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published in
Acta Ophthalmologica
2015

DOI (link to publisher)
10.1111/aos.12596

document version
Publisher's PDF, also known as Version of record

citation for published version (APA)
Darma, S., Kok, P. H. B., van den Berg, T. J. T. P., Abràmoff, M. D., Faber, D. J., Hulsman, C. A., Zantvoord, F., Mourits, M. P., Schlingemann, R. O., & Verbraak, F. D. (2015). Optical density filters modeling media opacities cause decreased SD-OCT retinal layer thickness measurements with inter- and intra-individual variation. *Acta Ophthalmologica*, *93*(4), 355-61. https://doi.org/10.1111/aos.12596

Acta Ophthalmologica

Optical density filters modeling media opacities cause decreased SD-OCT retinal layer thickness measurements with inter- and intra-individual variation

Stanley Darma,[1] Pauline H. B. Kok,[1] Thomas J. T. P. van den Berg,[2] Michael D. Abràmoff,[3] Dirk J. Faber,[4] Caroline A. Hulsman,[1] Frank Zantvoord,[1] Maarten P. Mourits,[1] Reinier O. Schlingemann[1,2] and Frank D. Verbraak[1,4]

[1]Department of Ophthalmology, Academic Medical Center, Amsterdam, The Netherlands
[2]Netherlands Institute for Neuroscience, Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands
[3]Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, USA
[4]Biomedical Engineering and Physics, Academic Medical Center, Amsterdam, The Netherlands

ABSTRACT.
Purpose: **To assess the effect of media opacities on thickness measurements of the peripapillary retinal nerve fibre layer (pRNFL) and macular inner retinal layer (mIRL) performed with spectral-domain optical coherence tomography (SD-OCT) using a set of filters with known optical density.**
Methods: **Spectral-domain optical coherence tomography volume scans of the optic disc and the macular area were performed in 18 healthy volunteers, using Topcon-3DOCT-1000 Mark II. A set of five filters with optical density ranging from 0.04 to 0.69 was used. The correlation was calculated between the percentage change in thickness measurements (%ΔpRNFL and %ΔmIRL) and the change in optical density. All scans and measurements were performed in duplicate by one operator.**
Results: **Eighteen right eyes of 18 healthy volunteers were included in this study. Percentage decrease in pRNFL and mIRL thickness correlated with change in optical density (Spearman's rho $r = 0.82$; $p < 0.001$ and $r = 0.89$; $p < 0.001$, respectively). The measured decrease in pRNFL thickness differed from the decrease in mIRL thickness, not only between individuals, but also within the same individual.**
Conclusions: **Optical coherence tomography thickness measurements of both pRNFL and mIRL are influenced by image degradation caused by optical density filters as a model for media opacities. An underestimation of the thickness of these layers was observed, caused by a shift of retinal layer boundary placement due to image quality loss. This underestimation is not the same for each individual and also differed between the pRNFL and mIRL thickness measurements. These individual and interindividual differences demonstrate that an individual approach will be necessary to correct for this underestimation per layer.**

Key words: image quality – macular inner retinal layers – peripapillary retinal nerve fibre layer – spectral-domain optical coherence tomography

Acta Ophthalmol. 2015: 93: 355–361

doi: 10.1111/aos.12596

Introduction

Optical coherence tomography (OCT) has become an important instrument in the diagnosis of glaucoma (Grewal & Tanna 2013). In glaucoma, there is a loss of retinal ganglion cells and thinning of the retinal nerve fibre layer (RNFL). Currently, peripapillary retinal nerve fibre layer (pRNFL) thickness measurements are used as an objective measurement of glaucomatous damage, for detecting early glaucoma and glaucoma progression in the management of patients with glaucoma (Grewal & Tanna 2013). More recently, the macular inner retinal layer (mIRL) thickness, consisting of the RNFL, ganglion cell layer (GCL) and inner plexiform layer (IPL), has also been shown to be a good diagnostic parameter for early glaucoma. It has demonstrated high reproducibility, good diagnostic performance and has the advantage of a central fixation (Wong et al. 2012). Both pRNFL and mIRL thickness measurements represent loss caused by damage to the retinal ganglion cell (RGC) axons in the optic nerve head in glaucoma. Before visual field defects become detectable, OCT can already demonstrate a decrease in thickness of the pRNFL and mIRL in glaucoma patients (Lee et al. 2012; Grewal & Tanna 2013). Preperimetric detection of glaucoma might allow for patients to be treated at an earlier stage of the disease.

Optical coherence tomography is an optical measurement technique that uses near-infrared light reflected from the retina to assess the thickness of the retina and its individual layers (Huang et al. 1991; van Velthoven et al. 2007). The time-domain optical coherence tomography (TD-OCT) system has been overtaken by spectral-domain optical coherence tomography (SD-OCT), which has major advances in imaging speed and sensitivity (Wojtkowski et al. 2004). Much like other imaging techniques, OCT is subject to artefacts and variability. Factors such as pupil dilation, medium opacity, scanning protocol, OCT device and software can influence the quality of the scans and the thickness measurements (Savini et al. 2006; Yoo et al. 2009). To overcome some of these limitations, we recently introduced a phantom eye model to calibrate individual systems (de Kinkelder et al. 2013).

