Choroidal Thickness in Healthy Japanese Subjects

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PURPOSE. To study posterior choroidal thickness and its profile based on location in healthy Japanese subjects and the correlation with axial length, refractive error (RE), and age.

METHODS. Eighty-six eyes of 43 healthy volunteers with no ophthalmic or systemic symptoms were examined with prototype high-penetration optical coherence tomography using a 1060-nm light source. Eyes with high myopia (exceeding −6 D) or with retinal/choroidal disease were excluded. The spherical equivalent RE was measured by autorefractometry, and the axial length was measured by partial coherence interferometry.

RESULTS. Mean choroidal thicknesses were 354 ± 111 μm at the fovea, 364 ± 86 μm superiorly, 345 ± 108 μm inferiorly, 227 ± 532 μm nasally, and 337 ± 102 μm temporally. Subfoveal choroidal thickness was significantly greater than nasal (P < 0.01) and temporal (P < 0.05) choroidal thickness; however, there was no significant difference compared with superior (P = 0.20) and inferior (P = 0.17) choroidal thickness. The temporal choroid was significantly (P < 0.01) thicker than the nasal choroid, and the inferior choroid was significantly (P < 0.01) thinner than the superior choroid. There was a significant negative correlation between foveal choroidal thickness and axial length (P < 0.05) but a borderline correlation with the RE (P = 0.086) and age (P = 0.07). Age was the factor that was most associated with the choroidal thickness (F = 20.86; P < 0.001), followed by RE (F = 5.37; P < 0.05); axial length was not a significant factor (F = 1.47; P = 0.22) by stepwise analysis.

CONCLUSIONS. The profile of choroidal thickness depends on its location, RE, axial length, and especially age are critical for evaluation of choroidal thickness. (Invest Ophthalmol Vis Sci. 2010;51:2173–2176) DOI:10.1167/iovs.09-4383

The choroid is the source of many vision-threatening diseases, such as age-related macular degeneration,1 polyoidal choroidal vasculopathy,2 central serous choriorretinopathy,3 and high myopia-related chorioretinal atrophies.4 In addition, the outer retina, including the photoreceptors, is nourished by the choroidal vasculature; extreme choroidal thinning and loss of the vascular tissues often lead to photoreceptor damage and visual dysfunction.2 Because choroidal abnormalities such as vascular hyperpermeability, vascular changes and loss, and thinning are critical to the onset and progression of such diseases, ophthalmologists and researchers are shifting their interest to the choroidal abnormalities.

Accurate measurement of choroidal thickness in vivo is an essential step in monitoring disease onset and progression that lead to choroidal thinning. Based on histologic study, choroidal thickness ranges from 170 to 220 μm.6 However, recent advances in technologies such as partial coherence interferometry7 and enhanced depth imaging8 using a Heidelberg system have shown an approximate subfoveal choroidal thickness of 300 μm in healthy volunteers. Choroidal thickness is affected by age9,10 and perhaps refractive abnormalities or ethnicity.

High-penetration optical coherence tomography (HP-OCT) using a long-wavelength light source of approximately 1050 nm11–17 allows visualization of the posterior choroid and sclera but are normally difficult to image with commercially available OCT using a shorter wavelength of approximately 840 nm, with higher scattering at the photoreceptors and pigment epithelium and a resultant lower signal from the deep choroidal tissue.18 The system provides more details of the microarchitecture of the posterior choroid and theoretically facilitates an understanding of the choroidal abnormalities underlying various chorioretinal diseases. We studied choroidal thickness in healthy Japanese volunteers to determine baseline choroidal thickness.

Subjects and Methods

Subjects

Eighty-six eyes of 43 healthy volunteers with no ophthalmic or systemic symptoms were examined with prototype HP-OCT, an autorefractometer (ARK-530A; Nidek, Gamagori, Japan), and a keratometer (IOLMaster; Carl Zeiss Meditec, La Jolla, CA). Exclusion criteria included high myopia or hyperopia (greater than ±6 or ±6 diopters [D]) of spherical equivalent refractive error (RE), any retinal or retinal pigment epithelial (RPE) detachment detectable with HP-OCT, poor image quality because of unstable fixation, and pseudophakia or severe cataract. Seven eyes were excluded because of high myopia (n = 4), poor HP-OCT image quality because of poor fixation (n = 2), and suspected central serous choriorretinopathy caused by a small pigment epithelial detachment (n = 1). Thus, data from 79 eyes of 43 patients were analyzed. All keratometry and autorefractometry examinations were performed by one author (KK), and HP-OCT examination was performed by one author (YI). All examinations were performed under nonmydriatic conditions. This study was conducted in accordance with the tenets of the Declaration of Helsinki.

