Macular Choroidal Thickness and Volume in Normal Subjects Measured by Swept-Source Optical Coherence Tomography

Masaya Hirata, Akitaka Tsujikawa, Akiko Matsumoto, Masanori Hangai, Sotaro Ooto, Kenji Yamashiro, Masahiro Akiba, and Nagabisa Yoshimura

Purpose. To study the choroidal thickness in healthy subjects by swept-source optical coherence tomography (SS-OCT) at longer wavelength.

Methods. The macular area of 31 eyes (31 healthy volunteers) was studied with an SS-OCT prototype system, which uses a tunable laser as a light source operated at 100,000 Hz A scan repetition rate in the 1-μm wavelength region. Three-dimensional volumetric measurement comprised of 512 × 128 A scans was acquired in 0.8 second. From a series of OCT images, a choroidal thickness map of the macular area was created by manual segmentation. To evaluate interoperator reproducibility, the choroidal thickness in each section from 10 subjects was determined independently by two observers.

Results. SS-OCT at the 1-μm wavelength region allowed visualization of the fine structure of the choroid as well as that of the retina. Mean choroidal thickness and volume in the macula area were, respectively, 191.5 ± 74.2 μm and 5.411 ± 2.097 mm³. The mean choroidal thickness of the outer nasal area was significantly thinner than that of all other areas (P < 0.05). The measurements by the two independent observers were significantly identical; the intraclass correlation coefficient in mean choroidal thickness was between 0.945 and 0.980 in each area. The macular choroidal thickness was significantly correlated with axial length after adjustment for age (P < 0.001), and with age after adjustment for axial length (P < 0.001).

Conclusions. SS-OCT system at 1 μm provides macular choroidal thickness maps and allows one to evaluate the choroidal thickness more accurately. (Invest Ophthalmol Vis Sci. 2011; 52:4971–4978) DOI:10.1167/iovs.11-7729

So far, the thickness of the choroid has been measured by ultrasound and magnetic resonance imaging (MRI), although their resolution of imaging within the choroid is limited. Recently, optical coherence tomography (OCT) has been used to obtain quantitative measurements of the retinal thickness and to detect morphologic changes in the retinal architecture. However, commercially available OCT, which functions at approximately 800 nm, can visualize the entire choroid only in eyes with high myopia because of low penetration and high backscattering at the level of the retinal pigment epithelium (RPE).

Since Spaide and associates introduced enhanced depth imaging (EDI–OCT) based on spectral-domain OCT technology, an increasing number of investigators have studied the choroidal thickness in both healthy eyes and eyes with various pathologies. In fact, EDI–OCT does allow visualization of the choroidal structure in detail and measurement of choroidal thickness. However, EDI–OCT requires averaging of 50 to 100 B scans to achieve high-contrast and low-speckle noise. In most studies that have used EDI–OCT, the “choroidal thickness” is a representative value obtained at one or even several different measurement points, often at the foveal center. However, measurement of a few sampling points tends to be influenced by focal thickening or thinning of the choroid or, more often, by irregularity of the inner chorioscleral border.

Recently, other investigators have reported the measurement of choroidal thickness with the use of OCT at a longer wavelength. In these more recent studies, higher penetration of the OCT probe light, which uses a center wavelength of 1040 to 1060 nm instead of the current OCT probing light operated at approximately 800 nm, allows us to visualize the entire choroid without the EDI system or multiaveraging.

Recently, Esmaeelpour and associates showed a two-dimensional (2D) choroidal thickness map with raster scan protocol using spectral-domain OCT at 1060 nm. Even more recently, Ikuno and associates reported the choroidal thickness of healthy subjects measured with swept-source (SS)–OCT at 1060 nm. SS-OCT, which is characterized by a high-speed scan rate and a relatively low sensitivity roll-off versus depth compared with the spectral-domain OCT, potentially allows one to obtain a three-dimensional (3D) high-contrast image of the choroid. However, Ikuno and associates reported the choroidal thickness only at the fovea.

