Subfoveal Choroidal Thickness: The Beijing Eye Study

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Purpose: To study subfoveal choroidal thickness (SFCT) in adult Chinese subjects and its correlation with ocular biometric parameters, refractive error, and age.


Participants: The population-based Beijing Eye Study 2011 included 3468 individuals with a mean age of 64.6±9.8 years (range, 50–93 years).

Methods: A detailed ophthalmic examination was performed, including spectral-domain optical coherence tomography (SD-OCT) with enhanced depth imaging for measurement of SFCT.

Main Outcome Measures: Subfoveal choroidal thickness.

Results: The SFCT measurements were available for 3233 subjects (93.2%). Mean SFCT was 253.8±107.4 μm (range, 8–854 μm). In multivariate analysis, SFCT increased with younger age (P<0.001; correlation coefficient r = 4.12; beta coefficient = 0.37), shorter axial length (P<0.001; r = 44.7; beta coefficient = 0.46), male gender (P<0.001; r = 28.5; beta coefficient = -0.13), deeper anterior chamber depth (P<0.001; r = 39.3; beta coefficient = 0.13), thicker lens (P<0.001; r = 26.8; beta coefficient = 0.08), flatter cornea (P<0.001; r = 46.0; beta coefficient = 0.11), and better best-corrected visual acuity (BCVA) (logarithm of minimal angle of resolution; P = 0.001; r = 48.4; beta coefficient = 0.06). In multivariate analysis, SFCT was not significantly associated with blood pressure, ocular perfusion pressure, intraocular pressure, cigarette smoking, alcohol consumption, serum concentrations of lipids and glucose, diabetes mellitus, and arterial hypertension. In the myopic refractive error range of more than −1 diopter (D), SFCT decreased by 15 μm (95% confidence interval [CI], 11.9–18.5) for every increase in myopic refractive error of 1 D, or by 32 μm (95% CI, 37.1–26.0) for every increase in axial length of 1 mm. For each year increase in age, the SFCT decreased by 4.1 μm (95% CI, 4.6–3.7) (multivariate analysis).

Conclusions: Subfoveal choroidal thickness with a mean of 254±107 μm in elderly subjects with a mean age of 65 years decreased with age (4 μm per year of age) and myopia (15 μm per diopter [D] of myopia). It was also associated with male gender and the ocular biometric parameters of a deeper anterior chamber and thicker lens. The association between SFCT and BCVA indicates a functional aspect of SFCT.

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The choroid, a highly vascularized structure between the lamina fusca of the sclera and the retinal pigment epithelium, is composed of the chooriocapillaris, the basal membrane of which forms the outer part of Bruch’s membrane; the middle layer of medium-sized vessels (Sattler’s layer) and the outer layer of large vessels (Haller’s layer); melanocytes interposed between the vessels of Sattler’s layer and Haller’s layer; a nicotinamide adenine dinucleotide phosphate diaphorase–positive and nitric oxide synthase–positive ganglion cell plexus located mainly in the temporal-central portion; and connective tissue and other cellular elements. 1, 2 The physiologic functions of the choroid include, among others, providing oxygen and nourishment to the outer retinal layers, which have one of the highest metabolic activities among all tissues in the body, and regulating temperature by conveying heat accumulated by the focused light onto the foveal region. The choroid receives approximately 95% of the ophthalmic artery blood. The choroid is primarily or secondarily involved in the pathogenesis of many diseases of the posterior segment of the eye, such as age-related macular degeneration, polypoidal choroidal vasculopathy, central serous chorioretinopathy, and myopic retinopathy.

Although the anatomy and physiologic functions have clearly shown the importance of the choroid for ocular diseases, and histomorphometric studies have already indicated that the thickness of the choroid changes in the course of some disorders such as the glaucomas, 3 it was the landmark study by Spaide et al 4 that demonstrated the choroidal thickness can be measured noninvasively in vivo using spectral-domain optical coherence tomography (SD-OCT). The images were obtained by positioning the SD-OCT device close enough to the eye to obtain an inverted representation of the fundus. Since that landmark study, several studies have measured the thickness of the choroid in nor-
mal subjects and patients with choroidal or retinal diseases. However, these studies were hospital-based studies with relatively few subjects and the possibility of a bias by the selection artifact. Therefore, we conducted the present investigation to measure the subfoveal choroidal thickness (SFCT) in a population-based study with a relatively large study population.

