The Impact of Lens Opacity on SD-OCT Retinal Nerve Fiber Layer and Bruch’s Membrane Opening Measurements Using the Anatomical Positioning System (APS)

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PURPOSE.
To evaluate the impact of lens opacity on retinal nerve fiber layer thickness (RNFLT) and Bruch’s membrane opening (BMO) measurements.

METHODS.
Fifty-nine randomly selected patients without any other relevant ocular pathology undergoing elective routine cataract surgery in two specialized eye clinics were enrolled. RNFLT, BMO area, and BMO minimum rim width (BMO-MRW) were assessed with the Heidelberg Engineering Spectralis OCT using the anatomical positioning system (APS) prior to and 1 day after cataract surgery using a ring scan at different eccentricities of the disc (3.5, 4.1 and 4.7 mm). Lens opacity was quantified using densitometry based on Scheimpflug images (Oculus Pentacam AXL).

RESULTS.
RNFLT, BMO area, and BMO-MRW were virtually identical before and following removal of the cataractous lens. This held when assessed overall, within the six sectors for the 3.5-mm scan, or at any other eccentricity. Baseline RNFLT was not associated with lens opacity.

CONCLUSIONS.
Using the APS, RNFLT remained unchanged following cataract surgery, contrary to results reported by previous studies. Our results imply that the APS may have contributed to more precise spectral-domain optical coherence measurements, minimizing the influence of cataract on RNFLT and BMO assessments in our cohort.

Keywords: lens opacity, retinal nerve fiber layer, Bruch’s membrane opening, anatomical positioning system

Spectral-domain optical coherence tomography (SD-OCT) measurements of the retinal nerve fiber layer thickness (RNFLT) and Bruch’s membrane opening minimal rim width (BMO-MRW) have become important tools for morphologic assessments in clinical practice. Analyses of RNFLT are frequently used in glaucoma diagnostics1–3 and hold promise as a biomarker for various neurodegenerative diseases.4,5 Alterations and thinning of different retinal layers have been associated with neurologic diseases such as multiple sclerosis or Parkinson’s disease.6,7

In order to evaluate glaucoma progression it is crucial to quantify RNFLT reliably. As OCT is an optical measurement technique, the image quality can be impacted by light attenuation in the optical path due to media opacities.8 Various studies have suggested that lens opacity may influence RNFLT measurements and reported an increased macular and peripapillary RNFLT after cataract surgery.9–15 Light scattering due to lens opacity was hypothesized to lead to reduced image quality and thus result in artificially reduced RNFLT.16–18 However, none of these studies included an objective assessment of lens opacity using, for example, Scheimpflug photography. Similarly, anatomical positioning of SD-OCT scans, which is particularly important when performing follow-up assessments, has been greatly improved since the aforementioned studies were conducted, for example, through using the anatomical positioning system (APS) of the Spectralis SD-OCT (Software Version 6.5.2.0; Heidelberg Engineering, Heidelberg, Germany). Whether the reported differences in RNFLT after cataract surgery persist when using the APS remains unclear.

We investigated whether and to what extent lens opacity influences SD-OCT measurements of RNFLT and BMO-MRW, using Scheimpflug photography to objectively quantify lens opacity as well as improved anatomic overlay at follow-up using the APS.

METHODS
Participants
We enrolled 59 cataract patients during their regularly scheduled visit for routine cataract surgery including phacoemulsification and intraocular lens implantation. We randomly selected patients without any relevant other eye disease (e.g., corneal opacities) scheduled in two eye clinics. The study followed the tenets of the Declaration of Helsinki and was...
approved by the local ethics committee. Informed consent was obtained from each subject.

**Participant Assessments**

The eye for which cataract surgery was planned was chosen as study eye. Preoperatively, all patients underwent a complete ophthalmic history and examination of both eyes, including slit-lamp examination, dilated fundus examination, SD-OCT imaging, and Scheimpflug photography (Oculus Pentacam AXL; Oculus GmbH, Wetzlar, Germany). Postoperatively, the study eye was examined with a slit lamp to screen for postoperative inflammation and SD-OCT imaging. All imaging was conducted by the same examiner (M.M.). Patients were dilated for funduscopy as well as all imaging using 0.5% tropicamide. Patients with any corneal or vitreous opacity were not enrolled; patients who did not have stable fixation during imaging resulting in insufficient image quality were excluded from the analyses retrospectively (see Results).