In using EDI–OCT or any other OCT that has a longer wavelength, the inner and outer borders of the choroid are determined manually by the observer, and it is essential to estimate the error in measuring the thickness from the obtained images. In the study described herein, we scanned the macular area of healthy eyes with SS-OCT at 1050 nm, using a 3D raster scan protocol, and produced a choroidal thickness map of the macular area. By applying the grid used by the Early Treatment Diabetic Retinopathy Study (ETDRS) to this map, we measured the mean choroidal thickness and volume in each area. In addition, to estimate the error in this evaluation,
interoperator reproducibility of the choroidal thickness measurements was assessed.

**MATERIALS AND METHODS**

This prospective study consisted of 31 eyes of 31 healthy volunteers, with no ophthalmic or systemic symptoms. The macular area of these 31 eyes was examined with an SS-OCT prototype system at Kyoto University Hospital between October 2010 and February 2011. All subjects underwent a thorough ocular examination, including an autorefractometer (ARK1; Nidek, Gamagori, Japan), best-corrected visual acuity measurement with a 5-m Landolt eye chart, axial length measurement using ocular biometry (IOLMaster; Carl Zeiss Meditec, Jena, Germany), slit-lamp examination, intraocular pressure measurement, and dilated funduscopy. Exclusion criteria included history or evidence of chorioretinal or vitreoretinal diseases, including age-related macular degeneration, diabetic retinopathy, central serous chorioretinopathy, epiretinal membrane, and macular dystrophy; best-corrected visual acuity < 20/25; history of intraocular surgery; evidence of glaucoma; and poor image due to cataract or unstable fixation were also reasons for exclusion. Subjects with systemic diseases or conditions that might affect retinal or choroidal thickness were also excluded, such as those with diabetes mellitus, Vogt–Koyanagi–Harada disease, or malignant hypertension, or those who were pregnant. The Institutional Review Board and Ethics Committee of Kyoto University approved this study, which adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each subject before examination.

**SS-OCT System and Scan Protocols**

We used an SS-OCT prototype system (Topcon Corp., Tokyo, Japan) with an axial scan rate of 100,000 Hz operated at the 1-μm wavelength region. In the current SS-OCT system, the light source was a wavelength-sweeping laser with a tuning range of approximately 100 nm centered at 1050 nm, yielding 8-μm axial resolution in tissue. Transverse resolution was set to approximately 20 μm. In a single OCT image consisting of 1000 A lines can be acquired in 10 ms. SS-OCT imaging at 1050 nm was conducted with approximately 1 mW on the cornea, which is well below the safe retinal exposure limit established by the American National Standards Institute. Sensitivity was measured to be approximately 98 dB at this input power.

SS-OCT examinations of the eligible volunteers were performed by trained examiners after pupil dilation. A 3D imaging data set was acquired on each patient by using a raster scan protocol of 512 (horizontal) × 128 (vertical) A-scans per data set (total 65,536 axial scans/volume) in 0.8 s. Each 3D scan covered an area of 6 × 6-mm² centered on the fovea, which was confirmed by an internal fixation and fundus camera integrated in the prototype instrument. To reduce a speckle noise, each image was denoised by applying weighted moving average from three consecutive single images. Owing to the invisible scanning light, the eye movement during 3D scan was minimal.

In each patient, fifty-times averaged horizontal and vertical scan images in 12 mm transverse scan range were obtained as well. Acquired 50 single images were registered and averaged by software to create an averaged image. The vertical scan was captured centered on the fovea while the horizontal scan was captured centered on the midpoint between fovea and optic disc.

**Choroidal Thickness Measurement**

The choroidal thickness was measured as the distance between the outer border of the hyper-reflective line, considered to be the RPE, and the choriocapillaris border. In each image of the 3D data set, lines of both RPE and the choriocapillaris border were determined manually by trained observers in a masked fashion. Automated built-in calibration software determined the distance between these two lines. The measurement points per image consisted of 512 points, with an interval of approximately 12 μm. From all 128 images of each 3D data set, the choroidal thickness map of 6 × 6-mm² area was created.

