OCT Measurements in Patients with Optic Disc Edema

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**PURPOSE.** This study investigated the influence of disc edema (DE) caused by inflammatory optic neuropathies or retinal vein occlusions on optical coherence tomography (OCT) retinal nerve fiber layer (RNFL) thickness measurements.

**METHODS.** OCT RNFL circle scans centered on the optic disc were made for 13 patients with DE (7 with retinal vein occlusions and 6 with inflammatory optic neuropathies) and 13 controls. RNFL thickness was assessed using the OCT normative database. The same circle scans were also used for peripapillary total retinal thickness measurements. The RNFL percentage of total retinal thickness was calculated, normalized (nRNFL%), and averaged separately for affected and unaffected regions of each eye.

**RESULTS.** Average RNFL thickness was 122 ± 23 μm in the DE group, and 91 ± 8 μm in the control group (P = 0.0001). Mean peripapillary total retinal thickness was 329 ± 56 μm in the DE group and 255 ± 12 μm in the control group (P < 0.001). Comparison of the averaged nRNFL% values at measurement locations above the range of the normative database with averaged nRNFL% values at measurement locations within the range of the normative database in the optic neuropathy group showed a significant difference (P = 0.024); however, the same analysis in the retinal vein occlusion group revealed no significant difference.

**CONCLUSIONS.** OCT measurements are influenced by DE and show significantly greater thickness values in those patients than in controls. The presence of a significant difference within the averaged nRNFL% values in the optic neuropathy group and the absence of such a difference in the retinal vein occlusion group could be explained by edema primarily affecting the RNFL in optic neuropathy in contrast to what occurs in retinal vein occlusion, where edema affects all retinal layers.

Optical coherence tomography (OCT) is a noninvasive, high-resolution imaging technique to measure total retinal thickness, retinal nerve fiber layer (RNFL) thickness, and optic nerve head morphology. It provides retinal cross-sectional images with an axial resolution of 8 to 10 μm. OCT imaging is analogous to ultrasound B-mode imaging but uses infrared light instead of ultrasound. The details of the OCT technique are described elsewhere. RNFL thickness measurements are extremely important in diseases such as optic neuropathies or ischemic branch and central retinal vein occlusions. These diseases can cause RNFL damage, which leads to visual field loss.

The reliability and reproducibility of OCT RNFL thickness measurements have been tested in studies on healthy subjects and patients with glaucoma. OCT has also been used to measure RNFL thickness in patients with demyelinating optic neuritis.

Acute stages of optic neuropathies and retinal vein occlusions, however, are often accompanied by episodes of optic disc edema (DE). Swelling of the optic nerve head and the surrounding retinal tissue might impair OCT cross-sectional analysis. The most common scan type for OCT RNFL analysis is based on a 1.73-mm radius circle scan centered on the optic disc to measure RNFL thickness. Because of the proximity of the scan to the disc, we suspected a direct influence of DE on OCT RNFL thickness measurements.

This study tested the hypothesis that DE leads to significantly greater RNFL thickness values in OCT measurements. We also investigated the hypothesis that OCT might show differences in RNFL thickness measurements depending on the cause of the edema. Given that retinal venous obstruction leads to blood flow blockage, one would expect primarily a diffuse type of retinal edema affecting all retinal layers. In contrast, inflammatory optic neuropathies might show more specific swelling of the neuroretinal layers.

**METHODS.** Thirteen patients (mean age, 58 years; 54% women) with previously diagnosed DE caused by inflammatory optic neuropathies (6 patients) or retinal vein occlusion (5 patients with central vein occlusions, 2 with branch vein occlusions) and 13 healthy age-matched subjects (mean age, 58 years; 54% women) were included in the study. The study protocol received institutional review board approval and followed the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject. All examinations were performed under pupil dilation. DE was diagnosed by slit lamp biomicroscopy, fundus photography, and OCT optic nerve head analysis. Figure 1 shows the results of OCT optic nerve head analysis of a healthy subject and a patient with DE. In the patient with DE, OCT shows an elevated neuroretinal rim and fluid accumulation around the disc (Fig. 1B). For OCT RNFL thickness measurement, software (Stratus OCT 3000, version 3.0; Zeiss, Oberkochen, Germany) was used. Each subject underwent standard OCT-RNFL circle scanning three times at the peripapillary retina using default settings (1.73-mm radius from the center of the disc with 512 A-scan measurement points). During the examination, the patient had to fixate on an internal fixation target. A real-time OCT fundus image allowed the examiner to observe the patient’s fixation and to target the circle scan on the optic disc. The scan with the strongest signal and the best centration on the nerve head was chosen for RNFL thickness analysis.

Scans were analyzed using the newly established normative database for RNFL thickness. For this database, a prospective, multicenter, noncomparative study was designed that included 625 RNFL scans on 328 healthy subjects. Data were implemented into OCT software package 3.0 (Zeiss). Figure 2A is an example of the analysis of normal RNFL thickness. A color-coded graph displays the actual RNFL measurements and compares them with the age-matched data of the normative database. Thickness values falling into the green area are considered normal. The yellow area marks thickness values that are 5% or less than all thickness values measured in the normative database. Thickness measurements in the red area are considered pathologic.
Less than 1% of all age-matched subjects included in the normative database had such thickness values. In addition, two circle diagrams are given by the software analysis that show the average RNFL thickness values in four quadrants and 12 sectors around the optic disc.

