Choroidal and Retinal Thickness in Children With Different Refractive Status Measured by Swept-Source Optical Coherence Tomography

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- PURPOSE: To investigate the choroidal and retinal thickness in myopic, emmetropic, and hyperopic Chinese children by swept-source longer-wavelength optical coherence tomography.
- DESIGN: Cross-sectional study.
- METHODS: Two-hundred and seventy-six schoolchildren aged 7-13 years underwent comprehensive ophthalmic examinations, including cycloplegic refraction, and swept-source optical coherence tomography measurements. The thickness of the choroid, retina, ganglion cell layer, and nerve fiber layer were compared among children of different refractive status. The topographic variation and factors related to the thickness of the choroid and retinal layers were analyzed.
- RESULTS: Compared to emmetropic subjects, those with myopia had a significantly thinner choroid in all regions ($P < .01$), and hyperopic subjects had a thicker choroid in most regions ($P < .05$). The myopic retinas were thinner than those of emmetropic or hyperopic subjects in the superior parafoveal and all 4 perifoveal subfields ($P < .05$), but no other subfields differed significantly among different refractive groups ($P > .05$). The axial length and refractive diopters were independently related to central foveal choroidal thickness ($R^2 = 0.17$, $P < .01$), while age and intraocular pressure were independently associated with central fovea retinal ($R^2 = 0.15$, $P < .01$) and ganglion cell layer thicknesses ($R^2 = 0.10$, $P < .01$) after adjustment for other systematic and ocular factors. Central foveal choroidal and retinal thickness were unrelated in children of different refractive status ($P > .05$).
- CONCLUSIONS: Choroidal thickness, but not retinal thickness, correlated closely with axial length and refractive diopters in Chinese children. Choroid thinning occurs before retina thinning early in myopic progression. (Am J Ophthalmol 2016;168:164–176. © 2016 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).)

Myopia is a global public health concern. It is estimated that one third of the world’s population may be affected by myopia by the year 2020.1 The pathophysiology of myopic progression is not well understood, although both genetic and environmental factors have been implicated in this apparent dysregulation of the emmetropization process.2,3 The choroid, which may facilitate axial growth by modulating the remodeling of the scleral extracellular matrix,4,5 has been implicated as playing an important role in the emmetropization of the eye during development. In animal models of induced myopia and hyperopia, changes in choroidal thickness precede changes in axial length and scleral remodeling.6–10 This implies that choroidal thickness may be an important marker in predicting myopia and myopic progression.

Morphologic changes in the choroid and retina of myopic eyes have been well studied in adults, but they are poorly understood in children.11–16 Few studies have described retinal and choroidal thickness in children with different refractive states,17–19 but none have studied both characteristics in the same cohort.

Swept-source optical coherence tomography (SSOCT) uses a long-wavelength swept light source to probe the amplitude and phase of backscattering of light from tissue. SSOCT has several advantages compared with spectral-domain optical coherence tomography (SDOCT), including higher resolution, greater imaging depth and breadth, and faster scan speed.20 SSOCT has been used for epidemiologic characterization of the fundus, with good repeatability.21

In this cross-sectional study, we investigated several retinal and choroidal characteristics, including the thickness of the retina, choroid, ganglion cell layer, and nerve...
fiber layer, using SSOCT in children aged 7-13 years, to elucidate the anatomic and topographic variations of the choroidal and retinal layers among children of different refractive status.

**METHODS**

- **SETTING AND PARTICIPANTS:** This cross-sectional study was conducted according to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Shanghai General Hospital, Shanghai Jiao Tong University. All of the children understood the study protocol, and written informed consents were provided by their parents or other guardians.