Prototype 1060-nm HP-OCT

The prototype HP-OCT was used to image the full-thickness choroid and retina. This HP-OCT is based on swept-source OCT technology,19 with a scanning speed of 50,000 A-scans/s. A 6 × 6-mm retinal region was scanned by a horizontal fast raster scanning protocol, and the A-scan density was 512 lines (horizontal) × 255 lines (vertical). The center wavelength of the probe beam was 1060 nm. This long-wavelength probe enables deep penetration to the choroid. The detailed profile of this instrument is described elsewhere.15,17 The axial resolution of this system is 10 μm in tissue. The use of this prototype

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HP-OCT was approved by the institutional review board of Osaka University Hospital.

Choroidal thickness was measured as previously described. The vertical distance between the hyperrefractive RPE layer and the chorioscleral interface was measured manually using a software caliper built into the custom-made OCT image viewer. If the line was blurred especially for chorioscleral interface, the center of the line was always traced and measured. Choroidal thickness was measured at the fovea and 3 mm nasal, temporal, superior, and inferior to the fovea.

Comparison with Conventional 840-nm OCT
To compare the image of the HP-OCT, the same healthy eye of 24-year-old woman was examined both with a conventional system using 840-nm wavelength (OCT-1000; Topcon, Tokyo, Japan) and with our HP-OCT. Images obtained were processed similarly and compared.

Statistical Analysis
The data were analyzed using a paired $t$-test to compare thickness at different points and by univariate regression analysis and multiple regression analysis using a statistical software package (JMP, version 7.0; SAS Institute Inc, Cary, NC). $P \leq 0.05$ was considered significant.

RESULTS

Demographic Data
Eighteen men and 25 women (mean age, 39.4 ± 16.0 years; range, 23–88 years) were enrolled. Forty-one right eyes and 38 left eyes were analyzed. Mean RE was $-1.9 \pm 2.3$ D (range, +4.0 to $-5.75$ D); mean axial length was $24.40 \pm 1.24$ mm (range, 21.76–27.35 mm).

OCT Image of HP-OCT
A typical B-scan image of HP-OCT is presented in Figure 1. Visualization of the posterior choroid and the sclera was markedly improved compared with the conventional 840-nm system.

Location and Choroidal Thickness
Mean choroidal thicknesses were $354 \pm 111$ μm (range, 80–641 μm) at the fovea, $364 \pm 86$ μm (range, 191–573 μm) superiorly, $345 \pm 108$ μm (range, 94–634 μm) inferiorly, $227 \pm 532$ μm (range, 61–532 μm) nasally, and $337 \pm 102$ μm (range, 102–634 μm) temporally. The subfoveal choroidal thickness was significantly greater than the nasal ($P < 0.01$) and temporal ($P < 0.05$) choroidal thickness; however, there were no significant differences compared with superior ($P = 0.20$) and inferior ($P = 0.17$) choroidal thickness. When compared horizontally or vertically, the temporal choroid was significantly ($P < 0.01$) thicker than nasal choroid, and the inferior choroid was significantly ($P < 0.01$) thinner than the superior choroid.

Relation to RE, Axial Length, and Age
Figure 2 shows a significant ($P < 0.05$) relationship between the foveal choroidal thickness and the axial length; however, the regression was low ($R^2 = 0.06$). Figure 3 shows the relation with the RE. Similarly, borderline significance was seen ($P = 0.086$); however its regression ($R^2$) was 0.046. Age tended to have a negative correlation of borderline significance (Fig. 4; $P = 0.07$). $R^2$ was as low as 0.04.

Multiple Regression Analysis
We performed stepwise analysis to determine the factors most associated with subfoveal choroidal thickness among patient
FIGURE 4. Scatterplot of age and subfoveal choroidal thickness of all subjects shows a borderline significant negative correlation \( (P = 0.07; y = -1.4x + 410.6; R^2 = 0.04) \).

age, RE, and axial length. Age was the factor most associated with choroidal thickness \( (F = 20.86; P < 0.001) \), followed by RE \( (F = 5.57; P < 0.05) \); axial length was not significantly \( (F = 1.47; P = 0.22) \) correlated with choroidal thickness. Table 1 shows the results of multiple regression analysis with age and RE.

**DISCUSSION**

A newly developed 1060-nm OCT system has higher penetration and consequently increased sensitivity for the posterior choroid and the sclera, allowing visualization of the choriocapillaris and choroidal interface in normal eyes compared with conventional systems in most cases. Thus, in vivo choroidal thickness has been measured accurately because of this technical advantage. Magnetic resonance imaging (MRI) may provide approximate choroidal thickness; however, MRI resolution is on the order of 100 \( \mu \)m, and the thickness measured is supposedly much less accurate. Commercial OCT with a 800-nm band can measure retinal thickness and provides useful information in various mucular diseases and glaucoma; this information is applicable in many clinical situations for decision making regarding the management and monitoring of disease progression. The rationale for measuring choroidal thickness remains controversial; however, detecting choroidal abnormalities beneath the RPE, which could not be done using conventional OCT systems, is assumed to provide an increased understanding of the pathogenesis and to facilitate identification of risk factors in vision-threatening chorioretinal diseases such as age-related macular degeneration or myopic degeneration. For example, myopic progression is accompanied by choroidal thinning, suggesting the importance of choroidal thickness measurement in vivo in at least some conditions.

