Comparisons of Choroidal Thickness of Normal Eyes Obtained by Two Different Spectral-Domain OCT Instruments and One Swept-Source OCT Instrument

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Purpose. We compared the subfoveal choroidal thickness (SFCT) measured on the images obtained by two spectral-domain optical coherence tomographic (SD-OCT) instruments and one swept-source OCT (SS-OCT) instrument.

Methods. A cross-sectional, prospective noninterventional study was done in which SFCT was measured in the images obtained by two SD-OCT instruments; Heidelberg Spectralis-OCT (Spectralis-SD-OCT) and Topcon 3D OCT-1000 Mark II (Topcon-SD-OCT). Images also were obtained with SS-OCT Atlantis DRI OCT-1 (DRI-SS-OCT). After manual segmentation, the measurements were made using the calipers embedded in each instrument. The intrarater, interrater, and intermachine agreements were assessed.

Results. We studied 35 subjects. The intrarater correlation coefficient (95% confidence interval) was 0.994 (0.988–0.994) for Spectralis-SD-OCT, 0.996 (0.993–0.998) for Topcon-SD-OCT, and 0.997 (0.991–0.998) for DRI-SS-OCT ($P < 0.001$). The interrater correlation coefficient was 0.995 (0.991–0.998) for Spectralis-SD-OCT, 0.995 (0.990–0.998) for Topcon-SD-OCT, and 0.996 (0.992–0.998) for DRI-SS-OCT ($P < 0.001$). The average SFCT was 273.2 μm with Spectralis-SD-OCT, 269.1 μm with the Topcon-SD-OCT, and 280.5 μm with DRI-SS-OCT. The intermachine correlation coefficient was 0.982 (0.964–0.991) for Spectralis-SD-OCT versus Topcon-SD-OCT, 0.907 (0.815–0.953) for Topcon-SD-OCT versus DRI-SS-OCT, and 0.911 (0.832–0.954) for DRI-SS-OCT versus Spectralis-SD-OCT ($P < 0.001$). The SFCT measured with DRI-SS-OCT was significantly thicker than that with Topcon-SD-OCT, with a mean difference of 11.41 ± 30.27 μm ($P = 0.032$).

Conclusions. In normal adult eyes, there was good reproducibility and repeatability of SFCT measurements obtained by the SD-OCT and SS-OCT instruments. However, the choroid measured with DRI-SS-OCT was thicker than that measured with both SD-OCT instruments, and, thus, the choroidal thickness should not be compared between the SD-OCT and SS-OCT instruments. (www.umin.ac.jp/ctr number, UMIN000011259.)

Keywords: choroid, penetration, diabetic retinopathy, retinal pigment epithelium

The choroid has important roles in the pathogenesis of various retinal diseases. In age-related macular degeneration and diabetic retinopathy, the choroidal abnormalities can be shown by fluorescein angiography and histopathology.[1–4] However, qualitative and quantitative evaluations of the choroidal morphology are not obtained easily by conventional clinical examinations.

This limitation was overcome partially by Spaide et al.,[5] who reported that examinations and measurements of the choroid in normal and pathologic states can be made by enhanced depth imaging optical coherence tomography (EDI-OCT). This has advanced greatly the field of retinochoroidal pathophysiology, and many studies have been published on choroidal pathology studied by EDI-OCT. Thus, the examination of the choroid by EDI-OCT has become a standard method for evaluating retinochoroidal diseases.[6–16]

Recently, a new type of OCT instrument, called a swept-source OCT (SS-OCT), was introduced. The SS-OCT uses a tunable laser (swept-source) as a light source with a longer wavelength of approximately 1 μm. The longer wavelength allows the light to penetrate deeper into tissues than the conventional spectral domain OCT (SD-OCT) instruments. This, then, enabled the imaging of the choroid,[17] and, thus, SS-OCT instruments should be more suitable for examining choroidal pathology than the present SD-OCT instruments. However, to our knowledge, it has not been determined whether the measurements made on the images obtained by SD-OCT and SS-OCT instruments are interchangeable, especially for adult eyes.

Earlier, we compared the choroidal thickness values obtained by different SD-OCT instruments and found that they were not significantly different.[18] However, we are not aware of any study comparing the choroidal thickness measurements obtained by SD-OCT to that obtained by SS-OCT instruments.

