Optical Coherence Tomography in Neuromyelitis Optica

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Background: Neuromyelitis optica (NMO) is an inflammatory disease with combined features of optic neuritis and myelitis. This pathologic entity may induce severe disability, including visual loss and paraplegia. Other than clinical follow-up, there is no marker for severity of the disease.

Objectives: To evaluate the use of optical coherence tomography (OCT) in NMO and to determine whether this new technique could be a good marker of axonal loss in NMO.

Design: Cross-sectional study.

Participants: Thirty-five patients with NMO or at a high risk for NMO (having optic neuritis or myelitis and who are positive for NMO antibody) were prospectively studied. Fifteen healthy individuals served as control subjects.

Main Outcome Measure: All patients underwent a complete ophthalmologic evaluation, including OCT, funduscopy, and visual field, visual acuity, and visual evoked potential testing. Expanded Disability Status Scale scores were assessed but without the visual data. Correlations between the visual test results and demographic or clinical characteristics were evaluated.

Results: Optical coherence tomography and visual field data were available for only 32 patients because 3 patients were blind. The mean retinal nerve fiber layer thickness was significantly reduced in patients with NMO compared with controls (P < .001). We found good correlation between the OCT results and visual field testing. We also found weak correlation between OCT results and both visual acuity and visual evoked potential latencies. We did not find any correlation between OCT results and age, sex, or disease duration. In contrast, retinal nerve fiber layer thickness was closely correlated with the Expanded Disability Status Scale score (P < .001).

Conclusions: Optical coherence tomography results are significantly altered in patients with NMO. Optical coherence tomography is easy to perform, and the results are well correlated with visual acuity and visual field findings. It could be considered a marker of axonal loss because we found good correlation between OCT and the Expanded Disability Status Scale score. These preliminary results will need to be confirmed in a longitudinal prospective study.

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NEUROMYELITIS OPTICA (NMO) is an inflammatory disease with combined features of optic neuritis (ON) and myelitis. In the past, NMO was frequently considered a form of multiple sclerosis (MS), but there is substantial evidence to suggest that they are different diseases. First, NMO is commonly restricted to the spinal cord and optic nerve. Second, NMO seems to be more severe than MS, especially with regard to ON, which usually has a better prognosis in MS than in NMO. Third, recent magnetic resonance imaging and neuropathologic study findings argue for early severe damage in NMO, including not only demyelination but also axonal loss and extended necrosis.

A serum autoantibody, anti-NMO, which binds specifically to aquaporin-4, the dominant central nervous system water channel protein, was recently found to be associated with NMO. Approximately 70% of patients with NMO test positive for NMO antibody. Aquaporin-4 is ubiquitous in the central nervous system, but primarily in the optic nerve and spinal cord. This antibody is highly specific to NMO, and its presence helps to define more precisely patients with NMO and to identify a group of patients with either myelitis or ON who are at a high risk of developing NMO.

Neuromyelitis optica may induce severe disability, including visual loss and paraplegia. However, except for clinical follow-up, there is no marker for severity of the disease. The lack of factors that predict the course of the disease is problem-
measuring the retinal layer thickness. Optical coherence tomography (OCT) in MS showed that OCT is easy to perform, reproducible, and could be a good marker for disability. 

Recently, several studies of optical coherence tomography (OCT) in NMO showed that OCT results were significantly different for many retinal areas. These results confirmed that visual field is a major problem in NMO. In previous studies, the RNFL thickness was strongly correlated with visual field testing and OCT. 

The main results of the OCT evaluation are given in Table 2. The mean retinal nerve fiber layer (RNFL) thickness was significantly thinner in patients with NMO (77.5 µm in the right eye and 78.3 µm in the left eye) compared with controls (101.9 µm in the right eye and 102.8 µm in the left eye) (P<.001). We also found significant differences for all retinal areas (Table 2). In the high-risk group, we also found a reduction in RNFL thickness in patients with recurrent ON but not in patients with isolated myelitis (Table 2).

We found good correlation between OCT results and visual field defects (r=−0.78; P<.001). We also found a correlation between OCT results and both visual acuity (r=−0.36; P<.01) and visual evoked potential latencies (r=0.57; P<.001). We did not find any correlation between OCT results and age, sex, disease duration, or NMO antibody status. The RNFL thickness was strongly correlated with the EDSS score (r=−0.72; P<.001) (Figure).

Findings at OCT are significantly altered in patients with NMO compared with controls. In addition, RNFL atrophy is an early and frequent phenomenon in NMO. Similar results were found in all retinal areas. These results are not surprising in view of the results of previous studies of OCT in MS. However, the level of alteration seems to be higher than that found in MS, confirming that visual defect is a major problem in NMO. In previ-
ous studies of OCT in MS, mean RNFL thickness was between 80 and 100 µm\(^1\) compared with a mean of 77 µm in our cohort with NMO. Trip et al\(^{18}\) found no relationship between RNFL and visual evoked potential latencies but did find a relationship with visual evoked potential amplitude, which suggests that pathophysiology of the disease process in MS optic neuropathy, both acute and chronic, is better linked with the process of retinal axonal degeneration than with demyelination. The retina lacks myelin and is, therefore, an ideal model to use to ascertain the effects of MS and NMO on retinal structural integrity.