The SD-OCT examination was performed using the Spectralis SD-OCT (Heidelberg Engineering GmbH, Heidelberg, Germany). The instrument combines OCT technology with a confocal scanning laser ophthalmoscope (cSLO) and provides an automatic real-time (ART) function that adjusts for eye movement and increases image quality.19

SD-OCT imaging included the APS function, which recognizes individual anatomic landmarks and provides exact alignment of the follow-up scans. At baseline examination the foveal pit was manually identified on two live B-scans, followed by identification of the BMO on two radial B-scans that were perpendicular to each other. These anatomic landmarks were used to define the fovea–BMO axis, which served as reference for the scans.20

For the BMO-MRW measurements, 24 radial scans, and for the RNFLT assessments, three circular scans (diameters 3.5, 4.1, and 4.7 mm, respectively), were acquired. Each radial BMO-MRW scan was averaged from 25 and each circle RNFL scan was averaged from 100 B-scans. These scans were centered onto the optic nerve head (ONH) and aligned to the previously determined fovea–BMO axis using the APS.21

The automated segmentation for BMO and RNFLT was revised manually by an experienced grader to guarantee accurate segmentation. Values for RNFLT and BMO-MRW were calculated globally (G) and for six sectors according to the legacy segmentation. Values for RNFLT at baseline and change in RNFLT (ΔRNFLT) and the Pentacam opacity parameters. Furthermore, we used linear regression analysis to investigate the association of lens opacity with the measurements of baseline RNFLT and ΔRNFLT. In these models we used the percentage of lens opacity in the 3D mode as the explanatory variable and baseline RNFLT and the change in RNFLT measurements (ΔRNFLT) as the dependent variables. All analyses were adjusted for age, and statistical significance was set at $P < 0.05$.

**RESULTS**

**Patient Characteristics and Densitometry**

Data were available for SD-OCT in all 59 patients and for lens densitometry in 54 patients; 5 patients had insufficient densitometry image quality in the 3D cube. Mean age was $73.0 \pm 8.9$ years; 29 patients were female. The mean percentage of lens opacity in the 3D cube was $13.1\% \pm 2.1\%$. Further patient characteristics and densitometry analyses are shown in Table 1. None of the cataract surgery was complicated and no relevant postoperative inflammation occurred.

**SD-OCT Measurements**

RNFLT was nearly identical before and following cataract surgery. Mean differences of global RNFLT for the 3.5-, 4.1-, and 4.7-mm scans were $0.0 \mu m$ (95% confidence interval [CI] $-1.2; 1.2, P = 1.0$), $-0.3 \mu m$ (95% CI $-1.3; 0.6, P = 0.47$), and $-0.1 \mu m$ (95% CI $-1.2; 1.0, P = 0.82$), respectively. RNFLT did not change in any of the respective sectors, either (Table 2). Similarly, we detected no changes in BMO-MRW and the BMO...
area as well as the internal quality score following cataract surgery (Table 3). Spearman correlation analyses showed no correlation between baseline RNFLT and lens opacity. Only D\RNFLT at 4.1-mm eccentricity and at 4.7-mm eccentricity were weakly correlated with mean (r = 0.31) and maximum (r = 0.30) lens density, respectively (Table 4). Linear regression models controlling for age demonstrated no association of lens opacity with baseline RNFLT measurements, either. The beta coefficients (P values) per percentage lens opacity for baseline RNFLT measurements in the 3.5- and 4.7-mm scans either (β = −0.02, P = 0.95 and β = −0.15, P = 0.59). However, in the 4.1-mm scan \RNFLT showed a small association with lens opacity (β = −0.62, P = 0.008).

**DISCUSSION**

In our study, lens opacity was not associated with RNFLT, and a reduction in lens opacity (i.e., cataract surgery) did not cause any change in RNFLT. The RNFLT measurements before and after cataract surgery were virtually identical, with any