Thus, the purpose of this study was to determine the choroidal thickness of normal adult eyes with two commonly used SD-OCT instruments to that obtained by one SS-OCT instrument. We showed that the choroidal thickness can be measured in the images obtained by both types of OCT

Table 1. Scanning Protocols of OCT Machines

Instrument	Protocol	Scan Areas, Lines	A-Scans per B-Scan	Average or Overlapping per Image
Spectralis SD-OCT	Line (enhanced depth imaging)	30° (length) cross lines	1024	100
Topcon SD-OCT	Line (enhanced choroidal mode)	6-mm line	1024	50
DRI SS-OCT	Line (enhanced choroidal mode)	6-mm line	1024	96

instruments, but the thickness measured by SS-OCT was significantly thicker than that by SD-OCT.

Methods

All of the procedures used complied with the tenets of the Declaration of Helsinki, and they were approved by the Institutional Ethics Committee of Kagoshima University Hospital (ID 25-9, April 8, 2013; Kagoshima, Japan) and registered with the University Hospital Medical Network (UMIN)–clinical trials registry: UMIN000011259 "A prospective, cross-sectional study of Repeatability and Reproducibility of Retina/Subfoveal Choroidal Thickness in Normal Eyes Using Different OCT Devices" (available in the public domain at https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&recptno=R000012685&type=summary&language=E, and at http://www.kufm.kagoshima-u.ac.jp/∼op/gairai/vit.html). All of the subjects signed a written informed consent form after a complete explanation of the procedures and possible complications.

Subjects

This was a prospective, cross-sectional study that was performed at a single institution from April 30 to May 30, 2013. Approximately 40 volunteers were projected to enroll in the study, and all subjects had a complete ocular examination, including the measurement of the refractive power (spherical equivalent) with an autorefractor keratometer (RM8900; Topcon, Tokyo, Japan), best-corrected visual acuity (BCVA), IOP with a pneumotonometer (CT-80; Topcon), slit-lamp biomicroscopy, and dilated funduscopy. The axial length was measured with optical interferometry (OA-1000; Tomey, Tokyo, Japan). Only the right eye was measured with the three OCT instruments.

The inclusion criteria were an age of $\geq$20 years and $<$50 years, BCVA of $\geq$20/20, and normal fundus by ophthalmoscopy and OCT. The exclusion criteria were history of ocular and systemic diseases, prior ocular surgery or intraocular injections, and high myopia $\geq$6.0 diopters (D).

All eyes were examined without mydriasis and two separate measurements were made on each eye with each of the three instruments by a single trained examiner. The order of the OCT instrument measurements was random for the patients, and the order for the second OCT examinations also was random. Because of the significant diurnal fluctuations of the choroidal thickness, all OCT recordings on a single patient were made within 1 hour on the same day.

Optical Coherence Tomography

All OCT examinations were performed according to the analysis protocol and variables for each device (Table 1).