Our study findings also demonstrated interesting results in the group of patients with high-risk syndromes (ie, those having isolated recurrent ON or myelitis and who tested positive for NMO antibody). We found an early retinal defect in patients with recurrent ON but not in patients with isolated spinal cord lesions. However, in the 4 patients with isolated spinal cord lesions, the disease was in the early stage (mean duration, 1.7 years). It would, therefore, be interesting to observe this subgroup longer to determine whether and when a retinal defect could be detected (ie, before or after the first visual symptoms).

Optical coherence tomography is easy to perform, reproducible, and well correlated with visual acuity and visual field. However, whether OCT is a good marker for neuropathologic processes in the retina is a matter of debate. There is strong evidence for a link between OCT results and axonal loss, as demonstrated in both MS and animal models. A recent study of OCT in MS showed good correlation between RNFL results and white or gray mat-

### Table 2. Results of OCT Evaluation\(^a\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With NMO (n=26(^b) [52 Eyes])</th>
<th>Patients With Optic Neuritis (n=12 [4 Eyes])</th>
<th>Patients With Myelitis (n=4 [8 Eyes])</th>
<th>Control Subjects (n=15 [30 Eyes])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total RNFL</td>
<td>77.9 (22.6)</td>
<td>74.2 (16.6)</td>
<td>101.8 (3.7)</td>
<td>102.3 (7.4)</td>
</tr>
<tr>
<td>Temporal RNFL</td>
<td>54.9 (16.7)</td>
<td>50.7 (10.1)</td>
<td>72.0 (18.6)</td>
<td>74.3 (13.1)</td>
</tr>
<tr>
<td>Inferior RNFL</td>
<td>98.0 (27.8)</td>
<td>91.0 (18.9)</td>
<td>124.4 (14.5)</td>
<td>130.9 (19.8)</td>
</tr>
<tr>
<td>Nasal RNFL</td>
<td>57.2 (17.7)</td>
<td>59.0 (13.4)</td>
<td>75.3 (10.5)</td>
<td>79.2 (15.4)</td>
</tr>
<tr>
<td>Superior RNFL</td>
<td>98.5 (28.2)</td>
<td>93.2 (13.2)</td>
<td>135.3 (8.1)</td>
<td>125.7 (16.3)</td>
</tr>
</tbody>
</table>

Abbreviations: NMO, neuromyelitis optica; OCT, optical coherence tomography; RNFL, retinal nerve fiber layer.

\(^a\) Optical coherence tomography was performed in 26 patients only because 3 patients were blind. Values are given as mean (SD).

\(^b\) Statistical comparisons are between the patients with NMO and the control subjects (all \(P<.001\)). Because of the small sample size, no statistical comparisons were made for the patients at high risk for NMO.

![Figure](https://example.com/figure.png)

**Figure.** Correlation between the mean retinal nerve fiber layer (RNFL) at optical coherence tomography and the Expanded Disability Status Scale (EDSS) score (without visual data).
ter atrophy, one of the best indirect markers of axonal loss in MS. Some authors have also clearly demonstrated a relationship between RNFL, vision, and disability and visual field. We found similar results in our cohort with NMO. Similarly, several investigators successfully used OCT in animal models to image retinal structures. Measures of retinal thickness obtained at OCT correlate with histologic analysis.

The most important result of our study is the correlation between disability and RNFL thickness. The underlying hypothesis was that RNFL thickness might be indicative of the widespread axonal damage in the central nervous system. However, because our study was cross-sectional, these preliminary results will need to be confirmed in a longitudinal prospective study before we can conclude that OCT is a good marker for disability evolution. Another limitation of our study is that the EDSS score has not been validated for use in NMO. However, there is no validated disability scale for NMO, and the EDSS score provides a good reflection of spinal cord damage. The visual data were excluded from the EDSS score calculation because they could have biased the correlation analysis.

Recent therapeutic studies found that patients with NMO responded better to therapy with immunosuppressive drugs (especially anti-B-cell drugs such as rituximab and mitoxantrone hydrochloride) than to therapy with immunomodulator agents. Immunosuppressive drugs have an anti-inflammatory effect, but to date there are no clear data for a specific effect on neurodegeneration and axonal loss. Even if NMO remains rare, therapeutic studies with both anti-inflammatory and neuroprotective drugs are warranted in this disease that specifically affects the spinal cord and optic nerve.

In conclusion, OCT evaluation seems to be a good technique for assessing the clinical follow-up and potential drug effects in patients with NMO. Retinal nerve fiber layer thinning in NMO could be one of several key measures of disease status. However, it is not known whether these data further delineate or define clinical or structural features that may be unique to NMO. A larger cohort may be required to determine this.

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Author Contributions: Dr de Seze had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: de Seze, Blanc, Labauge, Castelnovo, and Vermersch. Acquisition of data: de Seze, Blanc, Jeanjean, Zéphir, Labauge, Bouyon, Ballonzoni, Castelnovo, Fleury, Defoort, Vermersch, and Speeg. Analysis and interpretation of data: de Seze, Blanc, and Vermersch. Drafting of the manuscript: de Seze, Zéphir, Labauge, Castelnovo, and Speeg. Critical revision of the manuscript for important intellectual content: de Seze, Blanc, Jeanjean, Bouyon, Ballonzoni, Fleury, Defoort, Vermersch, and Speeg. Statistical analysis: de Seze. Obtained funding: Fleury and Speeg. Administrative, technical, and material support: Blanc, Labauge, Castelnovo, Vermersch, and Speeg. Study supervision: Labauge, Castelnovo, Vermersch, and Speeg.

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REFERENCES