Cataract is a common cause of media opacity and studies have shown that pRNFL and mIRL thickness measurements are affected by cataract, causing an underestimation of pRNFL and mIRL thickness (Lee et al. 2010; Mwanza et al. 2011; Kok et al. 2013; Nakatani et al. 2013). The loss of OCT image quality in patients with disturbances in the optical media is caused by attenuation of the light of the OCT scanning spot on the retina (Kok et al. 2009).

Cataract is often present in patients with glaucoma, especially in the eyes of older patients. It can act as a confounding factor and can lead to an incorrect diagnosis of glaucoma or glaucoma progression. Because both the pRNFL and the mIRL thickness measured with SD-OCT are important for early detection of glaucoma and detection of progression, it is of interest to know what the exact influence of media opacities is on both thickness measurements, and whether both measurements are influenced in the same way.

This study aimed to assess and quantify the influence of disturbances in the optical media on the SD-OCT thickness measurements of the pRNFL and the mIRL. Optical density filters were used to model a comparable range of optical density values as those observed in cataract patients, as described in previous studies (Kok et al. 2009, 2013). The main objectives were to determine whether the pRNFL and the mIRL were influenced in the same way. This information is needed to decide whether, and in which way, we are able to correct OCT layer thickness measurements affected by a lower image quality.

Materials and Methods

Subjects

Eighteen healthy right eyes of 18 healthy individuals were included in this study. The research followed the Tenets of the Declaration of Helsinki, and informed consent was obtained from all participants. The participants underwent an ophthalmic examination, including slit-lamp biomicroscopy, measurement of visual acuity, intraocular pressure and refractive error.

Image acquisition and thickness measurements

All OCT examinations were performed by one single experienced operator, with the Topcon 3D OCT-1000 Mark II (Topcon Medical Systems, Tokyo, Japan; 5–6 μm depth resolution). Of each eye, two volume scans were made of both the optic disc and the macular area, after pupil dilation with 0.5% tropicamide. These measurements served as reference values of the thickness measurements. Then, a set of five reflective filters (Balzers) was used to mimic light loss caused by media opacities of the eye, like cataract. Each scan was performed in duplicate, so a total of 12 volume scans of the optic disc and 12 of the macular area were made per eye. The volume scanning protocol was a raster scan consisting of 128 B-scans, each with 512 A-scans, covering a 6 × 6 mm region, centred at either the optic disc or the fovea. The quality parameter provided by the OCT software was also collected. Mean total retinal thickness (mRT), pRNFL and mIRL thickness were computed and extracted from the volume scans using the ETDRS grid area for macular scans and a 3.4-mm diameter virtual circle centred at the optic disc for optic disc scans. The thickness measurements were performed with the Iowa Reference Algorithm which uses a fully three-dimensional graph search approach (Garvin et al. 2009; Available on http://www.iibi.uiowa.edu/content/iowa-reference-algorithms-human-and-murine-oct-retinal-layer-analysis-and-display).

Light attenuation model

Similar to the model used in a previous study (Kok et al. 2009, 2013), a set of five reflective filters with a known optical density ranging from 0.04 to 0.69 was used to simulate a disturbance of the optical media (Fig. 1 and Table 1).

The optical density filter was positioned, manually, right in front of the eye. Accurate care was taken in positioning of the filters by checking for potential tilt of the filters. This tilt was estimated to be <10°. In this manner, a maximum error of 2% was accepted. The head of the individual was always positioned against the head rest during scanning. In a previous study, it was found that attenuation of the light in the OCT scanning spot on the retina, expressed as optical density, fully determined loss of OCT image quality as provided by the OCT system, irrespective of the nature of the filter, or type of cataract (Kok et al. 2009, 2013). Therefore, only one type of filters was used in this study to model the image quality decrease of the OCT image. The effects of the filters on the OCT images are visible in Fig. 2. These filters had the same range of optical density values that can be observed in cataract patients.

The mean layer thickness without filters was taken as baseline layer thick-

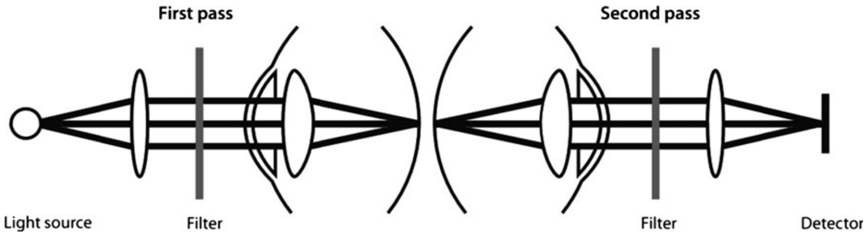

Fig. 1. Schematic illustration of filter placement in optical pathway.

ness. The difference between the baseline measurements and the measurements with the reflective filters was noted as ΔpRNFL and ΔmIRL, respectively. Using the percentage decrease of pRNFL and mIRL, the rate of decrease in both layer thickness measurements could be compared with each other. To illustrate the decrease in SD-OCT measured mIRL thickness in relation to the changes in the other retinal layers, the thickness measurement of all macular retinal layers is shown for each optical density filter in a stack diagram (Fig. 3). The differences in layer thickness change were assessed between individuals.