Materials and Methods

The Beijing Eye Study 2011 is a population-based, cross-sectional study in Northern China. The Medical Ethics Committee of the Beijing Tongren Hospital approved the study protocol, and all participants gave informed consent. The study was carried out in 5 communities in the urban district of Haidian in the North of Central Beijing and in 3 communities in the village area of Yufa of the Daxing District south of Beijing. The only eligibility criterion for inclusion in the study was an age of 50+ years. In 2011, the 8 communities had a total population of 4403 individuals aged ≥50 years. In total, 3468 individuals (1963 female, 56.6%) participated in the eye examination, corresponding to an overall response rate of 78.8%. The study was divided into a rural part (1633 subjects, 47.1%; 943 female, 57.7%) and an urban part (1835 subjects, 52.9%; 1020 female, 55.6%). The mean age was 64.6 ± 9.8 years (median, 64 years; range, 50–93 years).

All examinations were carried out in the communities, either in schoolhouses or in community houses. All study participants underwent an interview with standardized questions on their family status, level of education, income, quality of life, psychic depression, physical activity, known major systemic diseases such as arterial hypertension and diabetes mellitus, and quality of vision. Fasting blood samples were taken for measurement of blood lipids, glucose, and glycosylated hemoglobin. Blood pressure was measured. Body height and weight and the circumference of the waist were recorded. The ophthalmic examination included measurement of presenting visual acuity and uncorrected visual acuity. Best-correcting refractive error was assessed by automatic refractometry (Auto Refractometer AR-610, Nidek Co, Ltd, Tokyo, Japan). If uncorrected visual acuity was <1.0 (i.e., <5/5), subjective refractometry was also performed. A Snellen chart at a distance of 5 m was used, and visual acuity was recorded in decimal notation. Intraocular pressure was measured by pneumotonometry by an experienced ophthalmologist. A slit-lamp examination performed by an ophthalmologist assessed lid abnormalities, Meibomian gland dysfunction, corneal disorders, and peripheral anterior chamber depth using van Herick’s method. The anterior segment was measured by slit-lamp adapted optical coherence tomography (OCT) (Heidelberg Engineering Co, Dossenheim, Germany). By using optical low-coherence reflectometry (Lenstar 900 Optical Biometer, Haag-Streit, 3098 Koeniz, Switzerland), biometry of the right eye (or the left eye if measurements of the right eye were not possible) was performed for measurement of the anterior corneal curvature, central corneal thickness, anterior chamber depth, lens thickness, and axial length. The pupil was dilated using tropicamide 0.5% once or twice until the pupil diameter was at least 6 mm. A second slit-lamp–assisted biomicroscopy searched for pseudoexfoliation syndrome. Digital photographs of the cornea and lens were taken using the slit-lamp digital camera (Type BG-4, Topcon Medical Systems, Inc, Tokyo, Japan), and retroilluminated photographs of the lens were obtained using the Neitz CT-R camera (Neitz Instruments Co, Tokyo, Japan). Photographs of the macula and optic disc were taken using a fundus camera (Type CR6-45NM, Canon Inc, Lake Success, NY).

The SFCT was measured using SD-OCT (Spectralis, Wavelength: 870 nm; Heidelberg Engineering Co, Heidelberg, Germany) with enhanced depth imaging modality (Fig 1) after pupil dilation. Seven sections, each comprising 100 averaged scans, were obtained in an angle of a 5- to 30-degree rectangle centered onto the fovea. The horizontal section running through the center of the fovea was selected for further analysis. Subfoveal choroidal thickness was defined as the vertical distance from the hyperreflective line of the Bruch’s membrane to the hyperreflective line of the inner surface of the sclera. The measurements were performed using the Heidelberg Eye Explorer software (v. 5.3.3.0; Heidelberg Engineering Co, Heidelberg, Germany). Only the right eye of each study participant was assessed. The images were taken by 1 technician (CXC), and the images were assessed by 2 ophthalmologists (L.S., K.F.D.).