  A primary school located in Shanghai, China, was randomly selected using cluster sampling. All of the students aged 7-13 years were screened for enrollment into the study in January 2015. They were excluded if (1) there was a self-reported history of intraocular surgery or pathology (e.g., retinopathy of prematurity, congenital glaucoma, congenital cataract, etc); (2) the parents were unwilling or unable to give written informed consent; or (3) the participant was unwilling or unable to give verbal informed assent. The research team consisted of 1 ophthalmologist, 5 optometrists, and 2 public health physicians. The investigation site was set up within the school.
RESEARCH METHODS: Participants’ age and sex were recorded according to state-issued identification cards, and height and weight were measured. Body mass index (BMI) was calculated using the formula: weight (kg)/ [height (m)]². Self-reported background information, including the participants’ birth history, birth weight, and refractive status of the parents, were collected by means of a questionnaire.

Each participant underwent comprehensive ophthalmic examinations, including visual acuity, sensorimotor examination, slit-lamp biomicroscopy, tonometry, cycloplegic refraction, and fundus examination. This was followed by ancillary testing, including axial length, corneal curvature measurements, and SSOCT. Visual acuity was measured using a retroilluminated Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a distance of 4 m. Cycloplegia was achieved by administering 1 drop of topical 0.5% proparacaine (Alcaine; Alcon, Fort Worth, Texas, USA) followed by 2 doses of 1% cyclopentolate (Cyclogyl; Alcon) applied 5 minutes apart. After 30 minutes, if the pupils were still reactive to light and the pupil size was estimated to be less than 6 mm, a third drop of cyclopentolate was administered. Corneal curvature and refraction were determined using a desk-mounted auto-refractor (model KR-8900; Topcon, Tokyo, Japan). Spherical equivalent refraction (SER) was used to classify refractive status. Hyperopia was defined as SER ≥ 0.5 diopters (D) and myopia was defined as SER ≤ 0.5 D. Intraocular pressure was measured using a noncontact tonometer (model NT-4000; Nidek Inc, Fremont, California, USA) prior to dilation. Axial length was measured using noncontact optical biometry (IOLMaster, version 5.02; Carl Zeiss Meditec, Oberkochen, Germany).

SSOCT (model DRI OCT-1 Atlantis; Topcon), with a lateral resolution of 10 µm and a depth resolution of 8 µm, was used to measure the thickness of choroid and retinal layers. The machine uses a 1050-nm-wavelength light source and has a scanning speed of 100 000 A-scans per second. The 12-line radial scan pattern with a resolution of 1024 × 12 was used. Each image was an average of 4 overlapped consecutive scans, which covered an area of 12 mm × 9 mm, centered on the fovea.

Built-in software was used to segment layers and construct topographic maps. Choroidal thickness was measured as the distance between the Bruch membrane and the choroid-sclera interface; retinal thickness was measured as the distance between the internal limiting membrane and the interface between photoreceptor outer segments and retinal pigment epithelium. The ganglion cell layer thickness was measured as the distance from the interface between the nerve fiber layer and the ganglion cell layer to the interface between the inner plexiform layer and the inner nuclear layer. The nerve fiber layer thickness was measured as the distance between the internal limiting membrane and the interface between the nerve fiber layer and the ganglion cell layer (Figure 1).

All acquired images were inspected, and if automatic segmentation errors occurred or resulted in measurement artifacts, manual segmentation was performed. The ETDRS grid was applied once the tomography map was obtained, which divided the macula into 3 concentric circles centered on the fovea: the central foveal circle (diameter = 1 mm), the parafoveal circle (diameter = 3 mm), and the perifoveal circle (diameter = 6 mm). The parafoveal and the perifoveal region were further subdivided into superior, inferior, temporal, and nasal subfields (Figure 1). The average thickness of the choroid, retina, ganglion cell layer, and nerve fiber layer of each subfield was calculated with the built-in software.

A single technician performed all the SSOCT image acquisitions between 9 AM and 11 AM, to reduce variability. The machine used a 1050-nm-wavelength light source and has a scanning speed of 100 000 A-scans per second. The 12-line radial scan pattern with a resolution of 1024 × 12 was used. Each image was an average of 4 overlapped consecutive scans, which covered an area of 12 mm × 9 mm, centered on the fovea.