Reflectivity profiles

To explore the possible relationship between the height of the reflectivity peaks, the reflectivity decrease as result of the filter induced light attenuation and the filter induced mIRL thickness change, raw data were exported to analyse with custom software in LabVIEW 2010 (version 10.0.1; National Instruments, Austin, TX, USA) (Fig. 4). The reflectivity profiles of 25 adjacent A-scans located 1.5 mm nasally to the fovea out of the central B-scan going through the fovea were averaged and analysed. The initial heights of the reflectivity peaks of the IPL-INL transition and the posterior retinal pigment epithelium (RPE) border in the macular scans, and of the RNFL reflectivity peak in the optic disc scans, were measured, as well as the decrease of the peak height as result of the set of optical density filters.

Table 1. Single pass optical density values (in log units) of the reflective filters.

Transparency (%)	Optical density
79.2	0.04
63.0	0.11
51.2	0.26
25.4	0.54
19.6	0.67

Statistical analysis

Linear regression analysis was performed to determine the regression equation between optical density and change in thickness measurements. Correlations of optical density change with change in the thickness measurements, as well as reflectivity peak decrease with layer thickness decrease, were studied using Spearman's correlation test. Change in thickness measurements as result of optical density change was evaluated with a repeated-measurements anova test. Bland–Altman plots were used to assess the agreement of the in duplicate performed measurements. A p-value of ≤0.05 was considered as statistically significant, and this threshold was, where necessary, adjusted for multiple testing with Bonferroni corrections. Statistical software Microsoft Excel (Microsoft Office Excel 2003; Microsoft Corporation; Redmond, WA, USA) and spss (spss 16.0; SPSS Inc., Chicago, IL, USA) were used for data analysis.

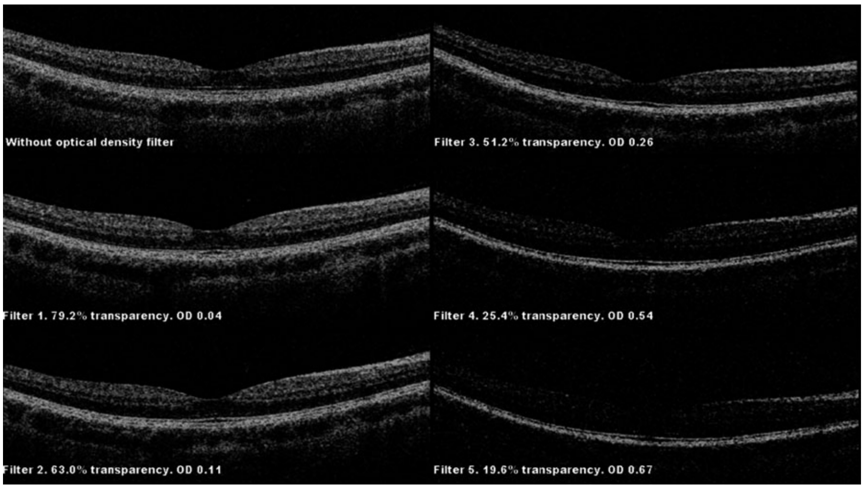

Fig. 2. OCT macular volume scans of one healthy eye with the application of optical density filters. OCT, optical coherence tomography.

Results

Four hundred and twenty-six SD-OCT volume scans of 18 right eyes of 18 healthy volunteers were included for analysis. Six scans were excluded due to motion artefacts; in these cases, only one scan was used. The means of the duplicate measurements were used in the analyses. Table 2 shows the characteristics of the study participants. All 18 healthy volunteers had a normal optic disc appearance and none of them suffered from any ophthalmological condition, with the exception of minor refraction errors. The mean pRNFL thickness was 101 μm ($\pm$10 μm), and the mean mIRL thickness was 103 μm ($\pm$8 μm). Table 3 shows the differences found in layer thickness measurements between scans made with different optical density filters.

Peripapillary RNFL thickness measurements

The increase in optical density was linearly correlated with the percentage decrease in RNFL thickness, as shown in Fig. 5A ($r = 0.82$, $p < 0.001$).

Peripapillary retinal nerve fibre layer thickness started to decrease with a difference greater than one standard deviation (SD) beyond a threshold optical density of 0.54 (Table 3). More than one SD was considered to be clinically relevant. The difference between the duplicate pRNFL thickness measurements is shown for each optical density value in a box plot (Fig. 5B). This demonstrates a higher variability with increasing optical density.

Macular measurements

The increase in optical density was also linearly correlated with the percentage decrease in mIRL thickness, as shown in Fig. 5C ($r = 0.89$, $p < 0.001$). mIRL thickness only decreased with a difference greater than one SD after a threshold optical density of 0.26 (Table 3). The difference between the duplicate mIRL thickness measurements and range of the difference is shown for each optical density value in a box plot (Fig. 5D). This demonstrates a higher variability with increasing OD. Total retinal thickness also decreased as a result of the increase in optical density, but the differences were smaller. Figure 3 shows a stack diagram to illustrate

