Measurement of the retinal nerve fibre layer with scanning laser polarimetry in patients with previous demyelinating optic neuritis

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Abstract

Objectives—Subjective visual deficits are common after demyelinating optic neuritis despite the frequent return of normal visual acuity. Visual and electrodiagnostic tests have demonstrated evidence of these persisting functional abnormalities, which are thought to be secondary to demyelination and variable axonal loss in the optic nerve. Scanning laser polarimetry (SLP) is a new image analysis technique which uses the polarising properties of the retinal nerve fibre layer (RNFL) to produce a quantitative measure of its thickness. This study was carried out to assess the prevalence, extent, and pattern of RNFL loss after demyelinating optic neuritis using SLP.

Methods—Twenty-four patients with a history of previous demyelinating optic neuritis were re-examined. Examination included measurement of logmar visual acuity, Pelli-Robson contrast sensitivity, and the presence of a relative afferent pupil defect and optic atrophy. SLP was performed and a mean RNFL profile from a series of three images from each eye was constructed. This was compared with normative data from 20 age-matched normal subjects. The lower 99.9% confidence limit of the normal data was calculated and used as the cut off criterion for abnormality.

Results—There were a total of 31 eyes with a history of demyelinating optic neuritis and SLP disclosed an abnormality in 29 (94%) of these. Twenty-three eyes recovered an acuity of 0.0 or better, 21 of which had evidence of RNFL loss on polarimetry. Scanning laser polarimetry was the only abnormality found in nine of the 31 eyes (29%). The pattern and extent of RNFL loss was very variable and there was no significant difference in these indices between patients with multiple sclerosis compared with those with isolated demyelinating optic neuritis.

Conclusion—Scanning laser polarimetry can provide a quantitative measure of RNFL loss after demyelinating optic neuritis, demonstrating its occurrence in a high percentage of patients recovering normal visual acuity.

Keywords: demyelinating optic neuritis; retinal nerve fibre layer; scanning laser polarimetry

Demyelinating optic neuritis is a common condition which generally has a characteristic course and a good prognosis for vision. About 75% of patients regain 6/6 vision but despite this, patients often complain of subjective visual deficits. Some visual tests can detect evidence of these residual functional abnormalities with variable sensitivity. Visual evoked responses have been used as an objective assessment of optic nerve function after recovery from demyelinating optic neuritis. Abnormal results have been demonstrated in 65% to 100% of cases recovering 6/6 vision or better. Similarly, Pelli-Robson contrast sensitivity, colour vision as tested with the Farnsworth-Munsell 100 hue test, and visual fields give abnormal results in 46%, 26%, and 20% of cases recovering 6/6 vision respectively.

The precise aetiology of these persisting abnormalities is unknown but variable atrophy of the optic nerve and retinal nerve fibre layer (RNFL) has been well described in multiple sclerosis and after demyelinating optic neuritis. The mechanism resulting in axonal loss is unknown but may be due to the retrograde atrophy of axons within plaques of demyelination. Kerrison et al showed RNFL atrophy at postmortem histologically in 35 of 49 eyes of patients previously diagnosed as having multiple sclerosis. Frisen and Hoyt considered that RNFL loss was universal after demyelinating optic neuritis although they admitted that this was not always detectable using techniques available at that time. Ophthalmoscopically visible optic disc pallor and RNFL defects have been shown to result from the direct loss of axons. Direct ophthalmoscopy and red free photography have enabled clinical observation of optic disc pallor in 50% to 71% of patients with a history of demyelinating optic neuritis and multiple sclerosis, and RNFL defects in up to 89%. However, it is known that RNFL atrophy is only detectable using red free photography after a 50% loss of neural tissue in a given area. Furthermore the evaluation of optic disc characteristics and RNFL assessment using the above techniques is thought to be qualitative, subjective, and inconsistent even among experienced observers.

Scanning laser polarimetry (SLP) is a new computerised image analysing technique which utilises the polarising properties of the RNFL to determine its thickness. Preliminary studies have investigated the use of SLP in the diagnosis of glaucoma with promising results. Comparison of the data from SLP in an individual patient to a normal age
matched database provides the potential to detect, quantify, and locate areas of RNFL loss. This study was designed to assess the prevalence, extent, and pattern of RNFL loss in patients, as measured with the SLP, in a cohort of patients who had recovered from an episode of demyelinating optic neuritis in at least one eye. Furthermore, it was carried out to compare this RNFL assessment with the findings of other clinical tests and to determine the sensitivity of SLP in the detection of optic nerve abnormalities as compared with the other methods.