After the choroidal thickness map was obtained, the ETDRS grid was applied to the map (Fig. 1A). The ETDRS grid divides the macula into inner and outer rings, with the inner ring being 1 to 3 mm and the outer ring being 3 to 6 mm from the foveal center. The ETDRS grid divides the macula area further into superior, inferior, temporal, and nasal quadrants. Thicknesses of all measurement points within each of nine areas based on the ETDRS grid were averaged, which allowed us to obtain the mean sectorial choroidal thickness. Further, on the basis of the choroidal thickness obtained, we calculated the choroidal volume within each area in the ETDRS grid.

In the present study, choroidal thickness at a single representative point of each area of the ETDRS grid was measured manually from the 3D data set with a caliper with which the machine was equipped; these representative points were located at the center (fovea) and at 1 and 2.25 mm temporal, superior, nasal, and inferior to the macula (Fig. 1B). These representative points were located at the center of each area of the ETDRS grid. In addition, choroidal thickness at these nine points was also measured manually from multiaveraged horizontal and vertical images (Fig. 1C).

**Measurement Reproducibility**

In the present study, the lines of both the RPE and the choriocapillaris border were determined manually, in a masked fashion, by the observers. To evaluate interoperator reproducibility of these measurements, the lines of both RPE and the choriocapillaris border were determined independently by two observers of each scan of the 3D data set obtained from 10 subjects. Thickness maps and mean choroidal thickness within the ETDRS grid were produced independently. In these 10 subjects, choroidal thickness at a representative point of each area of the ETDRS grid was determined from the 3D data set and horizontal and vertical images were multiaveraged independently by two observers.
The interoperator reproducibility of the choroidal thickness measurements was assessed by measuring the intraclass correlation coefficient (ICC) of each measuring procedure.

Statistical Analyses
Statistical analyses were performed by use of a commercially available software program (SPSS2: SPSS Japan, Tokyo, Japan; StatMate III: ATMS, Tokyo, Japan). All values are presented as mean ± SD. Repeated-measures ANOVA with Scheffe’s test was used to compare choroidal thickness (volume) at different areas; the ICC of the choroidal thickness (volume) obtained from three different measuring procedures was also used. Pearson’s correlation and partial correlation were calculated to assess the relationship of choroidal thickness of the macular area with age, refractive error, and axial length. Multiple linear regression analysis was used to evaluate the correlation between choroidal thickness of the macula and various factors. A P value < 0.05 was considered to be statistically significant.

RESULTS
In the present study, 31 eyes of 31 healthy volunteers (14 men and 17 women), ranging in age from 21 to 87 years (64.6 ± 17.3 years), were examined. Mean refractive error was −1.67 ± 5.1 dipters (range: −9.25 to +4.25 dipters). Mean axial length was 24.6 ± 2.1 mm (range: 21.35–28.66 mm).

The SS-OCT system with a center wavelength of 1050 nm clearly showed the deep structures of the posterior pole. Because of higher penetration due to longer operating wavelength and higher scan rate (100,000 Hz) of the light source, no eye was excluded from the present study because of a low-quality image due to cataract or eye movement during the scanning procedure. Multiaveraged scans of 12 mm in length revealed structures of the retina and choroid, which allowed precise identification in all eyes of chorioscleral border beyond the vascular arcade (Fig. 2). Using a raster scan protocol with 512 × 128 A scans, 3D imaging data of the 6 × 6-mm area were acquired. By weighted moving average, each image had quality sufficient to delineate both the outer border of the RPE and the chorioscleral border (Fig. 3). Based on 128 images of the 3D data set, a choroidal thickness map of the 6 × 6-mm area centered on the fovea was created for each eye (Fig. 4).

Choroidal Thickness
In our subjects, mean choroidal thickness in the macula (within a circle of 6.0-mm diameter) was 191.5 ± 74.2 μm. Table 1 shows the mean choroidal thickness of each area in the ETDRS grid as well as the choroidal thickness at a single representative point obtained from the 3D data set or multiaveraged SS-OCT images. Mean choroidal thickness within the central area was 202.6 ± 83.5 μm, which was virtually identi-
Choroidal Thickness