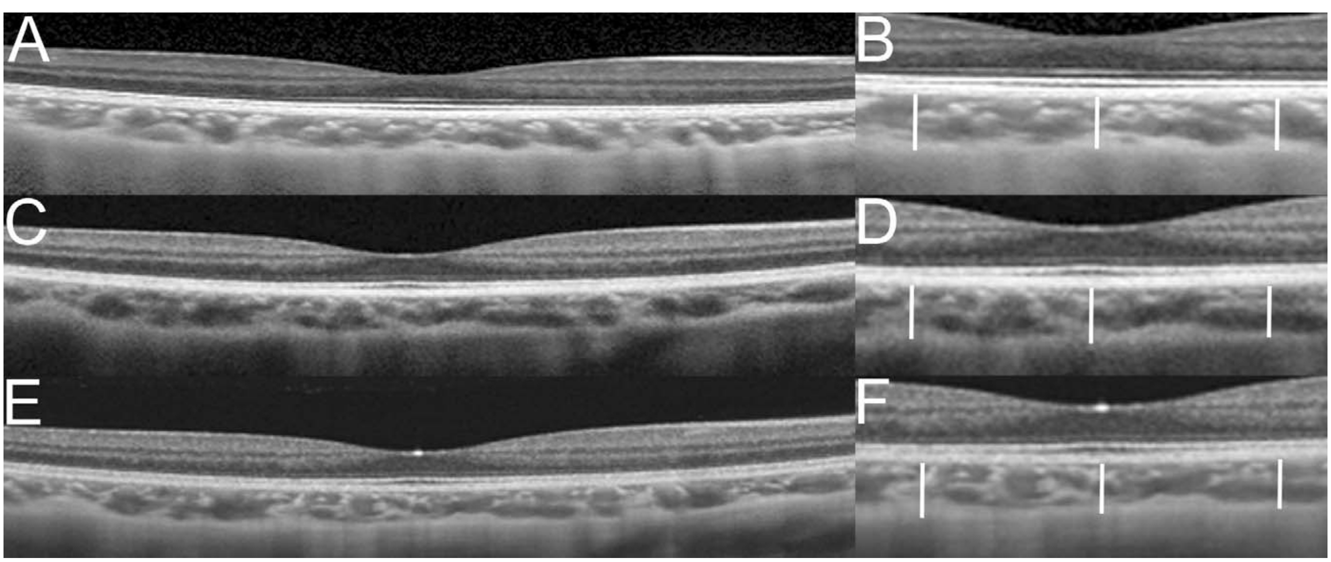

Figure 1. Representative choroidal images obtained from two SD-OCT instruments and one SS-OCT instrument from a normal eye (case 19). (**A**) Original image obtained by Spectralis SD-OCT. (**B**) Screen image of the Spectralis SD-OCT. (**C**) Original image of Topcon SD-OCT.0 (**D**) Screen image of the SD-OCT instrument. (**E**) Original DRI SS-OCT image. (**F**) Screen image of the DRI SS-OCT. *Scale bars* indicate the choroidal thickness measured using the tool embedded in each instrument.

Table 2. Choroidal Thickness Measurements by Three Different OCT Machines

Location	Choroidal Thickness Measurements, Average ± SD, μm: Spectralis SD-OCT	Topcon SD-OCT	DRI SS-OCT	1-Way ANOVA With Tukey's Post-Test *P*
Nasal	256.3 ± 70.49	255.5 ± 70.67	262.8 ± 74.47	>0.05
Subfoveal	273.2 ± 70.03	269.1 ± 70.54	280.5 ± 77.01	>0.05
Temporal	258.6 ± 70.38	256.1 ± 63.86	272.3 ± 75.31	>0.05

Choroidal images were obtained with the Heidelberg Spectralis-OCT (Spectralis SD-OCT; Heidelberg Engineering, Heidelberg, Germany) as reported.[5,18] Choroidal images also were obtained with the Topcon 3D OCT-1000 Mark II (Topcon SD-OCT; Topcon) with the enhanced depth imagining choroidal mode linear scans, and also with the Topcon deep range imaging swept-source OCT (DRI OCT-1 Atlantis, DRI SS-OCT; Topcon) using a standard protocol (Table 1). Detailed protocols are presented in Supplementary Material S1.

The transverse resolution is 14 μm and the axial resolution is 3.9 μm for the Spectralis SD-OCT. For the Topcon SD-OCT, the horizontal resolution is ≤20 μm, and the longitudinal resolution is 5 to 6 μm. For the DRI SS-OCT, the lateral resolution is 20 μm and the depth resolution is 8 μm.

After each examination, the best image was projected onto a computer screen and evaluated by two independent masked graders (HT, MS). The measurement of the choroidal thickness (rating) was done on the OCT screen. Because the original OCT images generally were too small to differentiate the RPE or other structures, the images were magnified on the OCT screen as described.[18]

If two graders determined that both inner and outer borders of the choroid of the image were clearly distinguishable, the image was accepted and used for the following analyses. If the determination was split, a third grader (TS) determined it. Measurements of the choroidal thickness were done in a masked fashion with no information of eyes. For intrarater comparisons, each image was measured two times independently by a single rater (YM) with no information of the eyes or the results by the other examination, as we have reported.[18] For interrater comparisons, each image was measured by two independent raters (YM, MT) with no information of the eyes or the results by the other rater as we have reported.[18] The two groups of data were used for the statistical analyses.