To investigate possible differences between RNFL edema related to inflammatory optic neuropathies or to retinal vein occlusions, we compared peripapillary total retinal thickness with RNFL thickness in each subject separately at 18 of 512 available A-scan locations. Measurements were taken at A-scan locations 1 and 30 and then in steps of 30 to 480. A-scan location 512 was chosen for the last measurement. Peripapillary total retinal thickness at the previously chosen A-scan location was measured in the RNFL circle scans by using the OCT retinal thickness single-eye analysis program. The percentage of RNFL (RNFL%) compared with total retinal thickness was calculated for each subject.
measurement point and then normalized by using the data of the corresponding age-matched healthy control subject using the formula: RNFL% normalized $(nRNFL\% ) = \frac{RNFL\%_{\text{PATIENT}}}{RNFL\%_{\text{CONTROL}}}$. Patients were divided into two subgroups, those with optic neuropathy and those with retinal vein occlusion. In each patient, all RNFL thickness measurement locations above the limits of the normative database were identified, and the average was calculated from the corresponding nRNFL% values. The average was also calculated from the nRNFL% values in the measurement locations that had values within the limits of the normative database. Unpaired t-tests were used for group and subgroup comparisons. $P \leq 0.05$ was considered statistically significant.

## RESULTS

OCT measured significantly greater RNFL thickness values in the DE group than in the control group. Average RNFL thickness in the DE group was $122 \pm 23 \, \mu m$ compared with $91 \pm 8 \, \mu m$ in the control group ($P = 0.0001$). Average RNFL thickness in the optic neuropathy subgroup was $111 \pm 15 \, \mu m$ compared with $131 \pm 25 \, \mu m$ in the retinal vein occlusion subgroup. The difference was not statistically significant. Superior, inferior, temporal, and nasal quadrants were separately compared with those of the age-matched control group. In each quadrant, the DE group showed significantly greater RNFL thickness values ($P < 0.0001$ to $P = 0.031$). Average thickness values, average thickness values of each quadrant, and corresponding $P$ values are given in Table 1. Figure 2 shows an example of RNFL analysis in a control subject and in a patient with DE.

In the DE group, RNFL thickness exceeded the normative database values in 22 of the 52 quadrants tested. The superior quadrant was the most frequent area of “supernormal” RNFL thickness. In the control group, all RNFL thickness measurement points were in the green area.

Mean peripapillary total retinal thickness in measurement locations exceeding the green area of the normative RNFL thickness database was $354 \pm 64 \, \mu m$ in the retinal vein occlusion group and $299 \pm 25 \, \mu m$ in the optic neuropathy group. The difference was not statistically significant. The control group had a mean peripapillary total retinal thickness of $255 \pm 12 \, \mu m$, which was significantly smaller than that in the optic neuropathy and vein occlusion groups ($P < 0.0001$). Figure 3 shows a box plot of peripapillary total retinal thickness values in the control and both DE subgroups.

Comparison of the averaged nRNFL% values of measurement locations outside the normal range of the normative database with averaged nRNFL% values at measurement locations within normal limits of the normative database in the optic neuropathy group showed a significant difference ($P = 0.024$). However, similar analysis in the retinal vein occlusion group revealed no significant difference.

## DISCUSSION

Results of our study indicated significantly larger RNFL thickness values for patients with DE than for healthy controls.

### Table 1. RNFL Thickness

<table>
<thead>
<tr>
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<th>DE Group (µm)</th>
<th>Control Group (µm)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior</td>
<td>156 ± 28</td>
<td>109 ± 12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inferior</td>
<td>143 ± 37</td>
<td>119 ± 13</td>
<td>0.0315</td>
</tr>
<tr>
<td>Temporal</td>
<td>88 ± 21</td>
<td>68 ± 10</td>
<td>0.0057</td>
</tr>
<tr>
<td>Nasal</td>
<td>100 ± 42</td>
<td>70 ± 12</td>
<td>0.0223</td>
</tr>
<tr>
<td>Average</td>
<td>122 ± 23</td>
<td>91 ± 8</td>
<td>0.0001</td>
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These findings are in agreement with the findings of Karam et al.22 showing greater RNFL thickness values in patients with papilledema or pseudopapilledema than in healthy controls. In our study the RNFL thickness in patients with DE frequently exceeded the normal RNFL thickness range for age-matched controls when using the normative database for RNFL thickness.

Multiple factors may contribute to the increased RNFL thickness values measured in patients with DE. One factor might be tissue swelling resulting from ischemia and increased fluid accumulation around the optic disc. Histopathologic studies by Tso et al.23,24 showed increased thickness of the peripapillary RNFL in patients with DE. Another study revealed slowed axoplasmic flow anterior to the laminar cribrosa to the point of extravasation of axoplasm into the perineural space in crowded optic nerves associated with drusen.25 In addition, Tso et al.24 demonstrated prelaminar axoplasmic flow stasis in experimental and clinical papilledema.