Statistical analysis was performed using a commercially available statistical software package (SPSS for Windows, v. 20.0, IBM-SPSS, Chicago, IL). In the first step, we examined the mean values (presented as mean ± standard deviation) of SFCT. In the second step, we performed a univariate linear regression analysis with SFCT as a dependent parameter and ocular and general parameters as independent parameters. In the third step, we performed a multivariate linear regression analysis, with SFCT as a dependent parameter and all those parameters as independent parameters that were significantly associated with SFCT in univariate analysis. All P values were 2-sided and considered

Figure 1. Optical coherence tomogram (enhanced depth imaging mode) of the subfoveal choroid.
tically significant when the values were less than 0.05; 95% confidence intervals (CIs) were presented.

**Results**

Of the 3468 participants, SFCT measurements were available for 3233 (93.2%) (1818 female, 56.2%). The mean age was 64.3 ± 9.6 years (median, 63 years; range, 50–93 years), the mean refractive error (spherical equivalent) was −0.18 ± 1.98 D (median, 0.25 D; range, −20.0 to +7.00 D). The group of subjects without SFCT measurements compared with the group of subjects with SFCT measurements was significantly (P<0.001) older (69.6 ± 10.9 years vs. 64.3 ± 9.6 years) and more myopic (−1.44 ± 4.75 D vs. −0.16 ± 2.02 D; P = 0.007) and did not vary significantly in gender (P = 0.12). Reasons why SD-OCT images for the measurement of the SFCT were not available were opacities of the optic media, such as cataract, and insufficient quality of the images for a reliable determination of the SFCT. Any ocular disease, including disorders of the optic nerve or macula, was no reason to exclude a subject if the quality of OCT image was sufficient to be evaluated. The mean axial length in the study population was 23.2 ± 1.11 mm (median, 23.13 mm; range, 18.96–30.88 mm), mean anterior corneal curvature radius was 7.62 ± 0.25 mm (median, 7.62 mm; range, 6.80–9.02 mm), mean anterior chamber depth was 2.49 ± 0.49 mm (median, 2.44 mm; range, 1.50–5.47 mm), and mean lens thickness was 4.56 ± 0.33 mm (median, 4.56 mm; range, 2.92–6.17 mm).

The mean SFCT was 253.8 ± 107.4 µm (median, 251 µm; range, 8–854 µm) (Fig 2). In univariate analysis, SFCT was significantly associated with the systemic parameters of younger age (P<0.001) (Fig 3, available at http://aaojournal.org); male gender (P = 0.02); greater body height (P<0.001), weight (P<0.001), and body mass index (P<0.001); rural region of habitation (P<0.001); higher diastolic (P<0.001) and mean (P<0.001) blood pressures; presence of arterial hypertension (P<0.001); higher ocular perfusion pressure (P = 0.001); higher serum concentrations of cholesterol (P = 0.03) and glucose (P = 0.01); smoking (P<0.001) and greater package years of cigarettes (P<0.001); higher alcohol consumption (P<0.001); less aspirin intake (P<0.001); and higher frequency of reported snoring (P = 0.01); and with the ocular parameters of shorter axial length (P<0.001) (Fig 4, available at http://aaojournal.org), hyperopic refractive error (P<0.001) (Fig 5, available at http://aaojournal.org), shorter anterior chamber depth (P<0.001), thinner lens (P<0.001), steeper cornea (P<0.001), higher best-corrected visual acuity (BCVA) (P<0.001), and higher intraocular pressure (P<0.001) (Table 1, available at http://aaojournal.org). The SFCT was not significantly (all P > 0.05) associated with the systemic parameters of systolic blood pressure, serum concentrations of high-density lipoproteins, low-density lipoproteins and triglycerides, and presence of diabetes mellitus; and with the ocular parameters of central corneal thickness, scleral spur distance, corneal diameter, and pupil diameter (Table 1, available at http://aaojournal.org).

