INTRODUCTION

Diffuse unilateral subacute neuroretinitis (DUSN) is an ocular disease caused by a nematode(1). It affects the retina, especially the posterior pole, and is one of the main causes of unilateral blindness in Northeast Brazil(2). The clinical course is characterized by periods of activity and remission. The acute phase consists of focal retinitis and vitreitis associated with inflammatory edema of the optic disk. In the chronic phase, if the nematoid is not destroyed, atrophy of the optic nerve, diffuse retinal degeneration and vascular narrowing occur(3-4). Early diagnosis and treatment are fundamental for preserving vision in the affected eyes(11).

The GDx nerve fiber analyzer (Laser Diagnostic Technologies, Inc) is a scanning confocal laser polarimeter, which uses a polarized light source to analyze the retinal nerve fiber layer thickness by measuring the delay of emitted light(5). The device was originally created to analyze retinal nerve fiber layer changes secondary to glaucomatous optic neuropathy(6-8).
Some studies have been performed in order to establish a correlation between GDx® and nerve fiber layer changes resulting from non-glaucomatous processes. Miyahara et al. verified a momentary increase in nerve fiber layer thickness, followed by a definitive, progressive decrease in patients with traumatic optic neuropathy. Lester et al. used the nerve fiber analyzer in an attempt to verify RNFL changes during the momentary increase (45 seconds) of intraocular pressure resulting from suction in the Lasik process. Tatlipinar et al. showed that druses visible at the head of the optic nerve lead to a decrease in RNFL delay.

The purpose of this study is to demonstrate the RNFL changes observed through polarimetry in chronic-phase DUSN eyes.

### METHODS

This is a retrospective case-control study, in which the examinations of retinal nerve fiber layer of 49 patients with clinical diagnosis of chronic-phase DUSN and 16 normal patients were analyzed and evaluated from May/97 to December/01 and in February/04, respectively.

All patients were submitted to applanation tonometry, gonioscopy and optic nerve evaluation through fundus biomicroscopy. None of these presented changes suggestive or suspected of glaucoma.

All DUSN patients were classified in the chronic phase according to the following criteria: optic nerve atrophy, diffuse retinal epithelium pigmentary atrophy, mild or moderate vitreitis, afferent papillary defect, multifocal choroiditis episodes, increase in the internal limiting membrane reflex (Oréfice’s sign), the presence of small white spots suggestive of calcification and evidence of tunnels in the subretinal space (Garcia’s signs).

All patients were submitted to the following technique to capture images in the Nerve Fiber Analyzer System, GDx®, Laser Diagnostic Technologies, Inc LDT P/N 591-0029B: ambient lights on, absence of medicamentous mydriasis, 3-image capture for each eye during the examination, exclusion of examinations which presented movement artifacts or off-centered optic disk. Images were considered valid if they presented an overall score greater than 90 (automatic evaluation of the device’s software version 2.0). Patients under 18 years had their ages adjusted for this value (the minimum accepted in the device’s data bank).

From the examinations performed between May/97 and December/01 the case (49 DUSN eyes) and control I (49 contralateral eyes) groups were determined. In February/04 control group II, consisting of 16 patients (32 eyes) without ocular disease, was evaluated.

Status denominators (within normal limits, borderline and outside normal limits) were obtained and analyzed, calculating the frequency of the data obtained for each GDx® parameter in DUSN eyes. A comparison was established between the qualitative and quantitative frequencies in the three groups (diseased, control I and control II). The quantitative frequencies were provided by the following parameters: symmetry, superior ratio, inferior ratio, superior/nasal, max. modulation, the number, average thickness, ellipse average, superior average and superior integral. Some patients underwent more than one examination at different time intervals, but only the first examination with reproducibility and software approval was considered.

Paired t test was used to evaluate statistical significance when comparing control group I and the case group. When comparing control group II and the case group a difference was observed between the number of eyes in each group. In this case, t test for independent samples was used.

For a better understanding of the examination, all analyzed parameters are briefly explained.

**Superior/nasal ratio** is the result of the ratio between average thickness of the 1,500 most delayed points in the superior quadrant and of the 1,500 points nearest to the median value of the nasal sector.

**Maximum modulation** is obtained through an equation which involves: (1) the average of 1,500 points peripheral to the ellipse with the greatest delay in the superior and inferior quadrants; (2) the lowest value obtained when calculating the average of the 1,500 points peripheral to the ellipse of nearest value to the median in the nasal and temporal quadrants.