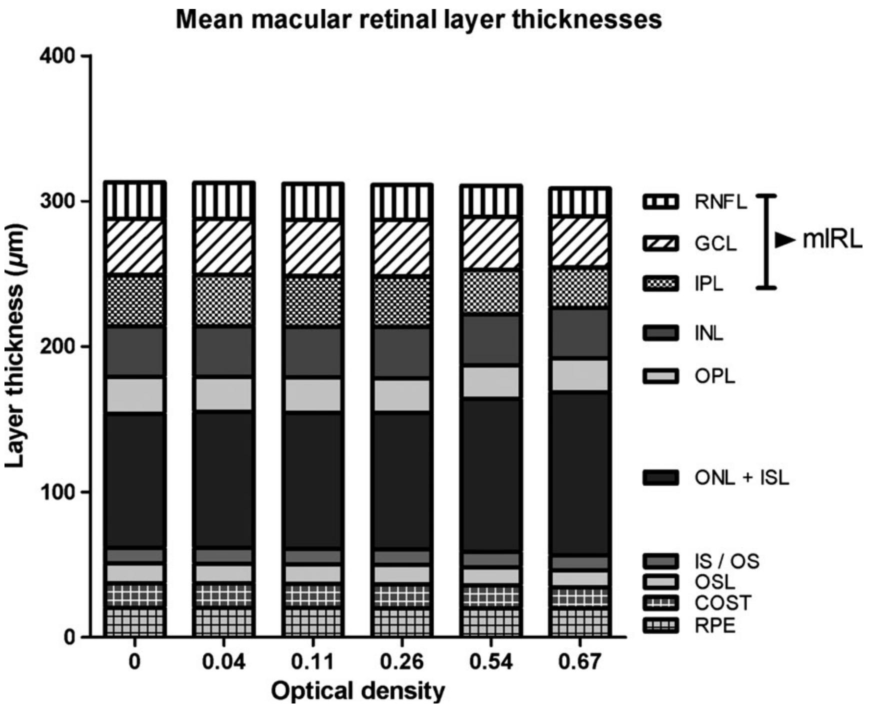

Fig. 3. Stack diagram representing the mean macular retinal layer thicknesses. INL, Inner nuclear layer; OPL, outer plexiform layer; ONL, outer nuclear layer; ISL, inner segment layer; IS/OS, inner segment/outer segments; COST, cone photoreceptor outer segment tips; RPE, retinal pigment epithelium.

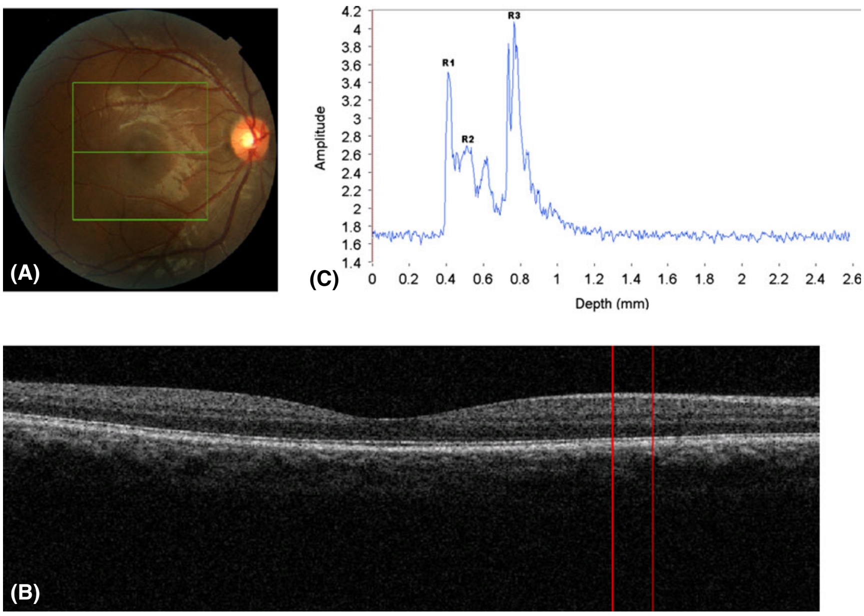

Fig. 4. (A) Fundus photograph: green square demarcates OCT scanning area and the central line the selected horizontal B-scan. (B) The selected 6 mm horizontal B-scan at the fovea. Red lines demarcate selected area of the 25 averaged A-scans analysis. (C) Averaged A-scan reflectivity profiles. *Y*-axis shows the reflectivity in arbitrary units. R1. RNFL peak; R2. IPL-INL peak; R3. RPE peak. IPL, inner plexiform layer; INL, inner nuclear layer; OCT, optical coherence tomography; RPE, retinal pigment epithelium.

the decrease of the retinal layers as measured in the macular volume scan. As can be seen, with an increasing optical density, the mIRL thickness decreases more than the total retinal thickness. The ganglion cell–inner plexiform layer (GC-IPL) thickness showed a similar decrease, of which the data are not shown. The measurements of the average mIRL of the whole ETDRS region are shown. Contrary to the mIRL, the mean ONL + ISL thickness measurements increased with an increasing optical density. Our measurements also showed that the layer thickness change was similar for the perifoveal, parafoveal and individual ETDRS areas within the same individual. Figure 6 shows an example of the segmentation lines in the SD-OCT image of the macula.

Individual difference in induced decrease of pRNFL and mIRL

Figure 5A,C show a scatter plot with the relationship between the increasing optical density and the decreasing retinal layer thickness of the pRNFL and the mIRL, as measured with SD-OCT. The spread in the measurements becomes larger with higher optical density, and each individual differed in the steepness of the linear relation between the change in optical density and % ΔpRNFL and % ΔmIRL. In other words, the rate of decrease of the thickness measurement as a result of the increase in optical density differed per individual. Two individual regression lines are shown in the figures, one with the steepest slope and one with the least steep slope.