In the first step of the multivariate analysis, we adjusted the SFCT for age and axial length, which were the 2 parameters with the highest regression coefficients, and we then added the systemic parameters of gender; body mass index; region of habitation; body height; diastolic blood pressure; serum concentration of glucose, low-density lipoproteins, and cholesterol; cigarette package years; and consumption of alcohol to the multivariate analysis. The results showed that SFCT remained significantly associated with younger age (P<0.001), shorter axial length (P<0.001), male gender (P<0.001), and cigarette package years (P = 0.04), whereas region of habitation (P = 0.55); body mass index (P = 0.36); serum concentration of low-density lipoproteins (P = 0.28); cholesterol (P = 0.18), and glucose (P = 0.07); diastolic blood pressure (P = 0.11); and frequency of alcohol consumption (P = 0.82) were no longer significantly associated. If ocular perfusion pressure was added, it was not significantly correlated with SFCT (P = 0.31). In the second step, we adjusted SFCT for age, gender, axial length, and cigarette package years, and added intraocular pressure, which was then not significantly associated (P = 0.96). When we added the remaining ocular biometric parameters and BCVA, we found that anterior chamber depth (P<0.001), lens thickness (P<0.001), anterior corneal curvature (P<0.001), and BCVA (P = 0.001) were all related with SFCT after adjustment for age (P<0.001), axial length (P<0.001), and gender (P<0.001). Cigarette package years were no longer correlated (P = 0.14).

The regressions of the associations of SFCT with axial length (Fig 4, available at http://aaojournal.org) or SFCT with refractive error (Fig 5, available at http://aaojournal.org) showed a curvilinear course. For the refractive error range of −1 toward hyperopia, the relationship between SFCT and refractive error was not statistically significant (P<0.05), whereas for the myopic refractive error range of more than −1 D, it was highly significantly correlated (P<0.001). For every increase in myopic refractive error of 1 D beyond a refractive error of −1 D, SFCT decreased by 15 µm (95% CI, 5.2–1.5) (Table 1, available at http://aaojournal.org). If the whole study population was stratified into age groups of 10 years each, the decrease in SFCT per year of age did not vary markedly between the age group of 50 to 59 years (decrease in SFCT of 3.3 µm [95% CI, 5.2–1.5] per year of age), the age group of 60 to 69 years (4.9 µm [95% CI, 7.1–2.8]), the age group of 70 to 79 years (3.8 µm [95% CI, 6.2–1.3]), and the age group of 80+
years (4.6 \mu m [95\% CI, 8.8–0.5]). In the multivariate analysis, the decrease in SFCT per year of age was 4.1 \mu m (95\% CI, 4.6–3.7) (Table 2).

### Discussion

In our population-based study on a relatively large study population, we found that that mean SFCT was 253.8 ± 107.4 \mu m, ranging from 8 to 854 \mu m. In multivariate analysis, SFCT was associated with younger age (P < 0.001; beta coefficient = 0.37), shorter axial length (P < 0.001; beta = 0.46), male gender (P < 0.001; beta = −0.13), deeper anterior chamber depth (P < 0.001; beta = 0.13), thicker lens (P < 0.001; beta = 0.08), flatter cornea (P < 0.001; beta = 0.11), and better BCVA (P = 0.001; beta = 0.06). In multivariate analysis, SFCT was not significantly associated with blood pressure, ocular perfusion pressure, intraocular pressure, cigarette smoking, alcohol consumption, serum concentrations of lipids and glucose, diabetes mellitus, and arterial hypertension. In the myopic refractive error range of more than −1 D, SFCT decreased by 15 \mu m (95\% CI, 11.9–18.5) for every increase in myopic refractive error of 1 D or by 32 \mu m (95\% CI, 37.1–26.0) for every increase in axial length of 1 mm. For each year increase in age, the SFCT decreased by 4.1 \mu m (95\% CI, 4.6–3.7) (multivariate analysis).