<table>
<thead>
<tr>
<th>Area</th>
<th>Mean Thickness of ETDRS Grid Area Obtained from 3D Data Set (μm)</th>
<th>Thickness at a Representative Point within ETDRS Grid Obtained from 3D Data Set (μm)</th>
<th>Thickness at a Representative Point Obtained from Multiaveraged Images (μm)</th>
<th>Choroidal Volume (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center</td>
<td>202.6 ± 83.5*</td>
<td>199.8 ± 85.6†</td>
<td>203.6 ± 86.1</td>
<td>0.159 ± 0.066</td>
</tr>
<tr>
<td>Inner temporal</td>
<td>204.5 ± 80.2†</td>
<td>201.6 ± 81.3†</td>
<td>197.0 ± 70.7</td>
<td>0.321 ± 0.126</td>
</tr>
<tr>
<td>Inner superior</td>
<td>206.6 ± 80.7†</td>
<td>206.6 ± 79.7†</td>
<td>205.1 ± 88.7†</td>
<td>0.324 ± 0.127</td>
</tr>
<tr>
<td>Inner nasal</td>
<td>186.8 ± 82.0‡</td>
<td>183.5 ± 85.7‡</td>
<td>187.9 ± 79.3</td>
<td>0.295 ± 0.129</td>
</tr>
<tr>
<td>Inner inferior</td>
<td>200.4 ± 81.7‡</td>
<td>203.9 ± 85.1‡</td>
<td>202.2 ± 76.7</td>
<td>0.315 ± 0.129</td>
</tr>
<tr>
<td>Outer temporal</td>
<td>200.2 ± 74.5†</td>
<td>200.6 ± 74.0†</td>
<td>182.4 ± 58.9</td>
<td>1.061 ± 0.394‡</td>
</tr>
<tr>
<td>Outer superior</td>
<td>215.5 ± 80.7‡</td>
<td>229.3 ± 86.4‡</td>
<td>214.0 ± 90.2‡</td>
<td>1.144 ± 0.428§</td>
</tr>
<tr>
<td>Outer nasal</td>
<td>152.5 ± 71.1</td>
<td>139.6 ± 74.8</td>
<td>147.8 ± 73.1</td>
<td>0.808 ± 0.377</td>
</tr>
<tr>
<td>Outer inferior</td>
<td>186.0 ± 75.2‡</td>
<td>190.4 ± 85.9‡</td>
<td>185.8 ± 82.6</td>
<td>0.986 ± 0.398‡</td>
</tr>
</tbody>
</table>

* P < 0.001, † P < 0.01, ‡ P < 0.05, compared with values of outer nasal area. § P < 0.05, compared with values of outer inferior area.

Choroidal Volume

By integrating choroidal thickness in each area, we could obtain values corresponding to the volume because of the many measurement points in the 3D data set. Table 2 shows the choroidal volume in each area. Mean choroidal volume of the center area (within a circle of 1.0-mm diameter) was 0.159 ± 0.066 mm³, 1.412 ± 0.507 mm³ within the inner ring (within a circle of 3.0-mm diameter), and 5.411 ± 2.097 mm³ within the outer ring (within a circle of 6.0-mm diameter).

**Interoperator Reproducibility of Choroidal Thickness Obtained by 3D SS-OCT**

To evaluate interoperator reproducibility, the lines of both RPE and chorioscleral borders in each image from 10 subjects were determined independently by two observers (Fig. 5). Table 2 shows the ICC in mean choroidal thickness of each area in the ETDRS grid, as measured by the two observers. ICC in mean choroidal thickness was between 0.945 and 0.980 (P < 0.001). In addition, choroidal thickness at a single point obtained from multiaveraged SS-OCT images also showed a high ICC (0.945–0.985) between the two observers, which was not statistically different from the ICC in mean choroidal thickness. However, choroidal thickness at a single point of each area obtained from the 3D data set showed a high ICC (0.919–0.967), which was statistically lower than the ICC in mean choroidal thickness (P < 0.01) or the ICC in choroidal thickness obtained from multiaveraged SS-OCT images (P < 0.001).

