in our opinion, were probably due to artifact and should be considered when using this instrument for developing scientific clinical studies, in order to avoid creating unintentional bias.

RESUMO

Objetivos: Comparar os resultados da polarimetria de varredura a laser da camada de fibras nervosas obtidas por meio do GDx Scanning Laser System® em brasileiros portadores de glaucoma primário de ângulo aberto e indivíduos não glaucomatosos acima de 40 anos, analisando também as diferenças obtidas entre olhos direitos e esquerdos. **Métodos:** Foram incluídos neste estudo 46 pacientes portadores de glaucoma primário de ângulo aberto e 44 pacientes normais. Os dados de retardo polarimétrico foram obtidos por meio do GDx Scanning Laser System®. As medianas dos parâmetros impressos no resultado foram comparadas nesses dois grupos, separadamente para olhos direitos e esquerdos, usando o teste de Mann-Whitney. A freqüência de parâmetros impressa como fora da normalidade e quadrantes estatisticamente alterados do gráfico "deviation from normal" foram comparados nesses dois grupos usando chi-quadrado e o teste exato de Fischer. **Resultados:** Todos os parâmetros obtidos pelo GDx diferiram de maneira estatisticamente significante entre esses dois grupos, exceto simetria nos olhos esquerdos. A freqüência do quadrante inferior com p<5% no gráfico "deviation from normal" foi maior no grupo glaucomatoso. Os parâmetros mais freqüentemente registrados como fora da normalidade no grupo glaucomatoso foram: modulação máxima, modulação da elipse, média superior e média inferior. Todos os parâmetros

exceto simetria e nasal/superior diferiram entre olhos direitos e esquerdos no grupo de indivíduos não glaucomatosos. **Conclusão:** Os parâmetros obtidos pelo GDx diferiram entre glaucomatosos e normais desta população. Alguns parâmetros desviaram da normalidade com maior freqüência no grupo de glaucomatosos. Foi observada diferença evidente entre olhos direitos e esquerdos de indivíduos não glaucomatosos nesse grupo.

Descritores: Glaucoma; Fibras Nervosas; Retina/patologia, Técnicas de diagnóstico oftalmológico, Perimetria

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