In the present study, the choroid was somewhat thicker than reported previously. Margolis and Spaide, who investigated 54 patients (mean age, 50.4 years) with normal vision using the enhanced depth imaging of the 840-nm OCT, reported choroidal thickness measurements of 287, 145, and 261 \( \mu \)m, respectively, for the subfovea, 3 mm nasal, and 3 mm temporal. Our results were 354, 227, and 337 \( \mu \)m subfoveally, 3 mm nasally, and 3 mm temporally, indicating that the current data are approximately 80 to 100 \( \mu \)m thicker. This difference between the studies may result from differences in the measuring software, differences in the OCT light source, differences in ethnicity (although Margolis and Spaide did not specify the ethnic group), or differences in patient profiles such as age, RE, or axial length. Theirs were patients without disease, and ours were healthy volunteers. It is still unknown what factors affect choroidal thickness; determining this is a high-priority task.

In the present study, we found that age was the factor most associated with subfoveal choroidal thickness by stepwise analysis. In a previous report, regression analysis showed an approximate decrease in thickness of 15 \( \mu \)m every 10 years. Univariate regression analysis in the present study showed 14.5 \( \mu \)m reductions every 10 years. Although the reductions were similar, the \( R^2 \) was as low as 0.04, suggesting great interindividual variations. A previous histologic study showed a similar trend \( (R^2 = 0.18; \text{regression}, -1.10 \mu \text{m/} \text{year}) \). Because choroidal thickness is affected by factors other than age, it may be difficult to evaluate the effect based simply on age. Studies with more patients of a wide range of ages are required for accurate analysis.

We also found a correlation with RE and axial length. Choroidal thinning is prominent in highly myopic eyes. Our previous report using a commercially available instrument (Cirrus HD-OCT; Carl Zeiss Meditec) indicated that the subfoveal choroidal thickness was 100.5 \( \mu \)m, which is approximately three times thinner in highly myopic eyes. Multiple regression analysis in the present study showed older age and myopic RE are significantly associated with choroidal thinning, indicating that aging and myopia shift are critical factors. RE had a great impact on choroidal thinning and on age in terms of regression \( (-4.16 \mu \text{m/year and 9.5} \mu \text{m/D}) \). Thus, preventing myopia progression is critical for avoiding choroidal thinning and consequent visual loss.

The present study also showed that the nasal choroid was significantly thinner than the subfoveal and temporal choroid and that the inferior choroid was significantly thinner than the superior choroid. A previous OCT study showed that the choroid is thicker at the macula than nasally or temporally probably because of high metabolic demand. The present data showed a significantly thicker choroid subfoveally than nasally and temporally; however, the thickness was similar to that of the superior and inferior choroid. There may be two reasons for relative choroidal thinning nasally and inferiorly. One is the choroidal watershed, which isolates the choroidal circulation, seen on fluorescein or indocyanine green angiography. Another could be the fetal choroidal fissure, which closes inferiorly at 16 weeks.

The optical geometry of the OCT probe beam is not symmetrical between the center and the perimeter of the area scanned because the pivot of the fan-beam scan of the probe is located at the pupil and not the center of the retinal curvature. In the scanning protocol used in the present study, subfoveal thickness was measured at the center, and the temporal, superior, nasal, and inferior thicknesses were measured at the perimeter. This asymmetry may cause a systematic error in the thickness measurement. At the fovea, the probe beam is per-
perpendicular to the retinal curvature; hence, the true thickness of the choroid is measured. However, at the perimeter, the probe beam impinges on the retina from a slightly oblique direction, which could result in a slight overestimation of choroidal thickness. However, this overestimation did not affect our conclusions because of the following reasons. First, this overestimation negatively affects the tendency we found, which was that thickness is greater at the subfovea than at other locations. Second, assuming that the axial length is 17 mm, the error in thickness is estimated to be 1.5%, which is sufficiently smaller than interseッション fluctuations.

Finally, investigators have just begun to study choroidal thickness, and more information is needed to gain a better understanding of choroidal abnormalities. In addition, it has not been totally agreed on that the hyperscattering line behind the choroidal vessels actually represents the choriocapillaris interface. It might be more accurate to use the polarization-sensitive, 1-μm swept-source OCT to trace the scleral interface. In addition, we believe it is important to determine the process of and risk factors for chorioretinal atrophy, a slowly progressing but vision-threatening condition worldwide, resulting from several factors, including myopic change.

References