Method

Approval from the local ethics committee was obtained along with informed consent from all of the patients. Forty-five patients were chosen at random from those who had attended the Bristol Eye Hospital with a documented history of demyelinating optic neuritis in the preceding 10 years. The original diagnosis was based on the criteria summarised by Glaser. Patients were excluded if there was a history of any other eye abnormality and if there was a history of more than one episode of optic neuritis in either eye. Twenty-five of these patients were able to attend for re-examination. This included the assessment of visual acuity, Pelli-Robson contrast sensitivity, the presence of optic disc pallor and a relative afferent pupillary defect, and scanning laser polarimetry on both eyes.

Visual acuity was tested with a full refraction in place, on a retroilluminated Bailey-Lovie chart at a distance of 4 m. Acuity was recorded in Logmar units. An acuity of 0.0 (equivalent to 6/6 on a Snellen chart) or lower was considered normal.

Contrast sensitivity was measured at a testing distance of 1 m on a standard Pelli-Robson chart. The chart consists of 16 rows of upper case letters of a constant size, arranged in triplets. Each triplet contains letters of equal contrast and each successive triplet declines in contrast in 0.15 log unit steps. The score was recorded as the lowest line at which the patient was able to correctly identify two of the three letters. A score of line 12 or higher was considered normal.

Previous studies have shown that the results of the Pelli-Robson test are highly correlated with peak contrast sensitivity measured with a sine wave grating.

Optic disc pallor was assessed using a direct ophthalmoscope and graded as absent, mild, moderate, or severe. The presence of a relative afferent pupillary defect was sought and measured using a neutral density filter as described previously. In addition to the above assessments, a general ophthalmic examination including the measurement of the intraocular pressure was carried out to exclude the presence of any other significant ocular disease.

Scanning laser polarimetry was performed using a Nerve Fiber Analyser (Laser Diagnostic Technologies Inc, San Diego, California). The birefringence of the RNFL is measured by a confocal scanning laser ophthalmoscope which has a polarisation modulator, corneal polarisation compensator, and polarisation detection unit integrated into the system. The polarisation state of the near infrared (780 nm wavelength) diode laser is altered by the birefringent RNFL and this is displayed as a 15° field of view image of the optic nerve head and peripapillary retina.

The change in the polarisation state, measured as the retardation in degrees, is converted in a linear fashion to the thickness of the RNFL and displayed in microns. Three measurements of each eye were made in a single session without pupillary dilation. The average time to perform a complete examination was 10 minutes. The thickness of the RNFL was retrieved from the image by placing a concentric circular zone (width of 1.5 to 2.0 optic disc diameters) within the peripapillary region and centred on the optic disc.

The resultant RNFL polar profile, comprising 360 individual values (one value per angular degree) was retrieved from each image and a mean profile for the series of three images from each eye was constructed and calculated. The within observer reproducibility for this
Table 2  Sensitivity of the tests used in this study

<table>
<thead>
<tr>
<th>Test</th>
<th>Total No</th>
<th>Abnormal visual acuity</th>
<th>Abnormal contrast sensitivity</th>
<th>RAPD detectable</th>
<th>Optic disc pallor</th>
<th>Scanning laser polarimetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual acuity n (%)</td>
<td>23 (74)*</td>
<td>NA</td>
<td>5 (22)</td>
<td>7 (30)</td>
<td>10 (43)</td>
<td>21 (91)†</td>
</tr>
<tr>
<td>Contrast sensitivity n (%)</td>
<td>21 (68)</td>
<td>3 (14)</td>
<td>NA</td>
<td>7 (33)</td>
<td>8 (38)</td>
<td>20 (95)</td>
</tr>
<tr>
<td>Normal pupil reactions n (%)</td>
<td>19 (61)</td>
<td>3 (16)</td>
<td>5 (26)</td>
<td>NA</td>
<td>8 (42)</td>
<td>17 (89)</td>
</tr>
<tr>
<td>Normal optic disc n (%)</td>
<td>14 (48)</td>
<td>1 (7)</td>
<td>1 (7)</td>
<td>NA</td>
<td>21 (86)</td>
<td>NA</td>
</tr>
<tr>
<td>Normal polarimetry n (%)</td>
<td>2 (6)</td>
<td>0</td>
<td>1 (50)</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

Results based on eyes with a previous episode of demyelinating optic neuritis (n = 31).