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the impact of diurnal variation. Images with signal strength below 60 were rejected and the test was repeated. On the first 20 participants, the SS-OCT was performed twice in order to assess measurement reproducibility.

- **Statistical Analyses**: SAS (version 8.0; SAS Institute, Cary, North Carolina, USA) was used for all the statistical analyses, and all data were doubly entered independently by 2 research associates and all discrepancies adjudicated. Although data were acquired from both eyes, only the right eye data were used for statistical analysis. The characteristics were presented as the means ± standard deviation for continuous variables that were normally distributed and as rates (proportions) for categorical data.

The data distribution was examined using Kolmogorov-Smirnov test. Comparisons among different measurement spots of the same eye were made using repeated measures analysis of variance (RMANOVA). Stepwise multiple regression analysis was performed to determine the independent factors of central foveal...
choroidal and retinal layers. Linear correlation testing was used to assess the relationship between the thickness of the retina and choroid and SER. Statistical significance was defined as $P < .05$ (2-tailed).

**RESULTS**

- **PATIENT CHARACTERISTICS:** Among the 299 participants enrolled in the study, 9 were excluded owing to poor cooperation, and another 14 were excluded because of poor SS-OCT images. Therefore, of enrolled participants, a final total of 276 (92.31%) were included in the study. There was no significant difference in sex or age between the included and excluded participants (all $P > .05$).

  The mean age of the participants was $9.69 \pm 1.17$ years (range: 7-13 years). Six children had best-corrected vision less than 20/25 equivalence, attributed to amblyopia; 18 children had best-corrected vision of 20/25 equivalence; and all remaining children had a best-corrected visual acuity of 20/20 equivalence. Axial lengths ranged between...
20.0 mm and 26.6 mm. The SER ranged between −9.00 D and +5.25 D, with a mean of −0.15 ± 1.60 D. Eighty-six of the participants had myopia (31.2%), and 99 had hyperopia (35.9%). The mean age and mean BMI of hyperopic participants were lower than those of emmetropic and myopic subjects (P < .01). More boys were emmetropic, while more girls were hyperopic or myopic. Compared with emmetropic subjects, those with myopia had a longer axial length, and those with hyperopia had a shorter axial length (Table 1).

The choroidal thickness measurement with SSOCT was highly reproducible in each subfield, with a test-retest correlation coefficient of 0.97-0.99 (n = 20). In the central foveal location, average choroidal thickness was thickest in hyperopic subjects, followed by that in emmetropic and myopic subjects. No statistical difference was observed in the central foveal thickness of the retina, ganglion cell layer, or nerve fiber layer between the different refractive groups (Table 2). There was no significant difference between the sexes in the central foveal choroidal thickness (261 ±

FIGURE 3. Whole retinal thickness in children of different refractive status.
65 μm vs 269 ± 68 μm, \( P = .37 \)) and central foveal retinal thickness (236 ± 25 μm vs 233 ± 27 μm, \( P = .13 \)). Age was negatively associated with central foveal retinal thickness (\( r = -0.23, \ P < .01 \)), ganglion cell layer thickness (\( r = -0.28, \ P < .01 \)), and nerve fiber layer thickness (\( r = -0.17, \ P < .01 \)), but there was no significant association between age and central foveal choroidal thickness (\( P = .34 \)).

- **TOPOGRAPHIC VARIATION OF CHOROID AND RETINAL LAYERS IN PARTICIPANTS OF DIFFERENT REFRACTIVE STATUS:** The thickness of the choroid increased from the nasal quadrant to the temporal quadrant, horizontally, while vertically the choroid in the parafoveal subfields was thicker than that in the perifoveal subfields (Figure 2). The total retinal thickness and the ganglion cell layer thickness of the parafoveal regions were highest, followed by those of the perifoveal areas, while those of the central fovea were the lowest (Figures 3 and 4). However, nerve fiber layer thickness increased with the distance to the fovea (Figure 5). All of the retinal layers were thicker in the nasal quadrant and thinner in the temporal quadrant.

