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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 diagnostics[1–3] 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 (MMM). 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 Glaucoma Module for 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 distribution of the Spectralis OCT (nasal [N], nasal superior [NS], nasal inferior [NI], temporal [T], temporal superior [TS], and temporal inferior [TI]), T and N twice the size of the other sectors.[21,22] BMO area was calculated per eye in square millimeters (mm^2). Signal strength was automatically determined as a quality score ranging from 0 (poor quality) to 40 (excellent quality).[16]

Scheimpflug imaging and densitometry were performed using the Pentacam AXL (Software Version 1.20r88; Oculus GmbH). The principles and performance of this technique have been described elsewhere.[23,24] We performed densitometry analyses with the three-dimensional (3D) cube using a central cylindrical block of 2 to 3 mm averaging all Scheimpflug images. Additionally, densitometry was calculated in three preset reference blocks (Pentacam Densitometry Zones [PDZ]) with diameters of 2, 4, and 6 mm, respectively, covering the whole lens depth.[25]

Data Analysis

Data of SD-OCT were automatically exported into a spreadsheet application with the inbuilt export function (Microsoft Excel 2010; Microsoft, Redmond, WA, USA). Densitometry data were extracted and entered into a database. All analyses were performed with the statistical software RStudio (RStudio, Inc., Boston, MA, USA; https://www.rstudio.com/, in the public domain). RNFLT, BMO-MRW, and BMO area before and after cataract surgery were compared using the Student's *t*-test for paired data. We calculated Spearman correlation coefficients of both 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 $P < 0.05$.

Table 1. Patient Characteristics, $n = 59$, and Lens Densitometry Analyses, $n = 54$

Characteristics	Mean ± SD or *n* (%)
Age, y	73.0 ± 8.9
Sex	
Male, *n* (%)	30 (51%)
Female, *n* (%)	29 (49%)
BCVA	
Preoperative*	0.5 ± 0.2
Postoperative†	0.7 ± 0.2
Densitometry	Mean ± SD
3D cube, 2 × 3 mm	
Average	13.1% ± 2.1
Maximum	38.7% ± 14.0
PDZ, 2 mm	12.4% ± 2.0
PDZ, 4 mm	11.9% ± 1.7
PDZ, 6 mm‡	11.6% ± 1.2
PNS, range, 0–5	1.5
RMS-HOA	0.60 μm ± 0.28

BCVA, best-corrected visual acuity; PNS, Pentacam Nucleus Staging; RMS-HOA, root mean square higher-order aberrations; SD, standard deviation.

* Data available in 47 patients.

† Data available in 42 patients.

‡ Data available in 39 patients.

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 ± 8.9 years; 29 patients were female. The mean percentage of lens opacity in the 3D cube was 13.1% ± 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 μm (95% confidence interval [CI] −1.2; 1.2, $P = 1.0$), −0.3 μm (95% CI −1.3; 0.6, $P = 0.47$), and −0.1 μm (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

Table 2. SD-OCT RNFLT Measurement Results, $n = 59$

Sector	Preoperative	Postoperative	Mean Difference (95% CI)	*P* Value
RNFLT 3.5 mm				
Global	93.3	93.3	0.0 (−1.2; 1.2)	1.00
Temporal	66.8	66.2	−0.6 (−2.0; 0.8)	0.39
Temporal superior	118.2	119.2	1.0 (−0.8; 2.8)	0.27
Temporal inferior	132.8	133.5	0.7 (−1.4; 2.8)	0.49
Nasal	79.5	79.0	−0.5 (−1.8; 0.8)	0.48
Nasal superior	115.4	116.9	1.5 (−0.4; 3.3)	0.12
Nasal inferior	105.3	104.3	−1.0 (−4.5; 2.6)	0.59
RNFLT 4.1 mm*				
Global	81.1	80.7	−0.3 (−1.3; 0.6)	0.47
Temporal	60.6	59.8	−0.8 (−2.0; 0.3)	0.13
Temporal superior	109.5	109.7	0.3 (−1.8; 2.3)	0.79
Temporal inferior	120.1	120.2	0.1 (−1.3; 1.5)	0.88
Nasal	66.7	66.3	−0.4 (−1.7; 0.9)	0.51
Nasal superior	95.2	95.6	0.4 (−1.0; 1.7)	0.59
Nasal inferior	85.2	84.5	−0.7 (−2.4; 1.1)	0.45
RNFLT 4.7 mm†				
Global	72.3	72.1	−0.1 (−1.2; 1.0)	0.82
Temporal	54.9	54.4	−0.5 (−2.0; 0.9)	0.47
Temporal superior	103.4	104.0	0.6 (−0.6; 1.9)	0.33
Temporal inferior	110.3	109.6	−0.8 (−2.6; 1.1)	0.43
Nasal	58.4	58.5	0.1 (−1.0; 1.2)	0.84
Nasal superior	81.2	81.5	0.3 (−0.7; 1.2)	0.57
Nasal inferior	70.9	71.6	0.6 (−1.4; 2.7)	0.54

All measurements are mean values in micrometers (μm).
* Data available in 58 patients.
† Data available in 55 patients.