*Of the 31 eyes with a history of optic neuritis 23 (74%) had normal visual acuity.
†Of the 23 eyes with normal visual acuity 21 (91%) had abnormal polarimetry.
NA=not applicable.

Table 3  Incremental detection values (n (%))

<table>
<thead>
<tr>
<th>Test</th>
<th>Total No</th>
<th>Abnormal visual acuity</th>
<th>Abnormal contrast sensitivity</th>
<th>RAPD detectable</th>
<th>Optic disc pallor</th>
<th>Scanning laser polarimetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>All eyes with previous DON (n = 31) p Value</td>
<td>+0.30 &gt; 0.7</td>
<td>−0.11 &gt; 0.9</td>
<td>−0.42 &gt; 0.6</td>
<td>+0.07 &gt; 0.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with previous unilateral DON (n = 17) p Value</td>
<td>+0.23 &gt; 0.8</td>
<td>+0.1 &gt; 0.9</td>
<td>+0.20 &gt; 0.8</td>
<td>+0.07 p &gt; 0.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DON=demyelinating optic neuritis.
Two of these eyes also had abnormal contrast sensitivity. The sensitivity of SLP is considerably higher than other commonly performed clinical tests such as contrast sensitivity. Indeed in 29% of our cases RNFL loss as shown with SLP was the only abnormality found. However, two patients with demyelinating optic neuritis showed no abnormalities on SLP. There are two possible explanations for this finding. Axonal loss may not be universal after demyelinating optic neuritis and therefore demyelination may occur on its own in some patients. Alternatively, the extent of axonal loss after demyelinating optic neuritis may be below the sensitivity of the SLP. Certainly the extent of axonal loss may have been insufficient to lower the retinal nerve fibre layer profile below our normal range in an individual eye.

The detection of abnormalities using SLP in the fellow normal eye was also similar to previous studies using visually evoked responses (30–82%), and red free photography (45–68%), and also again higher than other clinical tests of visual function. The occurrence of fellow eye abnormalities probably represents subclinical episodes of demyelination or subclinical bilateral involvement at the time of the initial episode of unilateral optic neuritis. With its speed and ease of use SLP may prove to be a good alternative to visual evoked responses in the diagnosis of multiple sclerosis in identifying the site of a second lesion in an otherwise visually asymptomatic person with no history of optic neuritis. However, as with evoked responses, RNFL loss is not specific for demyelination.

We found no consistent pattern of RNFL loss after demyelinating optic neuritis which concurs with the findings using red free photography and the absence of a characteristic field defect after demyelinating optic neuritis. Similarly, there was no significant difference in the extent and pattern of RNFL loss in patients with definite or probable multiple sclerosis against those with isolated demyelinating optic neuritis suggesting a similar pathogenesis.

The lack of correlation between SLP and visual acuity or contrast sensitivity is similar to the previously shown absence of correlation between VER latency and these two measures. There are several possible reasons for this finding. We used a global value of RNFL loss whereas abnormalities in visual function can be focal. Furthermore the exact relation between RNFL structure and visual function is not known and may vary between patients.

There was no significant correlation between the nerve fibre analysis and optic disc pallor or a relative afferent pupil defect. The presence of a relative afferent pupil defect is by definition made in relation to the contralateral eye and an assessment of optic disc pallor is often judged relative to the contralateral eye. The analysis was therefore repeated and limited to the 17 eyes with no previous history of demyelinating optic neuritis.
eyes with unilateral previous demyelinating optic neuritis. Despite this, there was no significant correlation. The presence of subclinical contralateral ocular abnormalities and the subjective and variable nature of assessment of optic disc pallor may partly explain this finding. Furthermore, the presence and magnitude of a relative afferent pupil defect will depend not only on the degree of axonal loss but also on the conduction delay resulting from demyelination.

The correlation between SLP and RNFL assessment using red free photography has been shown to be maximal at \( \rho = 0.53 \), and the information obtained with SLP and photography do not seem to be equivalent. The reasons for these disparities are not entirely clear. However, the reproducibility of SLP is high for these disparities are not entirely clear. There reasons information obtained with SLP and photogra-

Technologies Inc.

polarimeter (Nerve Fiber Analyser) or Laser Diagnostic

We have no financial or proprietary interest in the scanning laser polarimeter (Nerve Fiber Analyser) or Laser Diagnostic Technologies Inc.

21 Thompson HS, Corbett JJ, Cox TA. How to measure the relative afferent pupil defect. Surv Ophthalmol 1986;31:36.