<table>
<thead>
<tr>
<th>Sector</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>Mean Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFLT 3.5 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td>93.3</td>
<td>93.3</td>
<td>0.0 (−1.2; 1.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Temporal</td>
<td>66.8</td>
<td>66.2</td>
<td>−0.6 (−2.0; 0.8)</td>
<td>0.39</td>
</tr>
<tr>
<td>Temporal superior</td>
<td>118.2</td>
<td>119.2</td>
<td>1.0 (−0.8; 2.8)</td>
<td>0.27</td>
</tr>
<tr>
<td>Temporal inferior</td>
<td>132.8</td>
<td>135.5</td>
<td>0.7 (−1.4; 2.8)</td>
<td>0.49</td>
</tr>
<tr>
<td>Nasal</td>
<td>79.5</td>
<td>79.0</td>
<td>−0.5 (−1.8; 0.8)</td>
<td>0.48</td>
</tr>
<tr>
<td>Nasal superior</td>
<td>115.4</td>
<td>116.9</td>
<td>1.5 (−0.4; 3.3)</td>
<td>0.12</td>
</tr>
<tr>
<td>Nasal inferior</td>
<td>105.3</td>
<td>104.3</td>
<td>−1.0 (−4.5; 2.6)</td>
<td>0.59</td>
</tr>
<tr>
<td>RNFLT 4.1 mm*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td>81.1</td>
<td>80.7</td>
<td>−0.3 (−1.3; 0.6)</td>
<td>0.47</td>
</tr>
<tr>
<td>Temporal</td>
<td>60.6</td>
<td>59.8</td>
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<td>0.13</td>
</tr>
<tr>
<td>Temporal superior</td>
<td>109.5</td>
<td>109.7</td>
<td>0.3 (−1.8; 2.3)</td>
<td>0.79</td>
</tr>
<tr>
<td>Temporal inferior</td>
<td>120.1</td>
<td>120.2</td>
<td>0.1 (−1.3; 1.5)</td>
<td>0.88</td>
</tr>
<tr>
<td>Nasal</td>
<td>66.7</td>
<td>66.3</td>
<td>−0.4 (−1.7; 0.9)</td>
<td>0.51</td>
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<tr>
<td>Nasal superior</td>
<td>95.2</td>
<td>95.6</td>
<td>0.4 (−1.0; 1.7)</td>
<td>0.59</td>
</tr>
<tr>
<td>Nasal inferior</td>
<td>85.2</td>
<td>84.5</td>
<td>−0.7 (−2.4; 1.1)</td>
<td>0.45</td>
</tr>
<tr>
<td>RNFLT 4.7 mm†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td>72.3</td>
<td>72.1</td>
<td>−0.1 (−1.2; 1.0)</td>
<td>0.82</td>
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<tr>
<td>Temporal</td>
<td>54.9</td>
<td>54.4</td>
<td>−0.5 (−2.0; 0.9)</td>
<td>0.47</td>
</tr>
<tr>
<td>Temporal superior</td>
<td>103.4</td>
<td>104.0</td>
<td>0.6 (−0.6; 1.9)</td>
<td>0.33</td>
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<tr>
<td>Temporal inferior</td>
<td>110.3</td>
<td>109.6</td>
<td>−0.8 (−2.6; 1.1)</td>
<td>0.43</td>
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<tr>
<td>Nasal</td>
<td>58.4</td>
<td>58.5</td>
<td>0.1 (−1.0; 1.2)</td>
<td>0.84</td>
</tr>
<tr>
<td>Nasal superior</td>
<td>81.2</td>
<td>81.5</td>
<td>0.3 (−0.7; 1.2)</td>
<td>0.57</td>
</tr>
<tr>
<td>Nasal inferior</td>
<td>70.9</td>
<td>71.6</td>
<td>0.6 (−1.4; 2.7)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

All measurements are mean values in micrometers (µm).

* Data available in 58 patients.
† Data available in 55 patients.
Our study did not confirm the previously described differences in SD-OCT-measured RNFLT following cataract surgery. First studies on the effect of cataract surgery on RNFLT measurements used scanning laser polarimetry (GDxVCC, glaucoma diagnosis variable corneal compensation analyzer) and reported contradicting results. However, several studies have reported cSLO imaging to be less affected by cataract than standard fundus photography. Since OCT devices are working with cSLO techniques, the effect of light attenuation and scattering might be smaller than expected, and imprecise scan placement may have been the main cause of the reported difference in RNFLT following cataract surgery.

With the emergence of OCT imaging, various studies on the influence of cataract surgery on OCT-based RNFLT measurements were conducted. Early investigations by El-Ashry et al. and Savini et al. in 2006 indicated that using the time-domain (TD) Stratus OCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA), RNFLT assessments were indeed affected by cataract surgery in 24 and 25 patients, respectively. Further studies with larger numbers of patients by Pareja-Esteban et al. (74 patients) and Mwanza et al. (45 patients) confirmed these findings. It was hypothesized that signal and quality reductions due to lens opacities were the underlying mechanisms. Interestingly, image quality as reported by the SD-OCT device did not differ before and after the lens removal in our study.