**Ellipse modulation** is the modulation of the points inside the ellipse. It is calculated similarly to maximum modulation, but only the 200 points measured inside the ellipse are used.

**Superior ratio** is the ratio between the average thickness of the 1,500 pixels of greatest delay in the superior quadrant and of the 1,500 points nearest to the median value in the temporal sector.

**Inferior ratio** is the ratio between the average thickness of the 1,500 pixels of greatest delay in the inferior quadrant and of the 1,500 pixels nearest to the median value in the temporal sector.

**Average thickness** is the average of all 65,536 pixels with valid measures.

**Ellipse average** is the average of points inside the 10-pixel band delimited by the ellipse.

**Superior average** is the average of points inside the ellipse, located in the superior sector.

**Inferior average** is the average of points inside the ellipse, located in the inferior sector.

**Superior integral** is the total area below the curve of the nerve fiber layer graph regarding the ellipse points in the superior sector.

**The number** consists of the analysis of approximately 130 variables through the neural calculation of retrograde propagation.

### RESULTS

Of 49 evaluated DUSN patients, the mean age was 24.22±10.66 years (range= 8-48 years) (mode – 18 years).

In the case group, the right eye was affected in 57.1% of the cases. Thirty-three patients (67.3%) were males.
Table 1 shows that the frequency of "within normal limits" was higher in control groups 1 and 2 when compared to the DUSN group in practically all the parameters and that the frequency of de "borderline" and "outside normal limits" was greater in the DUSN group.

In control group II, the mean age was 33.3±10.81 years (range=19-46 years), (mode - 27 years). The frequency of the qualitative results of this group is illustrated in Table 1.

Table 2 presents averages obtained for each parameter in the 3 groups. It was observed that the mean of these values was greater in the control groups compared to the DUSN group. A statistically significant difference was found in practically all the parameters assessed (p<0.05), except for symmetry, average thickness and superior integral when comparing control group II and the DUSN group.

**DISCUSSION**

Only one case of strongly suspected clinical DUSN was histopathologically studied by Gass and Scelfo (1978)(17). The eye showed evidence of a non-specific inflammatory process, involving the vitreous body, optic nerve, retina and choroid. Histopathologic data were not sufficient to explain visual loss in this case, which contributed to speculation about the role of functional mechanisms in causing visual damage(3).

There are no reports suggesting a preferred region for the onset of the changes. The disease is characterized by diffuse inflammatory damage to the neuroretina. It presents a very characteristic and reproducible electoretinographic picture: negative electoretinogram (ERG) (b wave of maximum combined response is flat, with below normal response and a decrease in relation to b/a). This type of ERG is typically found in ischemic retinal cases(3). The mechanism of this interesting phenomenon is explained by Oréfice and Gonçalves as being a consequence of a possible autoimmune, inflammatory and/or toxic aggression towards retinal bipolar cells(3). These changes are found in the chronic phase and are similar to other ischemic retinal cases where information on characterizing DUSN is limited(3).

The case group consisted of young patients, which confirms literature data(1,18).

In the researched literature (Pubmed, Medline, LILACS, SciELO, Webof Science) no reports on the use of GDx® in patients with DUSN were encountered. This device is used as a diagnostic tool in suspected glaucoma patients. Its conception

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**Table 1. Frequency of the qualitative status of the case group and control I, II groups**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Within normal limits</th>
<th>Outside normal limits</th>
<th>Borderline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case I</td>
<td>Case II</td>
<td>Case I</td>
</tr>
<tr>
<td>Symmetry</td>
<td>53.1%</td>
<td>62.2%</td>
<td>62.5%</td>
</tr>
<tr>
<td>Superior ratio</td>
<td>38.8%</td>
<td>64.4%</td>
<td>90.6%</td>
</tr>
<tr>
<td>Inferior ratio</td>
<td>59.2%</td>
<td>91.1%</td>
<td>96.9%</td>
</tr>
<tr>
<td>Superior/nasal ratio</td>
<td>38.8%</td>
<td>55.6%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Maximum modulation</td>
<td>42.9%</td>
<td>82.2%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Ellipse modulation</td>
<td>67.3%</td>
<td>97.8%</td>
<td>96.9%</td>
</tr>
<tr>
<td>Average thickness</td>
<td>77.6%</td>
<td>91.1%</td>
<td>90.6%</td>
</tr>
<tr>
<td>Ellipse average</td>
<td>75.5%</td>
<td>91.1%</td>
<td>90.6%</td>
</tr>
<tr>
<td>Superior average</td>
<td>53.1%</td>
<td>77.8%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Inferior average</td>
<td>71.4%</td>
<td>91.1%</td>
<td>93.8%</td>
</tr>
<tr>
<td>Superior integral</td>
<td>67.3%</td>
<td>88.9%</td>
<td>81.3%</td>
</tr>
</tbody>
</table>