Statistical Analyses

All statistical analyses were performed with a commercial analytical package (SPSS statistics 19 for Windows; SPSS, Inc., IBM, Somers, NY). The coefficient of variation (SD/mean) also was calculated. A 1-way ANOVA with Tukey's multiple comparison tests was used to compare choroidal thickness at the subfoveal, nasal, and temporal sites obtained by the three instruments. Because of the clinical importance, the comparisons often were performed between two instruments.[18–20] Therefore, the subfoveal choroidal thickness was compared between two instruments (Spectralis SD-OCT versus Topcon SD-OCT; Topcon SD-OCT versus DRI SS-OCT, and DRI SS-OCT versus Spectralis SD-OCT) by paired *t*-test. This section was titled "Comparison between two instruments for subfoveal choroidal thickness." The intrarater correlation coefficients were calculated using 1-way random-effects model for measurements of agreement. Interinstrument and interrater correlation coefficients were calculated using 2-way mixed-effects model for measurements of absolute agreement. Bland-Altman plots were used to assess the agreement of the measurements between two of the three instruments.[21] Differences in thickness between instruments were plotted against mean choroidal thickness measurements on these graphs. If the difference of an eye measured with two instruments was more than the average ±3 SD, it was regarded to be an outlier. A value of $P < 0.05$ was considered to be statistically significant.

Results

We screened 43 Japanese volunteers, but six eyes were excluded because of high myopia, one eye because of a history of intraocular surgery, and one because of poor OCT quality. In the end, we studied 35 eyes in 18 men and 17 women. Clear choroidal images were obtained from all of the eyes from each of the three OCT instruments. The mean ± SD age of all of the volunteers was 32.5 ± 6.5 years, with a range of 22 to 47 years. The mean refractive error (spherical equivalent) was −2.6 ± 1.8 D, with a range from −5.75 to −0.75 D. The mean IOP was 13.9 ± 2.0 mm Hg, with a range from 10 to 19 mm Hg, and the mean axial length was 24.7 ± 1.3 mm, with a range from 22.51 to 27.68 mm.

Table 3. Comparison Between Two Instruments for Subfoveal Choroidal Thickness

Instruments	Mean Difference, μm ± SD	Range of Difference, μm	95% CI	*P* Value, Paired *t*-test	ICC	95% CI	*P* Value
Spectralis SD-OCT vs. Topcon SD-OCT	4.1 ± 12.72	−28.5 to 43.5	−0.27 to 8.47	0.065	0.982	0.964–0.991	<0.001
Topcon SD-OCT vs. DRI SS-OCT	−11.41 ± 30.27	−148.0 to 24.0	−21.81 to −1.01	0.032*	0.907	0.815–0.953	<0.001
DRI SS-OCT vs. Spectralis SD-OCT	7.31 ± 30.66	−19 to 140	−3.21 to 17.84	0.167	0.911	0.832–0.954	<0.001

CI, confidence interval; ICC, intraclass correlation coefficients.
* $P < 0.05$.

TABLE 4. Intrarater Comparison

Location	Spectralis-SD-OCT ICC	CV	*P* Value	Topcon SD-OCT ICC	CV	*P* Value	DRI SS-OCT ICC	CV	*P* Value
Nasal	0.998 (0.995–0.999)	0.27	<0.001	0.995 (0.990–0.997)	0.27	<0.001	0.997 (0.994–0.999)	0.28	<0.001
Subfoveal	0.994 (0.988–0.994)	0.26	<0.001	0.996 (0.993–0.998)	0.26	<0.001	0.997 (0.991–0.998)	0.27	<0.001
Temporal	0.997 (0.993–0.998)	0.27	<0.001	0.997 (0.994–0.999)	0.25	<0.001	0.998 (0.995–0.999)	0.27	<0.001

CV, coefficient of variation.

Representative images obtained from each of the three OCT instruments are shown in Figure 1. The subfoveal choroidal thickness measured with the Spectralis SD-OCT was 273.20 ± 70.03 μm, compared to 269.1 ± 70.54 μm with the Topcon SD-OCT, and 280.5 ± 77.01 μm with the DRI SS-OCT. The differences in the mean choroidal thickness were not significant. There was no significant difference of either the nasal or temporal choroidal thicknesses (Table 2).