**Correlations between Age and Choroidal Thickness**

Table 3 shows Pearson’s correlation coefficient and partial correlation coefficient between mean choroidal thickness of

**Correlations between Age and Choroidal Volume**

Table 3 shows Pearson’s correlation coefficient and partial correlation coefficient between mean choroidal volume of...
the macular area and age, axial length, and refractive error. The mean choroidal thickness within the macula (within the outer circle) had a weakly negative correlation with age ($r = -0.400, P = 0.026$) and with axial length ($r = -0.375, P = 0.045$), whereas it had no correlation with refractive error ($r = 0.238, P = 0.214$). The macular choroidal thickness was correlated significantly with age after adjustment for axial length ($r = -0.684, P < 0.001$) and with axial length after adjustment for age ($r = -0.684, P < 0.001$). In addition, similar correlations were seen in the mean choroidal thickness in the central area and within the inner circle. Table 4 shows the partial correlation coefficient between mean choroidal thickness at each quadrant and age, axial length, and refractive error. In each quadrant, choroidal thickness was negatively correlated with axial length after adjustment for age ($r = -0.720$ to $-0.597, P < 0.001$) and with age after adjustment for axial length ($r = -0.690$ to $-0.613, P < 0.001$).

**Multiple Linear Regression Analysis**

Table 5 shows results of the multiple linear regression analysis for mean choroidal thickness of the macula. A stepwise method was used to determine the most unexpected factors. The model determined by age and axial length had the best regression. The model showed a good coefficient of determination, which was $0.736 (R^2 = 0.542)$; the coefficients of age and axial length were $-3.04$ and $-24.95\,\mu m$, respectively (Fig. 6).

**DISCUSSION**

In the present study, the macular area of healthy volunteers was viewed with a raster scan protocol in a prototype SS-OCT at 1050 nm. The tunable laser source has a longer wavelength, higher penetration, and lower scattering at the RPE than those at the conventional spectral-domain OCT operating at the 800-nm region, and thus allows for full-depth imaging of the choroid.\(^7\) In addition, the tunable laser source of the SS-OCT has lower signal decay versus depth than does the existing spectral-domain OCT system.\(^7\) This advantage of the SS-OCT probably allowed the clear imaging of the entire choroid within the area scanned and also allowed the highly reproducible measurements of choroidal thickness.

Importantly, high-speed scanning coupled with the high sensitivity of the SS-OCT allowed highly reproducible measurements of choroidal thickness, even in single B-scan-based imaging on a 3D raster scan protocol. In the present study, the 3D imaging data sets were acquired by using a raster scan protocol of 512 × 128 in 0.8 second. An invisible scanning line of 1-μm wavelength contributes to reduced eye motion and to patient comfort during the scan. Based on the 3D data set, we produced a 2D choroidal thickness map of the macular area for each subject and, by applying the ETDRS grid to the map, we could then obtain a mean choroidal thickness and choroidal volume in each area of the ETDRS grid. EDI–OCT is usually coupled with multiple averaging to achieve high-contrast and low-speckle noise,\(^7\) but it does not provide as many sections as does the 3D imaging. Previously, Spaide and associates\(^7\) reported that the choroidal thickness in the fovea of a healthy subject was 318 μm in the right eye and 335 μm in the left eye. As shown in Figure 4, choroid in the macula can show focal thickening or thinning\(^6,17\) and, if measured from a single A scan may be influenced by irregularity or by focal indistinctness of the choriocentral border.\(^6,17\)

**Table 3. Pearson’s Correlation Coefficient and Partial Correlation Coefficient between Mean Choroidal Thickness of the Macula Area and Age, Axial Length, and Refractive Error**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Pearson’s Correlation Coefficient</th>
<th>$P$</th>
<th>Partial Correlation Coefficient</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>-0.282</td>
<td>0.125</td>
<td>-0.707</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>-0.476</td>
<td>0.009</td>
<td>-0.628</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>0.379</td>
<td>0.042</td>
<td>0.070</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Within inner circle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>-0.325</td>
<td>0.074</td>
<td>-0.647</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>-0.437</td>
<td>0.018</td>
<td>-0.695</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>0.322</td>
<td>0.089</td>
<td>0.006</td>
<td>0.978</td>
</tr>
<tr>
<td>Within outer circle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>-0.400</td>
<td>0.026</td>
<td>-0.684</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>-0.375</td>
<td>0.045</td>
<td>-0.684</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>0.238</td>
<td>0.214</td>
<td>-0.510</td>
<td>0.806</td>
</tr>
</tbody>
</table>