Figure 7 shows a scatter plot of the coefficients of the regression lines of Fig. 5A,C, per individual. This shows that the coefficients of the slope of the change in mIRL and pRNFL, caused by optical density change, are not the same in each individual. Also, the individuals with most and least percentage change differ between Fig. 5A,C. Thus, the rate of decrease of the thickness of the mIRL and that of the pRNFL was not identical for one individual.

Reflectivity profiles

The mean initial RPE reflection peak over all persons (R3 in Fig. 4C) was higher and decreased slightly more than the IPL-INL transition peak (R2 in Fig. 4C). Comparing the reflectivity peaks of the RPE and the IPL-INL transition per individual, the relationship of a faster decrease in case of higher initial reflection peaks was not found. Some individuals had higher initial reflectivity peaks than others, but the decrease in reflectivity was the same for each individual. We did find a correlation between the height of the initial IPL-INL reflectivity peak and the decrease in mIRL layer thickness (Spearman's rho $r = -0.68$; $p \leq 0.01$): a lower initial reflectivity peak was associated with a faster decrease in mIRL layer thickness. This was not found in the relation between initial reflectivity peak height of the pRNFL and the pRNFL thickness (Spearman's rho $r = 0.48$; $p = 0.23$).

Discussion

The results of this study showed that OCT-measured pRNFL and mIRL thickness is affected by a set of optical density filters with increasing optical density. The differences in retinal layer thickness measurement were statistically significant beyond an optical density value of 0.11 or higher for mIRL and 0.26 or higher for pRNFL. However, only with an optical density value used higher than 0.26 for mIRL and 0.54 for pRNFL, the retinal layer thickness measurement showed a decrease larger than 1 SD, which we considered to be clinically relevant. These optical density values corresponded with an image quality factor of 53 for the mIRL and 32 for the pRNFL, respectively (Table 3). The reproducibility of the measurements was good for all measurements, with an increasing variability with higher optical density values.

Table 2. Baseline characteristics.

	Mean	SD
Age (years)	25	3
Visual acuity (logMar)	−0.04	0.1
IOP (mmHg)	13	2
SE (dioptres)	−2.2	2.3
pRNFL (μm)	101	10
mIRL (μm)	103	8
RT (μm)	313	16
Quality factor (macula)	85	7
Quality factor (optic nerve head)	83	6
Male (%)	56	

mIRL, macular inner retinal layer; pRNFL, peripapillary retinal nerve fibre layer.

Our findings confirm that in case of low image quality, one should be aware of the possibility of underestimation of the retinal layer thicknesses, both the pRNFL and the mIRL (Mwanza et al. 2011; Kok et al. 2013; Nakatani et al. 2013). An underestimation of these layer thicknesses can influence glaucoma diagnosis and progression detection using OCT.

Inducing an optical disturbance with a known optical density value can also point the way to a method to correct for measurement errors caused by cataract. However, the individual differences of the relationship between optical density and retinal layer thickness found in this study suggest this should be corrected for each individual differently. Probably, the cause of this individual variation is explained by an interindividual difference in reflectivity of the retinal layers. A possible correction for the influence of optical density is even more complex, because the percentual decrease in layer thickness of pRNFL and mIRL is not equal within one individual.

Cataract is a common cause of optical disturbances affecting image quality of OCT scans. Image quality is an important factor in the reliability of OCT test results, as a high-quality image ensures accurate diagnosis. The effect of cataract on OCT measurements has been studied in both TD-OCT and SD-OCT. Several studies have measured a thinner pRNFL thickness in cataract patients prior to surgical removal of the cataract, compared with postoperative pRNFL thickness (El-Ashry et al. 2006; Savini et al. 2006; Mwanza et al. 2011; Kim et al. 2012; Kok et al. 2013). This underestimation of pRNFL thickness was correlated with a lower image quality. The more advanced the cataract, the lower the image quality and the thinner the pRNFL thickness. As image quality mainly depends on the amount of light that passes through the optical media to reach a focussed OCT scanning spot, the increase in image quality after cataract surgery is a result of an increased light transmittance and improved focussing. These findings are confirmed by the results of the present study. Our data showed a decreasing image quality factor and decreasing pRNFL thickness with increasing optical density. Of all scans included in the analysis, the segmentation software was still able to distinguish all the individual layers of the retina, without gross artefacts leading to border assignment errors.

Recently, Nakatani et al. (2013) described the effect of the removal of cataract on both pRNFL and mIRL measurements with the Optovue RTVue-100 SD-OCT, in patients with and without glaucoma. They found segmentation errors in mIRL and pRNFL measurements performed in the preoperative OCT imaging, due to a lower image quality leading to underestimation of the measured retinal layer thickness. They also found that the mIRL measurements were affected more than the pRNFL measurements. Segmentation errors due to low image quality and posterior subcapsular opacity were pointed out as the cause for a thinner mIRL measurement, as well as the possibility that a wider measurement area can lead to a higher error rate in case of the mIRL measurements. In the present study, we also found that the mIRL is affected more than the pRNFL, and for both measurements, we used data from 6 × 6 mm volume scans.