**Table 2. Quantitative averages obtained in each group**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case group</th>
<th>Control group I</th>
<th>Control group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetry</td>
<td>0.979</td>
<td>1.010 (p=0.60)</td>
<td>0.962 (p=0.34)</td>
</tr>
<tr>
<td>Superior ratio</td>
<td>1.830</td>
<td>2.284* (p&lt;0.01)</td>
<td>2.705* (p&lt;0.01)</td>
</tr>
<tr>
<td>Inferior ratio</td>
<td>1.908</td>
<td>2.525* (p&lt;0.01)</td>
<td>2.833* (p&lt;0.01)</td>
</tr>
<tr>
<td>Superior/nasal ratio</td>
<td>1.649</td>
<td>1.908* (p&lt;0.013)</td>
<td>2.185* (p&lt;0.01)</td>
</tr>
<tr>
<td>Maximum modulation</td>
<td>1.185</td>
<td>1.549* (p&lt;0.01)</td>
<td>1.980* (p&lt;0.01)</td>
</tr>
<tr>
<td>Ellipse modulation</td>
<td>2.345</td>
<td>3.226* (p&lt;0.01)</td>
<td>3.315* (p&lt;0.01)</td>
</tr>
<tr>
<td>The number</td>
<td>50.51</td>
<td>24.92* (p&lt;0.01)</td>
<td>17.03* (p&lt;0.01)</td>
</tr>
<tr>
<td>Average thickness</td>
<td>62.94</td>
<td>69.27* (p&lt;0.01)</td>
<td>62.72 (p=0.30)</td>
</tr>
<tr>
<td>Ellipse average</td>
<td>64.00</td>
<td>73.01* (p&lt;0.01)</td>
<td>67.56* (p=0.037)</td>
</tr>
<tr>
<td>Superior average</td>
<td>68.16</td>
<td>81.64* (p&lt;0.01)</td>
<td>77.41* (p&lt;0.01)</td>
</tr>
<tr>
<td>Inferior average</td>
<td>72.37</td>
<td>84.84* (p&lt;0.01)</td>
<td>81.16* (p&lt;0.01)</td>
</tr>
<tr>
<td>Superior integral</td>
<td>0.20994</td>
<td>0.23953* (p&lt;0.01)</td>
<td>0.21838 (p=0.124)</td>
</tr>
</tbody>
</table>

*p<0.05 (statistically significant) in relation to the difference in values between the case and control groups.
Retinal nerve fiber layer analysis using GDx® in 49 patients with chronic phase DUSN

Objective: Describe the alterations observed in the lamina cribrosa of patients with chronic DUSN and compare them with normal eyes.

Methods: 49 patients with chronic DUSN were studied. The control group consisted of 20 eyes of 10 normal individuals.

Results: The group with chronic DUSN showed lower values for superior/nasal ratio and number compared to the control group. The parameters of the nerve fiber layer (RNFL) were also compared between the vertical and horizontal meridians. The decrease in RNFL thickness and the delay in light transmission were found to be higher in the chronic DUSN group.

Conclusion: The RNFL analysis using GDx® can be a useful tool in the early diagnosis and monitoring of chronic DUSN.

Resumo

Objetivo: Descrever as alterações observadas na camada de fibras nervosas da retina de olhos portadores de neurorretinite subaguda unilateral difusa (DUSN) em fase crônica e compará-las aos valores obtidos em olhos normais pelo analisador de fibras nervosas da retina (GDx®). Métodos: Trata-se de um estudo retrospectivo caso-controle, no qual foram avaliadas 49 camadas de fibras nervosas retinianas em 20 olhos normais e 20 olhos de pacientes com DUSN em fase crônica. Resultados: Os olhos com DUSN apresentaram valores mais baixos para a razão superior/nasal e número em comparação com os olhos normais. Conclusão: O GDx® é um útil ferramenta na diagnóstico e monitoramento de DUSN em fase crônica.
Retinal nerve fiber layer analysis using GDx® in 49 patients with chronic phase DUSN