Comparisons of Subfoveal Choroidal Thicknesses

The subfoveal choroidal thickness determine by any one instrument was significantly correlated with the thickness obtained by the other two instruments (Table 3). The intraclass correlation coefficient was >0.95 for the Topcon SD-OCT versus Spectralis SD-OCT. The intraclass correlation coefficient was 0.907 for the Topcon SD-OCT versus Spectralis SD-OCT, and it was 0.911 for the DRI SS-OCT versus Spectralis SD-OCT. The mean subfoveal choroidal thickness measured with the Topcon SD-OCT was 4.1 μm thinner than that with the Spectralis SD-OCT, but the difference was not significant ($P = 0.065$). The subfoveal choroidal thickness measured with the Spectralis SD-OCT was 7.31 μm thinner than that obtained with the DRI SS-OCT, but this difference was not significant ($P = 0.167$). The choroidal thickness measurement with the Topcon SD-OCT was 11.41 μm thinner than that obtained by the DRI SS-OCT, and this difference was significant ($P = 0.032$, Table 3).

Repeatability of Examinations: Intrarater Comparisons

The coefficient of variation varied from 0.25 to 0.28 for all three instruments. The results of choroidal thickness measurements were significantly correlated by the two raters. The intraclass correlation coefficient was high with each instrument (Table 4).

Reproducibility of Examination: Interrater Comparisons

The coefficient of variation was 0.26 to 0.28 for all three instruments in the subfoveal area. The results of choroidal thickness measurements were correlated significantly by the two raters. Interrater correlation coefficient was high with each instrument (Table 5).

Bland-Altman Plot Analysis

There were no significant trends, such as a proportional error or variation of method depending on the magnitude of measurements, between the Topcon SD-OCT and the Spectralis SD-OCT (Fig. 2A). The mean choroid measured with the SS-OCT was thicker than that measured with the Topcon SD-OCT or Spectralis SD-OCT (Figs. 2B, 2C).

There was one outlier (case 3) in the Spectralis SD-OCT versus DRI SS-OCT, and the DRI SS-OCT and Topcon SD-OCT. This was a 27-year-old man with a refractive error of −1.75 D and axial length 23.64 mm (Fig. 3). Although the retinal structures were identifiable clearly and the RPE layer was evident, the outer border of the choroid was not clear in the SD-OCT images. The intrachoroidal structures and choroidal border were clearer and more sharply defined with the SS-OCT than with both SD-OCT instruments. The subfoveal choroidal thickness as measured by SS-OCT (407 μm) was much thicker than that by Spectralis SD-OCT (261 μm) or by Topcon SD-OCT (261 μm).

DISCUSSION

The choroidal thicknesses were measured on the images obtained by the commonly used SD-OCT instruments, Spectralis SD-OCT and Topcon SD-OCT, and the newly developed DRI SS-OCT in normal subjects. Our results showed that the two separate measurements had good reproducibility and repeatability with each instrument.

We found that the coefficient of correlation between any two of the three OCT instruments was high, and significant for the subfoveal and parafoveal choroidal thickness measurements. The choroid measured with the DRI SS-OCT was significantly thicker than that with the Topcon SD-OCT (280.5 ± 77.01 μm with DRI SS-OCT versus 269.1 ± 70.54 μm with Topcon SD-OCT, $P = 0.032$).

TABLE 5. Interrater Comparison

Location	Spectralis SD-OCT ICC	CV	*P* Value	Topcon SD-OCT ICC	CV	*P* Value	DRI SS-OCT ICC	CV	*P* Value
Nasal	0.993 (0.986–0.996)	0.27	<0.001	0.993 (0.987–0.997)	0.28	<0.001	0.997 (0.995–0.999)	0.28	<0.001
Subfoveal	0.995 (0.991–0.998)	0.26	<0.001	0.995 (0.990–0.998)	0.27	<0.001	0.996 (0.992–0.998)	0.28	<0.001
Temporal	0.992 (0.985–0.996)	0.27	<0.001	0.997 (0.994–0.999)	0.25	<0.001	0.998 (0.996–0.999)	0.28	<0.001