Table 3. Mean layer thicknesses, percentual thickness change and quality factor (QF) per filter.

Optical density	Macula QF	ONH QF	mIRL (μm)	p*	%ΔmIRL 95% CI (%)	pRNFL (μm)	p*	%ΔpRNFL 95% CI (%)	mRT (μm)	p*	%ΔmRT 95% CI (%)
0.00	85 ± 7	83 ± 6	103 ± 8			101 ± 10			313 ± 16		
0.04	76 ± 9	76 ± 9	102 ± 7	0.666	0.4 (0.1–0.7)	101 ± 11	1.000	0.4 (0.3–1.4)	312 ± 16	0.048	0.2 (0.0–0.3)
0.11	70 ± 10	73 ± 6	102 ± 8	0.023	0.8 (0.4–1.2)	100 ± 11	0.526	0.9 (0.3–1.4)	312 ± 16	0.023	0.3 (0.1–0.5)
0.26	53 ± 8	55 ± 7	101 ± 8	<0.001	1.9 (1.6–2.2)	98 ± 11	0.002	2.7 (1.8–3.6)	311 ± 16	<0.001	0.7 (0.4–0.9)
0.54	28 ± 6	32 ± 7	95 ± 7†	<0.001	7.6 (6.1–9.0)	94 ± 11	<0.001	7.6 (6.3–9.0)	307 ± 16	<0.001	1.5 (1.1–2.0)
0.67	19 ± 5	23 ± 4	89 ± 7†	<0.001	13.5 (11.5–15.5)	86 ± 11†	<0.001	15.0 (12.4–17.6)	305 ± 14	<0.001	2.1 (1.8–2.5)

mIRL, macular inner retinal layer; mRT, mean total retinal thickness; pRNFL, peripapillary retinal nerve fibre layer.

* Bonferroni corrected p-value of repeated-measurements anova. p is significant at 0.05.

† Difference with baseline measurement larger than one SD.

Contrary to the pRNFL and the mIRL, the full thickness measurements of the retina did not decrease much with increasing optical density. Even at an optical density of 0.67, only a slight decrease within one SD of the baseline measurement was observed. A possible explanation may be found in the fact that in OCT scanning, the boundaries of the retina are highly reflective as compared to the surrounding tissue. Therefore, the border of the RNFL with the vitreous, as well as the RPE with the choroid, can be correctly identified, even with impaired light transmittance. However, the intraretinal layer borders are less clear and therefore more susceptible for segmentation errors due to a lesser image quality. This can also explain the increase in ONL + ISL thickness with increasing optical density. The ONL + ISL are in general less reflective than the surrounding layers, the outer plexiform layer (OPL) and the inner segment/outer segments (IS/OS) transition or ellipsoid zone. This is shown in OCT images as a darker area. The ONL + ISL thickness increase is most likely due the overall image quality deterioration, making the intraretinal layer borders less clear. We see that this leads to a shift of the borders, leading to a falsely thinner OPL and IS/OS transition line, and as a consequence, a falsely thicker ONL + ISL measurement.

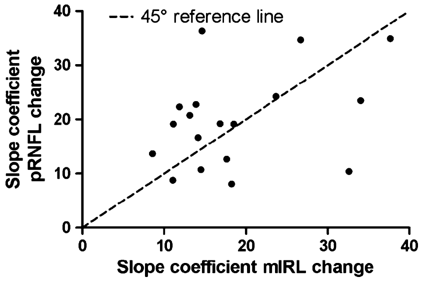

Fig. 7. Slope coefficients of % mIRL and % pRNFL change per individual. Each dot represents one individual. Identical slope coefficients would have been lying on the 45-degree reference line. mIRL, macular inner retinal layer; pRNFL, peripapillary retinal nerve fibre layer.

The multiple surfaces in the Iowa Reference Algorithm are detected simultaneously through the computation of a minimum-cost closed set in a vertex-weighted graph constructed using edge and regional information (Antony et al. 2010). Our results did not show a decrease in retinal thickness. However, one can speculate that the full thickness measurement of the retina will decrease with a higher optical density value than used in this study. This would be in accordance with results of studies investigating the effect of cataract and image quality on macular thickness (van Velthoven et al. 2006; Samarawickrama et al. 2010). We are currently improving the segmentation algorithm to decrease the effects of lower image contrast due to media opacities on layer thicknesses.

Tappeiner et al. (2008) reported that in Stratus OCT data of macular line scans, highly reflective peaks in the averaged A-scan reflectivity profiles decreased more than less reflective peaks, as a result of light attenuation. These results could serve as a possible explanation of the individual differences in our results. But we found that the mean initial reflectivity peak of the RPE border was higher and decreased slightly more, compared with the IPL-INL transition. However, this difference was small, and the relationship was not found comparing the reflectivity profiles per individual. We could not confirm this to be a cause of the individual differences in the relation between change in optical density and % ΔmIRL, nor for the differences found between the percentage decrease between mIRL and pRNFL. It has been suggested that the RNFL consists of both neuronal and non-neuronal