**Figure 5.** Choroidal thickness map of a healthy subject. (A) Fundus photograph of the right eye of a 77-year-old woman; visual acuity was 20/25, axial length was 22.87 mm, and refractive error was +2.0 diopters. (B) Multiaverage horizontal (upper) and vertical (lower) images clearly show choroidal structures and the choriocentral border. The choroid seems to be thin around the optic disc and beyond the vascular arcade. (C) The choroidal thickness maps (6 × 6 mm) were measured by two independent observers and were almost identical. By applying the ETDRS grid to the map, mean choroidal thickness was obtained for each area. Choroid in the outer superior area is thicker than that of the outer lower area. In addition, there is regional thickening seen in the outer superior area and in the inner nasal area.
In the study described herein, similar to what has been reported previously, 10–26 lines of both RPE and the chorioscleral border were determined manually by the observers, so it is essential to estimate the error that may have occurred. In multiaveraged images obtained by the SS-OCT at 1050 nm, the chorioscleral border was clearly seen because of the reduction in speckle noise, even without use of the EDI system. Similar to the previous studies that used EDI–OCT, 9,11 the ICC in choroidal thickness at a single point obtained from multiaveraged images was very high (0.945–0.994). In addition, the ICC of choroidal thickness at the same point obtained from the 3D data set was sufficiently high (0.919–0.971), but was lower than the ICC of choroidal thickness at a single point obtained from multiaveraged images. Less clarity of the chorioscleral border on each image of the 3D data set compared with multiaveraged images probably accounted for less reproducibility. However, using the 3D data set, the ICC of mean choroidal thickness was also quite high (0.945–0.980). Averaging of thickness values obtained at many measurement points in each area probably contributed to minimize the error in determining choroidal thickness at each point.

To date, there have been several reports of the foveal choroidal thickness in normal eyes obtained by use of various systems. 9,11,23,28,31,39,40 This has been reported to be between 272 and 448 μm in healthy eyes. In the present study, mean choroidal thickness in the macula (within a circle of 6.0-mm diameter) was 191.5 ± 74.2 μm, and thickness in the nasal quadrant (152.5 ± 71.1 μm) was less than that in the other quadrants. In addition, the choroid in the superior temporal quadrant (215.5 ± 80.7 μm) was thicker than that in the outer inferior area (186.0 ± 75.2 μm). In our study, the subfoveal choroidal thickness was comparable to that in the superior temporal quadrant, whereas it was greater than that in the inferior nasal quadrant.

The subfoveal choroidal thickness was less than that reported previously, 9,11,23,28,31,39,40 although age of eligible subjects may be involved in this difference. The average age was much higher (64.6 ± 17.3 years) than that in previous studies (53.4–55.5 years). 9,11,23,28,31,39,40 Margolis and Spaide 11 reported that increasing age was correlated significantly with axial length (r = 0.375), whereas it had no correlation with refractive error (r = 0.046); in the present study, mean choroidal thickness in the macula had a negative correlation with age (r = −0.400) and with axial length (r = −0.375), whereas it had no correlation with refractive error (r = 0.238). In addition, the correlation with age became more significant with an adjustment for axial length (r = −0.684), and the correlation with axial length became more significant with an adjustment for age (r = −0.684). However, whereas the central choroidal thickness showed a weak correlation with refractive error (r = 0.379), no correlation was seen after adjustment for axial length (r = 0.070). There have been some previous reports of a correlation between choroidal thickness and refractive er-

### Table 4. Partial Correlation Coefficient between Mean Choroidal Thickness of Each Quadrant and Age and Axial Length

<table>
<thead>
<tr>
<th>Factor</th>
<th>Temporal</th>
<th>Superior</th>
<th>Nasal</th>
<th>Inferior</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>−0.657</td>
<td>−0.672</td>
<td>−0.597</td>
<td>−0.720</td>
<td>&lt;0.001 (adjusted for axial length)</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>−0.656</td>
<td>−0.690</td>
<td>−0.613</td>
<td>−0.678</td>
<td>&lt;0.001 (adjusted for age)</td>
</tr>
</tbody>
</table>

Each quadrant includes both inner and outer areas.