Table 2 shows the comparison of topographic variations among participants in the different refractive groups.
Compared to emmetropic participants, myopic subjects had significantly thinner choroid in all the regions. The retinal thickness of participants with myopia were lower than in those with emmetropia in the superior parafoveal and in both the superior and inferior perifoveal subfields, while their ganglion cell layer thickness was lower in the perifoveal subfields. However, there was no difference in the nerve fiber layer thickness between myopic and emmetropic subjects. On the other hand, the choroid of hyperopic subjects was significantly thicker than that of emmetropic subjects in most regions, except for the temporal and inferior quadrants. Although no significant difference was observed in the retinal thickness between emmetropic and hyperopic participants, the inferior parafoveal ganglion cell layer thickness and the inferior perifoveal subfield nerve fiber layer thickness was lower in hyperopic participants.

**FACTORS ASSOCIATED WITH RETINAL AND CHOROIDAL THICKNESS:** Among systematic and ocular factors included in the stepwise multiple regression analysis, such as age, sex, BMI, refractive error, axial length,
intraocular pressure, history of preterm birth, birth weight, and the refractive status of parents, only axial length and SER were independently related to central foveal choroidal thickness. The correlation $R^2$ of the regression model was 0.17 ($P < .01$). According to the model, every 1-mm increase in axial length is associated with a 14-mm decrease in central foveal choroidal thickness, and each diopter toward myopia is associated with a 10-mm decrease in central foveal choroidal thickness. On the other hand, age and intraocular pressure were independently associated with the central foveal thickness of retina and ganglion cell layer. The thickness of the retina and ganglion cell layer decreased with age, and increased with the intraocular pressure, while nerve fiber layer thickness only decreased with age. The correlation $R^2$ of the regression model and its significance is listed in Table 3.

Linear correlation testing revealed a close correlation between SER and choroidal thickness in all of the regions, including the central fovea ($R^2 = 0.11, P < .01$), parafoveal circle ($R^2 = 0.11, P < .01$), and perifoveal circle ($R^2 = 0.11, P < .01$). Although SER was not associated with central foveal or parafoveal retinal thickness, there was a positive correlation between SER and retinal thickness in the perifoveal regions ($R^2 = 0.09, P < .01$, Figure 6). There was no statistical relationship between central foveal retinal and choroidal thickness in myopic ($P = .63$), emmetropic ($P = .66$), or hyperopic participants ($P = .89$).

**DISCUSSION**

Our results indicated that myopic children had a thinner choroid in most areas and thinner retina in the superior quadrants and inferior perifoveal subfields. Central foveal choroidal thickness was closely correlated with axial length and refractive status, while central foveal retinal thickness decreased with age and increased with intraocular pressure. To the authors’ knowledge, this study is the first to investigate the SS-OCT findings of retinal and choroidal thickness together in pediatric groups of different refractive status.

Compared to a prior study of older, mostly white children, the choroidal thickness of our participants was much lower. The mean central foveal choroidal thickness of myopic, emmetropic, and hyperopic children in our study were 227 mm, 253 mm, and 271 mm, respectively, while a study of 104 Australian children (10-15 years old) reported a mean subfoveal choroidal thickness of 304 mm in myopic subjects and 360 mm in nonmyopic subjects.22 This discrepancy might be due to population differences, and is consistent with a prior report of Asians with myopia having thinner choroids than whites, Hispanics, and African Americans.23 The choroidal thickness of temporal areas is significantly thicker than that of the nasal areas, which is consistent with prior studies.24–26

Our findings indicated a close correlation between SER and choroidal thickness, and the central foveal choroidal thickness decreased with AL and SER, independently. This result was consistent with previous reports in both adult and pediatric patients.5,17,22,24,27–33 No statistical correlation between central foveal choroidal thickness and retinal thickness was observed, which is consistent with a previous retrospective adult study.34