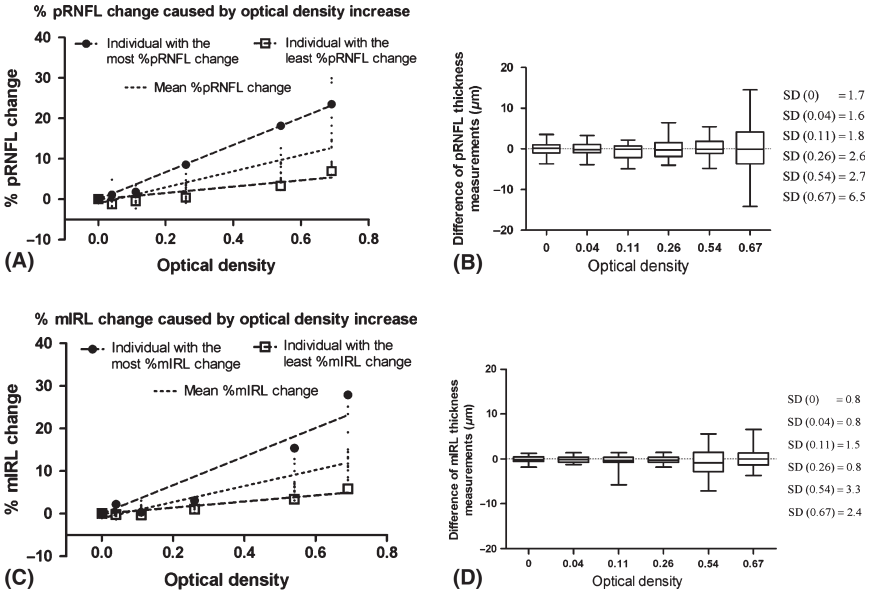

Fig. 5. (A) Linear relationship between the optical density and the % ΔpRNFL. Each dot represents an individual measurement. Mean change is the mean % change of all persons. (B) Box plot of the difference between the in duplicate performed pRNFL thickness measurements. Upper and lower whiskers show the maximum and minimum difference. The SD per optical density filter is shown on the right side. (C) Linear relationship between the optical density and the % Δ macular inner retinal layer (mIRL). Each dot represents an individual measurement. Mean change is the mean % change of all persons. (D) Box plot of the difference between the in duplicate performed mIRL thickness measurements. Upper and lower whiskers show the maximum and minimum difference. The SD per optical density filter is shown on the right side. pRNFL, peripapillary retinal nerve fibre layer.

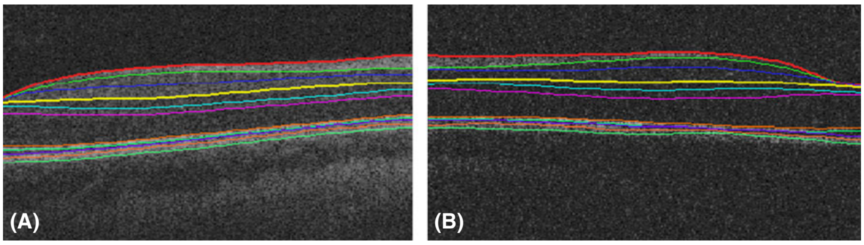

Fig. 6. Example of the layer segmentation of SD-OCT images of the macular area. (A) Without optical density filter; (B) With optical density filter 0.67. SD-OCT, spectral-domain optical coherence tomography.

tissue (Kanamori et al. 2013). This could be a cause of the interindividual variance, if these tissues are differently affected in OCT measurements, and the amount of non-neuronal tissue varies between individuals.

A limitation of our study is the relatively small size of our study population; nevertheless, significant differences between subjects were found in retinal thickness changes. Also, all our measurements have been carried out with a single OCT device and a single segmentation algorithm. Therefore, the results may be different, if another OCT device or another segmentation algorithm is used. Other studies using different devices demonstrated identical changes in measurement errors of the mIRL and pRNFL thickness, although the amount of induced error differed (El-Ashry et al. 2006; Savini et al. 2006; Kok et al. 2009, 2013; Lee et al. 2010; Mwanza et al. 2011; Kim et al. 2012; Nakatani et al. 2013). The model is not the real life situation, and cataract or other media opacities will degrade the image quality in different ways, but it all adds up to a loss of reflected light. The used filters with known optical density provide more precise calculations of the effect of media disturbance and can be used as a basis to correct for image degradation.

Future measurements with corrections based on this filter model in cataract patients, before and after cataract removal, could provide ways to correct for cataract-induced measurements errors.

Similar to the mIRL, the GC–IPL thickness is also used as an indicator to estimate the severity of glaucoma. Our results show the decrease in mIRL thickness. In our data, we found a similar change in GC-IPL thickness in the macular area, indicating that thickness measurements of the GC-IPL are affected in a similar way as the mIRL. However, as this study was aimed at measurements of the mIRL, analyses of the GC-IPL are not shown in the results.

In summary, this study demonstrates a linear relationship between an increase in optical density, and a decrease in mIRL and pRNFL thickness measurements. Similar to the pRNFL, the OCT measured mIRL thickness is influenced by a set of increasing optical density filters, acting as a model for media opacities, like cataract. An underestimation of these layer thicknesses was observed, caused by a shift of retinal layer boundary placement due to image quality loss caused by the set of filters. One should take into account the decrease in image quality caused by cataract on retinal layer thickness, as this effect of cataract can mimic glaucomatous change based on pRNFL and mIRL measurements by SD-OCT. Following cataract surgery, it is mandatory to define a new baseline for the SD-OCT measurements. The results found in the present study can help to correct retinal layer thickness measurements for the effects of cataract, which will be the subject of future studies.