In the present study, 3D imaging of the choroid using SS-OCT allowed calculation of the choroidal volume of the macular area. So far, no previous reports have provided in vivo data on the volume of the choroid. 42 Choroidal volume reflects vascular changes such as the vascular hyperpermeability or vasodilation seen in central serous chorioretinopathy, 43 the inflammation seen in Vogt–Koyanagi–Harada disease, 44 and the decrease of vessels seen in pathologic myopia 45; moreover, changes in the foveal choroidal thickness have been reported recently in various diseases, including central serous chorioretinopathy, 14,25 Vogt–Koyanagi–Harada disease, 13,18 polypoidal choroidal vasculopathy, 16,17 and age-related macular degeneration. 16,17 Maruko and associates 14,20 reported that choroidal thickness in the fovea becomes decreased after photodynamic therapy. In their studies, foveal choroidal thickness reflected pathophysiology of the choroid after treatment. However, still more information may be obtained by the evaluation of choroidal volume. In the present study, we applied the ETDRS grid only to the choroidal thickness maps. With some modification of the algorithm, choroidal volume within arbitrary areas could be obtained (e.g., choroidal volume within the laser-irradiated area to which photodynamic therapy is to be applied).

Previously, Ikuno and associates 31 reported that foveal choroidal thickness is weakly correlated with age (R² = 0.04), axial length (R² = 0.06), and refractive error (R² = 0.046); in the present study, mean choroidal thickness in the macula had a negative correlation with age (r = −0.400) and with axial length (r = −0.375), whereas it had no correlation with refractive error (r = 0.238). In addition, the correlation with age became more significant with an adjustment for axial length (r = −0.684), and the correlation with axial length became more significant with an adjustment for age (r = −0.684). However, whereas the central choroidal thickness showed a weak correlation with refractive error (r = 0.379), no correlation was seen after adjustment for axial length (r = 0.070). There have been some previous reports of a correlation between choroidal thickness and refractive er-

### Table 5. Multiple Linear Regression Analysis for Choroidal Thickness of the Macula* by Axial Length and Age

<table>
<thead>
<tr>
<th>Factor</th>
<th>Coefficient</th>
<th>P</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1001.70</td>
<td>&lt;0.001</td>
<td>153.50</td>
</tr>
<tr>
<td>Age, y</td>
<td>−3.04</td>
<td>&lt;0.001</td>
<td>0.64</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>−24.95</td>
<td>&lt;0.001</td>
<td>5.20</td>
</tr>
</tbody>
</table>

R = 0.736; R² = 0.542.

* Macular choroidal thickness = 1099.3 − 3.05 × Age − 28.53 × Axial length.
and it is possible that axial length or age has some influence on this correlation. Using stepwise multiple regression analysis, we showed with great accuracy ($R^2 = 0.542$) that the choroidal thickness in the macula is determined by age and axial length, so it is essential that both age and axial length be taken into account when choroidal thickness is evaluated. After this model is modified and its accuracy is confirmed in future studies, it may serve to compare the macular choroidal thickness in eyes of different ages and with different axial lengths.

Compared with spectral-domain OCT at approximately 800 nm, SS-OCT at longer wavelength is reported to provide superior visualization of the posterior pole in cataractous eyes. In the present study with SS-OCT at 1050 nm, no eyes were excluded because of poor images due to cataract. However, the present study does have some limitations. Primary among these is that it consisted of only Japanese subjects; thus, choroidal thickness and volume need to be confirmed in other ethnic groups. In addition, the small sample size might be insufficient to evaluate the mean choroidal thickness (volume) in normal eyes. In the present study, the line of RPE and the chorioscleral border were determined manually. The raster scan protocol with over 60,000 measurement points may have minimized the error in the measurements made by the observers, thus leading to the high ICC. To further standardize this evaluation, software to determine these lines automatically is essential. Regardless of the limitations, however, our study did show that 1050-nm SS-OCT provides a unique opportunity to study macular choroidal thickness in three dimensions. Furthermore, our results have confirmed the asymmetric nature of macular choroidal thickness. Further studies using pathologic eyes are, of course, necessary to establish the validity and usefulness of choroidal thickness maps obtained with SS-OCT at this longer wavelength.

References