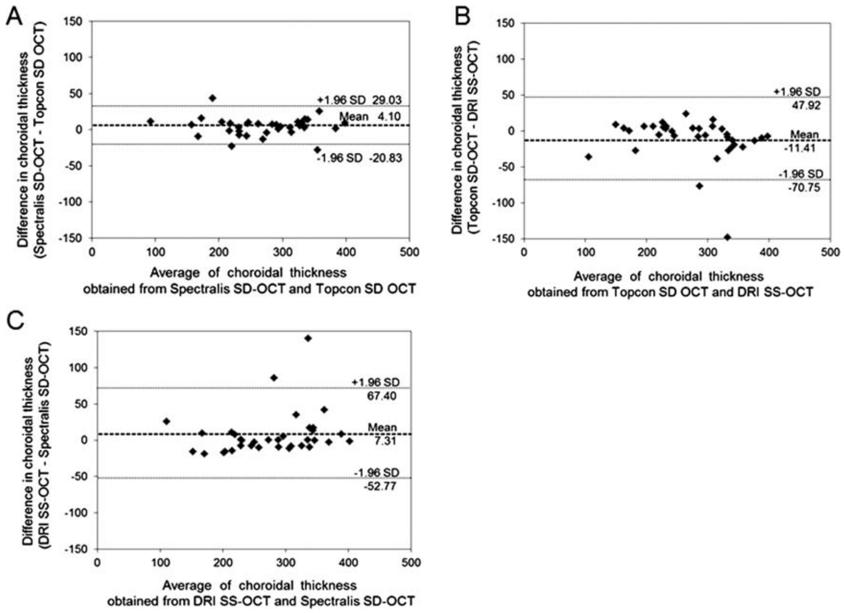

Figure 2. Bland-Altman plot analyses. There was no significant trend, such as a proportional error or variation of method depending strongly on the magnitude of measurements between Topcon SD-OCT and Spectralis SD-OCT (**A**). The mean choroidal thickness measured with the SS-OCT was thicker than that with Topcon SD-OCT or Spectralis SD-OCT (**B**, **C**).

The Bland-Altman analyses also showed that the mean choroidal thickness measured by SS-OCT was greater than that by either of the SD-OCT instruments. We did not determine the exact reason for this observation, but the raters noted that the outer border of the choroid was more distinct, probably because SS-OCT can record choroidal images deeper than the SD-OCT (Fig. 3). In many cases, the sclera-choroidal border in the SD-OCT images may not necessarily be the true border.

The largest difference in the choroidal thickness was 43.5 μm (−28.5–43.5 μm) for Spectralis SD-OCT versus Topcon SD-OCT, 148 μm (−148.0–24.0 μm) for Topcon SD-OCT versus DRI SS-OCT, and 140 μm (−19.0–140.0 μm) for DRI SS-OCT versus Spectralis SD-OCT. By eliminating the one outlier from the DRI SS-OCT measurements, these differences were reduced to 43.5, 75, and 91 μm, respectively. In an earlier analyses of choroidal thickness with different SD-OCT instruments, the largest difference was approximately 90 μm.[18,20] Therefore, it is possible to say that the difference in the choroidal thickness measured by SD-OCT or SS-OCT was not significant. The slight differences in the choroidal thickness determined by different SD-OCT or SS-OCT instruments probably are not important for clinical trials at present. However, when detailed analysis is necessary, this difference might be more important.

Of importance was the presence of an outlier in the SS-OCT data. In our earlier study comparing three different SD-OCT instruments in 43 normal subjects, the choroidal thickness measurements were not significantly different among all of the SD-OCT instruments, and no outliers were observed.[18] In the SD-OCT images, the choroidal border appeared as a linear structure (as indicated by the arrows in Figs. 3A, 3B), but in the SS-OCT images, another layer of tissue was observed outside of that border. This additional tissue made the choroid thicker. We were not able to determine why this eye showed the different images with the two types of OCT instruments. Because the images of choroids more than 500 μm did not have a clear choroidal boundary with any SD-OCT instrument, the choroidal thickness might be the factor.[18] However, the choroidal thickness in this case was less than 500 μm; thus, unidentifiable factors, such as pigmentation or vascular structures, might have caused the inconsistent results between the SD-OCT and SS-