The results of the mean SFCT as measured in our study are lower than those reported previously. In the landmark study by Spaide et al. on 17 healthy and young volunteers with a mean age of 33.4 years, the SFCT was 318 \mu m. If one takes into account the age difference between both study populations, with a mean decrease in SFCT of approximately 5 \mu m per year of age, the measurements in the study by Spaide et al are even lower than the results of the present study. Likewise, the study by Rahman et al. on 50 healthy subjects with a mean age of 38.5 years showed a mean SFCT of 332 \mu m, which becomes comparable to our results if the age difference is taken into account. Correspondingly, Ikuno and Tano. measured the SFCT in 43 healthy Japanese with a mean age of 39.4 years and found a mean value of 354 \mu m, which is similar to our result after correction for age. In the recent study by Ding et al. on 210 healthy Chinese volunteers with a mean age of 49.7 ± 17.9 years, the mean SFCT was 262 ± 88 \mu m. Other reasons for differences between various studies in the SFCT measurements could be differences in the refractive error of the study populations and ethnic differences in the anatomy of the globes.

The 2 parameters with the highest influence on SFCT were axial length (standardized coefficient beta = −0.46) and age (beta = −0.37) (Table 2). The association between SFCT and age was also reported by Ding et al., who found a thinner SFCT in subjects aged less than 60 years (294.6 ± 75.9 \mu m) than in subjects aged older than 60 years of age (196.5 ± 74.4 \mu m). However, a significant correlation between age and SFCT was found only for the subjects aged ≥60 years. In our study, the study population were 50 to 60 years of age, and showed a significant decline in SFCT, with a decrease in SFCT of 3.3 \mu m (95\% CI, 5.2–1.5) per year of age. Also, the age-related decrease in SFCT was similar in all age groups in our study population, with a rate of 3.3 \mu m in the age group 50 to 59 years, 4.9 \mu m in the age group 60 to 69 years, 3.8 \mu m in the age group 70 to 79 years, and 4.6 \mu m in the age group 80+ years. An age-related decline in SFCT also was reported by Margolis and Spaide. (SFCT decrease by 15.6 \mu m for each decade of life), Ikuno and Tano. (SFCT decrease by 14 \mu m per decade of life), and Ding et al. (SFCT decrease by 54 \mu m per decade of life). These intravital measurements were confirmed in a histomorphometric study by Ramrattan et al.

Parallel to age, axial length (or myopic refractive error) was the most influential parameter on SFCT in the current study (Table 1, available at http://aaojournal.org; Table 2) (Figs 4 and 5, available at http://aaojournal.org). The axial elongation–associated thinning of the subfoveal choroid is paralleled by an axial elongation–related thinning of the sclera. With a mean decrease in SFCT of 15 \mu m for every increase in myopic refractive error of 1 D, a myopic refractive error of −20 D results in an SFCT of approximately zero, a value that can also be found in the histology of highly axially elongated globes. The marked thinning of the SFCT in highly myopic eyes may be one of the reasons for the development of myopic retinopathy.

Parallel to the association between SFCT and axial length, SFCT was correlated with refractive error, which confirms previous studies. The association between SFCT and axial length or refractive error was not linear.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P Value</th>
<th>Regression Coefficient B</th>
<th>95% CI</th>
<th>Standardized Coefficient Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>&lt;0.001</td>
<td>−4.12</td>
<td>−4.55 to −3.70</td>
<td>−0.37</td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td>&lt;0.001</td>
<td>−44.7</td>
<td>−49.2 to −40.2</td>
<td>−0.46</td>
</tr>
<tr>
<td>Gender</td>
<td>&lt;0.001</td>
<td>−28.5</td>
<td>−35.9 to −21.6</td>
<td>−0.13</td>
</tr>
<tr>
<td>Anterior chamber depth (mm)</td>
<td>&lt;0.001</td>
<td>39.3</td>
<td>25.5–53.0</td>
<td>0.13</td>
</tr>
<tr>
<td>Lens thickness (mm)</td>
<td>&lt;0.001</td>
<td>26.8</td>
<td>14.8–38.9</td>
<td>0.08</td>
</tr>
<tr>
<td>Corneal curvature radius (mm)</td>
<td>&lt;0.001</td>
<td>46.0</td>
<td>29.8–62.2</td>
<td>0.11</td>
</tr>
<tr>
<td>BCVA</td>
<td>0.001</td>
<td>−48.4</td>
<td>−76.9 to −20.1</td>
<td>−0.06</td>
</tr>
</tbody>
</table>