When technologically more advanced SD-OCTs became available, several SD-OCT devices were used in similar studies to reassess the influence of lens opacity on RNFLT measurements. The Stratus OCT uses a super luminescence diode (SLD) with a wavelength of 820 nm; the Cirrus OCT (Carl Zeiss Meditec, Inc.) and the Spectralis OCT use SLDs with wavelengths of 840 and 870 nm, respectively. The Spectralis OCT defines the optic disc based on the BMO and aligns the OCT scans accordingly. Hence, the discrepant findings between our and previous studies may be explained by our SD-OCT system using the APS. This software allows for precise imaging of the exact same retinal area at follow-up examinations, avoiding incorrect scan placement and contributing to more precise imaging.

A recent study by Celik et al. investigated the effect of uneventful cataract surgery on RNFLT and choroidal thickness measurements using the Cirrus OCT. The authors concluded that both retinal and choroidal thickness assessments increased after cataract removal and recommended new baseline measurements. In contrast to our study, Celik et al. did not place the OCT scans according to the patients’ individual anatomic landmarks, which may explain the different results. Precise RNFLT assessments require the correct placement of the OCT scan onto the ONH, which thus far had to be performed manually by the device operator. The correct recognition of the optic disc margins can be a challenging task and was demonstrated to result in variability of RNFLT measurements. Defining the optic disc margins based on the BMO as a clear anatomic structure has been suggested to be more reliable and consistent. The APS of the Spectralis SD-OCT defines the optic disc based on the BMO and aligns the OCT scans accordingly. Hence, the discrepant findings between our and previous studies may be explained by our SD-OCT system using the APS. This software allows for precise imaging of the exact same retinal area at follow-up examinations, avoiding incorrect scan placement and contributing to more precise imaging.

As mentioned above, light attenuation and light scattering due to cataract were hypothesized to cause the previously found differences in RNFLT before and after cataract surgery. However, several studies have reported cSLO imaging to be less affected by cataract than standard fundus photography. Since OCT devices are working with cSLO techniques, the effect of light attenuation and scattering might be smaller than expected, and imprecise scan placement may have been the main cause of the reported difference in RNFLT following cataract surgery.

Since the very early studies indicated the possible influence of cataract on GDxVCC and TD-OCT RNFLT assessments, a potential publication bias may have led to only positive results being published later on with SD-OCT. The magnitude of lens opacity in this study was comparable to that in other studies, reducing the probability of cataracts in our study being too mild to have an effect on OCT measurements. However, the influence of severe cataract on RNFLT measurements using the APS remains unclear and needs further investigation.

To date we are unaware of any study investigating the influence of cataract removal on BMO-based SD-OCT RNFLT assessments. The strengths of this study consist of the well-characterized patient sample and the APS to guarantee exact scan placement. With 59 eligible patients with SD-OCT imaging, the authors reported a better repeatability in the Spectralis OCT compared to the Cirrus OCT, which was explained by the Spectralis eye tracking technology (Tru Track) while scanning. Wilson et al. have compared the Cirrus and Spectralis OCT devices with regard to RNFLT measurements and reported differences to also depend on pathology and population.

### Table 4. Spearman Correlation Analyses Between Lens Densitometry Parameters and RNFLT, n = 50

<table>
<thead>
<tr>
<th>SD-OCT Scan</th>
<th>Mean Density</th>
<th>Maximum Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline RNFLT</td>
<td>r</td>
<td>P Value</td>
</tr>
<tr>
<td>3.5-mm scan</td>
<td>0.06</td>
<td>0.68</td>
</tr>
<tr>
<td>4.1-mm scan</td>
<td>0.15</td>
<td>0.27</td>
</tr>
<tr>
<td>4.7-mm scan</td>
<td>0.05</td>
<td>0.70</td>
</tr>
</tbody>
</table>

RNFLT, retinal nerve fiber layer thickness in μm; ΔRNFLT, difference in RNFLT before and after cataract removal.
In conclusion, our data indicate that a change in lens opacity (i.e., cataract removal) does not result in a change of RNFLT and BMO parameters in SD-OCT measurements using the APS. The previously described changes in RNFLT may have occurred due to small variations in the positioning of OCT measurements between visits. With the APS the anatomic structure of an individual is recognized by the device, and subsequent measurements are conducted on this basis. The noise and physical light attenuation caused by lens opacity cannot be eliminated by the APS, but accurate follow-up scan placement may reduce variability considerably. Our results imply that the previously hypothesized influence of lens opacity on retinal SD-OCT measurements can be disregarded when exact follow-up scan placement is guaranteed.

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