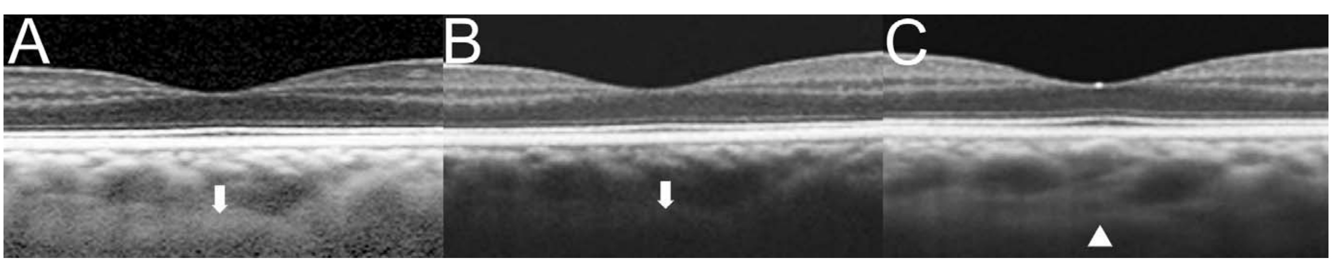

Figure 3. An outlier (case 3) with choroidal images from SD-OCTs and SS-OCT. (**A**) Spectralis SD-OCT image. (**B**) Topcon SD-OCT image. (**C**) DRI SS-OCT image. Both raters decided the border indicated by an *arrow* as the outer border of the choroid ([**A**, **B**], *arrow*). While in the DRI SS-OCT image, the raters detected another choroidal layer and the point indicated by an *arrowhead* was determined to be the border (**C**). As a result, subfoveal choroidal thickness was measured with DRI SS-OCT (407 μm) was thicker than that with Spectralis SD-OCT (261 μm) or with Topcon SD-OCT (261 μm).

OCT instruments. Considering the image quality, the image obtained by the SS-OCT likely was to be the true choroidal boundary more than the SD-OCT. Thus, the SS-OCT instrument might be better for evaluating choroidal thickness than the SD-OCT instruments.

The design of our experiments did not allow us to determine the sensitivity of each instrument. In an earlier report, the subfoveal choroidal thickness could be measured in all the subjects even from different ethnic groups,[22] and clear images of the choroid could be obtained from 39 of 43 eyes with all of the SD-OCT instruments.[18] We measured a similar population in this study, and we were able to record clear images from all eyes. To compare the sensitivity of different instruments correctly, interinstrument comparisons should be done on a larger number of eyes and by more graders.

There are strengths of the study, one of which was its prospective design, which allowed us to recruit a number of healthy subjects with a wide range of choroidal thicknesses. Scans of each eye were performed within a limited time, which minimized the possibility of choroidal thickness changes caused by circulating catecholamines, diurnal variations, or fluctuations of the intraocular pressure.[23,24]

There also are several limitations of this study. Scans were acquired from comparatively young subjects with no ocular pathology, and the values may not reflect those of patients seen in a routine outpatient setting. For example, the clarity of images of patients could be hindered by an ocular pathology, such as significant media opacity, or masking of choroidal reflectance by intraocular tissue. These issues, especially the age differences, should be remembered in interpreting our results. Second, we used manual segmentation, and this always is a concern because of uncontrollable bias among examiners. We performed interrater comparisons which were found to be high. However, the raters were well-trained and experienced. If the agreement ratio of many different raters is proved to be high on each device, the present results should be more generalized and the present instruments could be used interchangeably with confidence. Third, we only evaluated the specific scanning protocol of two SD-OCT instruments commonly used and one SS-OCT. It is not certain whether our observations can be generalized to other SD-OCT instruments or other scanning protocols. In addition, our results apply only to the choroidal thickness of the subfoveal or parafoveal areas. We do not have any evidence of the choroidal thickness of other areas. This also should be remembered when interpreting the present data.

In conclusion, the subfoveal choroidal thickness measurements obtained with the Spectralis SD-OCT and with the Topcon SD-OCT were significantly correlated with values obtained by the DRI SS-OCT in most of the cases. Although the difference might be clinically insignificant, it should be noted that the choroidal thickness measured with the DRI SS-OCT was thicker than that obtained with the SD-OCT instruments and some of them reached the statistical significance. Because OCT is an easy, reproducible, and noninvasive examination, it will be used more often in a clinical setting. Our results should be indispensable to interpreting the data of each SD-OCT or SS-OCT instruments and a better understanding of ocular diseases, which will further increase the value of this examination.

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