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 ΔRNFLT 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-, 4.1-, and 4.7-mm scans were $\beta = 0.96$ ($P = 0.44$), $\beta = 1.53$ ($P = 0.14$), and $\beta = 0.69$ ($P = 0.45$). Furthermore, ΔRNFLT was not associated with lens opacity in the 3.5- and 4.7-mm scans either ($\beta = -0.02$, $P = 0.95$ and $\beta = -0.15$, $P = 0.59$). However, in the 4.1-mm scan ΔRNFLT showed a small association with lens opacity ($\beta = -0.62$, $P = 0.008$).

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 3. SD-OCT BMO Measurement Results, $n = 59$

Sector	Preoperative	Postoperative	Mean Difference (95% CI)	*P* Value
BMO area				
Total area	1.98	1.96	−0.01 (−0.04; 0.01)	0.25
BMO-MRW				
Global	300.4	300.9	0.5 (−1.6; 2.5)	0.66
Temporal	207.6	207.5	−0.2 (−2.3; 1.9)	0.86
Temporal superior	278.4	279.1	0.8 (−2.2; 3.7)	0.60
Temporal inferior	305.8	306.4	0.5 (−4.9; 6.0)	0.84
Nasal	341.6	342.2	0.7 (−3.0; 4.3)	0.73
Nasal superior	339.4	341.8	2.4 (−1.3; 6.0)	0.20
Nasal inferior	373.9	372.8	−1.2 (−4.8; 2.5)	0.53
Scan quality				
3.5-mm scan	21.6	20.6	−1.0 (−2.3; 0.4)	0.16
4.1-mm scan	20.9	20.5	−0.4 (−1.8; 0.9)	0.52
4.7-mm scan	20.9	20.1	−0.9 (−2.3; 0.6)	0.23

BMO-MRW measurements are mean values in μm, BMO area in μm², scan quality is unitless.

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

	3D Cube Densitometry			
	Mean Density		Maximum Density	
SD-OCT Scan	*r*	*P* Value	*r*	*P* Value
Baseline RNFLT				
3.5-mm scan	0.06	0.68	−0.07	0.61
4.1-mm scan	0.15	0.27	0.01	0.98
4.7-mm scan	0.05	0.70	0.03	0.86
ΔRNFLT				
3.5-mm scan	0.11	0.42	0.19	0.16
4.1-mm scan	0.31	0.02	0.17	0.23
4.7-mm scan	0.19	0.20	0.30	0.03

RNFLT, retinal nerve fiber layer thickness in μm; ΔRNFLT, difference in RNFLT before and after cataract removal.

differences being very small and with narrow CIs. For the BMO assessments we did not find any change following cataract surgery, either. The correlation and association of ΔRNFLT with lens opacity are likely spurious, since absolute values for RNFLT did not differ before and after surgery. Hence, our results indicate that cataract surgery does not impact APS-guided SD-OCT measurements of RNFLT and BMO.

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.[26,27] Vetrugno et al.[26] did not find any significant changes after cataract surgery in 68 patients. In contrast, Iacono et al.[27] demonstrated significant RNFLT variations postoperatively in a smaller sample (28 patients), suggesting new baseline measurements after 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.[15] and Savini et al.[28] 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.[13] (74 patients) and Mwanza et al.[12] (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.[16–18,29] 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.[30–32] Scan speed improved from 400 A-scans per second in Stratus TD-OCT to 27,000 A-scans in Cirrus SD-OCT and 40,000 A-scans per second in Spectralis SD-OCT. Axial and transverse resolution improved from 10 and 20 μm in Stratus OCT[30] to 5 and 15 μm in the Cirrus OCT[31] and 7 and 14 μm in the Spectralis OCT.[32] In addition, improved eye tracking technologies were introduced. Bambo et al.[16] reported that most RNFL measurements differed significantly before and after cataract surgery in both the Cirrus and the Spectralis OCT; macular thickness differed only in the Cirrus OCT. However, 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.[33] have compared the Cirrus and Spectralis OCT devices with regard to RNFLT measurements and reported differences to also depend on pathology and population.

A recent study by Celik et al.[34] 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.[34] 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,[35,36] 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.[37] Defining the optic disc margins based on the BMO as a clear anatomic structure has been suggested to be more reliable and consistent.[2,20,38–40] 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.[41,42] 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.[23,24] 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 RNFTL 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 cohort was indeed only moderately sized but of a similar magnitude to that in all other studies published to date. Also, the CIs of our data were already narrow at this moderate sample size. Postoperative measurements were performed earlier than in other studies, namely on the first day after surgery. Yet, since all patients were examined for relevant signs of inflammation or hemorrhage by an ophthalmologist, the influence of these can be ruled out. Another limitation to be considered is that we did not collect data on the influence on macular RNFLT. As the measurement is the same including the APS, we expect there to be no change in macular RNFLT following cataract surgery, either. However, further investigations need to confirm this.

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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