BCVA = best-corrected visual acuity; CI = confidence interval.
(Figs 4 and 5, available at http://aaojournal.org). For the refractive error range of \(-1\) toward hyperopia, the relationship between SFCT and refractive error was not statistically significant \((P > 0.05)\), whereas for the myopic refractive error range of more than \(-1\) D, it was highly significantly correlated \((P < 0.001)\). However, if the statistical analysis included only subjects with a hyperopic refractive error of \(>1\) D, SFCT increased significantly by 30 \(\mu m\) for every decrease of 1 mm in axial length. This finding may be associated with the observation of an increased prevalence of a uveal effusion syndrome in markedly hyperopic eyes.\(^{22,23}\)

In univariate analysis, SFCT was significantly associated with higher diastolic blood pressure and higher mean blood pressure, and with the presence of arterial hypertension. This finding agrees with the results of the study by Tan et al.\(^{24}\) who examined 12 healthy volunteers on 2 separate days at 5 fixed, 2-hour time intervals, and found significant correlations between the amplitude of choroidal thickness measurements and systolic blood pressure \((P = 0.03)\), in addition to age \((P = 0.03)\), axial length \((P < 0.001)\), and refractive error \((P < 0.001)\). Usui et al.\(^{25}\) examined 38 eyes of 19 healthy volunteers and reported on a circadian variation in SFCT that was significantly negatively correlated with systolic blood pressure. It was not significantly related to the diastolic blood pressure, ocular perfusion pressure, and intraocular pressure.

### Study Limitations

Potential limitations of our study should be mentioned. First, a major concern in any prevalence study is nonparticipation. The Beijing Eye Study 2011 had a reasonable response rate of 78.8%; however, differences between participants and nonparticipants may have led to a selection artifact. Second, studies by Chakraborty et al.\(^{26}\) Tan et al.\(^{24}\) and Usui et al.\(^{25}\) have shown a circadian (diurnal) rhythm of approximately 20 to 30 \(\mu m\) in choroidal thickness measurements by OCT. The participants of our study underwent the OCT examinations at various times of the day. Because these examinations were performed in a randomized manner with respect to when they were performed, it is unlikely that the reported dependence of the choroidal thickness measurement on the time of the day introduced a bias into our study. Third, choroidal thickness was examined only in the right eye of each study participant, so that inter-eye differences and their associations with inter-eye differences of other parameters could not be assessed. Fourth, as for any new technology, it is necessary to assess the reproducibility of SD-OCT for measurement of the SFCT. In a recent separate study (own data), SFCT measurements showed a repeatability for 10 reexaminations with an intraclass coefficient of 1.00 and a mean coefficient of variation of 0.85% (own data). Fifth, as in any population-based study, our investigation included all eligible and participating subjects from the study region; thus, patients with diseases, such as disorders of the optic nerve and macula, also were included. These diseases may have affected the choroidal thickness, either in relation to thickening or in relation to a thinning.

Future studies may address whether these diseases were associated with abnormalities of choroidal thickness.

In conclusion, an SFCT with a mean of \(254 \pm 107\) \(\mu m\) in elderly subjects with a mean age of 65 years decreased with age (4 \(\mu m\) per year of age) and myopia (15 \(\mu m\) per D of myopia). It was also associated with male gender and the ocular biometric parameters of a deeper anterior chamber and thicker lens. The association between SFCT and BCVA indicates a functional aspect of SFCT.

### References


Footnotes and Financial Disclosures

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