Because of the different pathophysiology of disc edema caused by retinal venous obstruction compared with inflammatory optic neuropathies, we suspected differences in OCT RNFL thickness measurements between these subgroups.

Figure 4 is a schematic of the different edema types and their impact on OCT RNFL thickness measurements. We hypothesize that in inflammatory optic neuropathies, edema is found predominantly in the retinal nerve fiber and the ganglion cell layers. Comparing total retinal thickness with RNFL thickness in these locations reveals an increase in the RNFL thickness/total retinal thickness (TR) ratio (RNFL/TR ratio) with relation to unaffected locations. Our results in the optic neuropathy subgroup are in agreement with this hypothesis. In retinal vein occlusion, we expected edema predominantly affecting all retinal layers. We did not expect a significant change in the RNFL/TR ratio in affected areas compared with unaffected measurement locations. The results of our study are in agreement with this hypothesis.

In this study we introduced, for the first time, RNFL percentages of peripapillary total retinal thickness. These values had to be normalized to account for the normal age-related thinning of the RNFL. Although there was no significant difference in average RNFL thickness between the vein occlusion group and the optic neuropathy group, we found a significant difference between the averaged nRNFL% values at measurement locations above the range of the normative database and averaged nRNFL% values at measurement locations within the limits of the normative database in the optic neuropathy group. As indicated in Figure 4, this difference was not seen in the...
In addition, one would expect thicker peripapillary total retinal thickness values in retinal vein obstructions compared with inflammatory optic neuropathies (Fig. 4). Our results (Fig. 3) in fact showed a tendency toward thicker peripapillary total retinal thickness in the vein occlusion group than in the optic neuropathy group, but the difference did not reach the level of significance. Additional studies with larger groups might verify these findings. Peripapillary total retinal thickness values at measurement locations with values exceeding the range of the normative RNFL database in both DE groups were significantly greater than peripapillary total retinal thickness values in controls, indicating that peripapillary total retinal thickness and RNFL thickness are affected by DE.

Another possible explanation for the greater RNFL thickness values might be attributed to a change in the structural appearance of the retinal tissue caused by fluid accumulation. Retinal hemorrhages close to the disc caused by retinal vein occlusions might also alter the structural appearance. These changes could affect the OCT scan image by changing the tissue reflectivity patterns, causing a more homogeneous, undifferentiated scan image. The OCT RNFL thickness measurement algorithm might, therefore, be fooled by the changed tissue reflectivity patterns because it could not correctly identify the RNFL. However, because our averaged nRNFL% analysis is in good agreement with the pathophysiologic concept of different types of edema, we suspect that changes in the tissue reflectivity pattern of the OCT scan image do not have a significant impact on RNFL thickness measurements.

Other authors have investigated the influence of DE on RNFL measurements obtained by scanning laser polarimetry. This technique is thought to assess form birefringence properties of the ganglion cell axons of the RNFL that correspond to the number of nerve fiber cells. This leads to an elevated RNFL/TR ratio. However, because scanning laser polarimetry measurements correspond to the number of nerve cells in patients with DE must be clarified. In contrast, our study showed that OCT measurements most likely correspond to the real RNFL thickness. Whether scanning laser polarimetry measurements correspond to the number of nerve cells in patients with DE must be clarified. In contrast, our study showed that OCT measurements most likely correspond to the real RNFL thickness. Therefore, OCT evaluation of possible RNFL defects is not possible during DE.

To avoid this problem in patients with isolated DE or crowded discs, RNFL thickness measurements further away from the disc might be useful to avert measurement interference and to assess RNFL defects more reliably. However, central and branch vein occlusions are often accompanied by additional macular edema that might interfere with RNFL thickness measurements temporal to the disc. In addition, few data on normal RNFL thickness at distances away from the disc are available, making it difficult to compare the findings to normal RNFL thickness values. The normative database is available only for the standard 1.73-mm radius measurements. In this study we did not test larger scan radii to evaluate RNFL thickness.

Bartz-Schmidt et al. used red-free photography to identify RNFL defects to distinguish between ischemic and nonischemic types of branch vein occlusion. Other authors also reported RNFL loss in patients with retinal vein occlusion. Reliable techniques to assess RNFL thickness in these early stages of retinal vein occlusion would be extremely important and might help in diagnosing more severe types of ischemic retinal vein occlusions at earlier stages to adjust the clinical management of these patients. However, our study showed that cross-sectional OCT RNFL measurements cannot be used to assess RNFL loss in patients with retinal vein occlusion accompanied by DE. Our findings also show the importance of checking for DE before evaluating RNFL thickness in any patient to rule out any influence on measurements.

In conclusion, care must be exercised in interpreting OCT RNFL thickness measurement in patients with optic disc edema. RNFL loss cannot be assessed by OCT during episodes of DE. However, OCT might be used to distinguish edema that is predominantly of the nerve cell from edema affecting all retinal layers.

References


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