References

Antony BJ, Abràmoff MD, Lee K et al. (2010): Automated 3D segmentation of intraretinal layers from optic nerve head optical coherence tomography images. SPIE Medical Imaging. International Society for Optics and Photonics; 76260U-76260U-12.

El-Ashry M, Appaswamy S, Deokule S & Pagliarini S (2006): The effect of phacoemulsification cataract surgery on the measurement of retinal nerve fiber layer thickness using optical coherence tomography. Curr Eye Res **31**: 409–413.

Garvin MK, Abramoff MD, Wu X et al. (2009): Automated 3-D intraretinal layer segmentation of macular spectral-domain optical coherence tomography images. IEEE Trans Med Imaging **28**: 1436–1447.

Grewal DS & Tanna AP (2013): Diagnosis of glaucoma and detection of glaucoma progression using spectral domain optical coherence tomography. Curr Opin Ophthalmol **24**: 150–161.

Huang D, Swanson EA, Lin CP et al. (1991): Optical coherence tomography. Science **254**: 1178–1181.

Kanamori A, Nakamura M, Tomioka M et al. (2013): Structure-function relationship among three types of spectral-domain optical coherent tomography instruments in measuring parapapillary retinal nerve fibre layer thickness. Acta Ophthalmol **91**: 196–202.

Kim NR, Lee H, Lee ES et al. (2012): Influence of cataract on time domain and spectral domain optical coherence tomography retinal nerve fiber layer measurements. J Glaucoma **21**: 116–122.

de Kinkelder R, de Bruin DM, Verbraak FD et al. (2013): Comparison of retinal nerve fiber layer thickness measurements by spectral-domain optical coherence tomography systems using a phantom eye model. J Biophotonics **6**: 314–320.

Kok PH, van Dijk HW, van den Berg TJ & Verbraak FD (2009): A model for the effect of disturbances in the optical media on the OCT image quality. Invest Ophthalmol Vis Sci **50**: 787–792.

Kok PH, van den Berg TJ, van Dijk HW et al. (2013): The relationship between the optical density of cataract and its influence on retinal nerve fibre layer thickness measured with spectral domain optical coherence tomography. Acta Ophthalmol **91**: 418–424.

Lee DW, Kim JM, Park KH et al. (2010): Effect of media opacity on retinal nerve fiber layer thickness measurements by optical coherence tomography. J Ophthalmic Vis Res **5**: 151–157.

Lee K, Kwon YH, Garvin MK et al. (2012): Distribution of damage to the entire retinal ganglion cell pathway: quantified using spectral-domain optical coherence tomography analysis in patients with glaucoma. Arch Ophthalmol **130**: 1118–1126.

Mwanza JC, Bhorade AM, Sekhon N et al. (2011): Effect of cataract and its removal on signal strength and peripapillary retinal nerve fiber layer optical coherence tomography measurements. J Glaucoma **20**: 37–43.

Nakatani Y, Higashide T, Ohkubo S et al. (2013): Effect of cataract and its removal on ganglion cell complex thickness and peripapillary retinal nerve fiber layer thickness measurements by fourier-domain optical coherence tomography. J Glaucoma **20**: 447–455.

Samarawickrama C, Pai A, Huynh SC et al. (2010): Influence of OCT signal strength on macular, optic nerve head, and retinal nerve fiber layer parameters. Invest Ophthalmol Vis Sci **51**: 4471–4475.

Savini G, Zanini M & Barboni P (2006): Influence of pupil size and cataract on retinal nerve fiber layer thickness measurements by Stratus OCT. J Glaucoma **15**: 336–340.

Tappeiner C, Barthelmes D, Abegg MH et al. (2008): Impact of optic media opacities and image compression on quantitative analysis of optical coherence tomography. Invest Ophthalmol Vis Sci **49**: 1609–1614.

van Velthoven ME, van der Linden MH, de Smet MD et al. (2006): Influence of cataract on optical coherence tomography image quality and retinal thickness. Br J Ophthalmol **90**: 1259–1262.

van Velthoven ME, Faber DJ, Verbraak FD et al. (2007): Recent developments in optical coherence tomography for imaging the retina. Prog Retin Eye Res **26**: 57–77.

Wojtkowski M, Bajraszewski T, Gorczynska I et al. (2004): Ophthalmic imaging by spectral optical coherence tomography. Am J Ophthalmol **138**: 412–419.

Wong JJ, Chen TC, Shen LQ & Pasquale LR (2012): Macular imaging for glaucoma using spectral-domain optical coherence tomography: a review. Semin Ophthalmol **27**: 160–166.

Yoo C, Suh IH & Kim YY (2009): The influence of eccentric scanning of optical coherence tomography on retinal nerve fiber layer analysis in normal subjects. Ophthalmologica **223**: 326–332.

Received on March 24th, 2014.
Accepted on October 12th, 2014.

Correspondence:
Frank D. Verbraak, MD, PhD
Department of Ophthalmology
Academic Medical Center
D2 room 420
Meibergdreef 9
1105 AZ Amsterdam
The Netherlands
Tel: +3120 5663811
Fax: +3120 5669048
Email: f.d.verbraak@amc.nl