The mean central foveal retinal thickness of the myopic participants in our study was 234 μm, which is very close to the 240 μm mean retinal thickness reported in a former study that was also conducted in Chinese children.35 The topography findings of retinal layers in our study is

### Table 3. Systematic/Ocular Independent Variables Associated With Central Foveal Choroid and Retinal Layers

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>Variable’s $P$ Value</th>
<th>Equation’s $P$ Value</th>
<th>$R^2$</th>
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</thead>
<tbody>
<tr>
<td><strong>Choroid thickness</strong></td>
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<tr>
<td>AL</td>
<td>-13.86</td>
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<td>SER</td>
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<td>.02</td>
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<td><strong>Retina thickness</strong></td>
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<tr>
<td>Age</td>
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<td>-0.30</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
<td>0.1464</td>
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<tr>
<td>IOP</td>
<td>1.79</td>
<td>0.20</td>
<td>&lt;.01</td>
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<tr>
<td><strong>Ganglion cell</strong></td>
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<tr>
<td>layer thickness</td>
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<tr>
<td>Age</td>
<td>-2.96</td>
<td>-0.25</td>
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<td>&lt;.01</td>
<td>0.1011</td>
</tr>
<tr>
<td>IOP</td>
<td>0.68</td>
<td>0.15</td>
<td>.01</td>
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<tr>
<td><strong>Nerve fiber</strong></td>
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<tr>
<td>layer thickness</td>
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<tr>
<td>Age</td>
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<td>0.46</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
<td>0.0308</td>
</tr>
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</table>

$AL =$ axial length; $IOP = $ intraocular pressure; $SER = $ spherical equivalent refraction.
FIGURE 6. Linear correlation between spherical equivalent refraction and choroidal/retinal thickness in the central fovea, parafoveal circle, and perifoveal circle.
consistent with those of emmetropic and myopic adults in previous studies.\textsuperscript{3,6,26,36,37}

Prior studies yielded conflicting data on retinal thickness in myopic subjects. While some studies have shown retinal thickness to be significantly decreased in myopic subjects,\textsuperscript{38,39} other studies found it to be thicker in the central fovea but thinner in the parafoveal and perifoveal regions.\textsuperscript{12,35,40,41} Moreover, some studies found no relationship between retinal thickness and SER, age, or axial lengths.\textsuperscript{3,7,37,38} In our cohort, compared to emmetropic subjects, thinner retinal thickness was observed in myopic subjects in the superior parafoveal and perifoveal subfields and in the inferior perifoveal subfield. We found no relationship between subfoveal/parafoveal retinal thickness and either SER or AL, although subfoveal retinal thickness was seen to decrease with age and increase with IOP, which is consistent with previous studies performed in adult populations.\textsuperscript{3,7,37,38,43} The significance of these observations is unclear.

The results of previous studies on factors influencing the thickness of the ganglion cell layer and nerve fiber layer have been conflicting. While some suggested that the thickness of the ganglion cell layer and peripapillary nerve fiber layer is correlated with SER and AL in adults,\textsuperscript{44–48} others did not observe this relationship.\textsuperscript{49} In our cohort, ganglion cell layer thickness of myopic participants was lower in the perifoveal subfields in all 4 quadrants than in emmetropic or hyperopic participants, but there was no difference in nerve fiber layer thickness.

In summary, our data suggest that in Chinese children, the thickness of the subfoveal choroid, but not the retina, correlates closely with SER and AL. The perifoveal retinal and ganglion cell layer thickness is less in myopic subjects than in emmetropic or hyperopic subjects, while there was no difference in nerve fiber layer thickness among the different refractive groups. In the context of previous studies suggesting that choroidal changes precede scleral changes in induced ametropia, we propose that, during the early stage of myopia progression, choroid thinning occurs first, which is then followed by retinal thinning in the perifoveal area, which progresses centripetally. The ganglion cell layer thinning occurs either concurrently with or sequential to retinal thinning, while the nerve fiber layer is not affected in the early stages of myopic progression.

Our study has several limitations. First, it has been suggested that the choroid thickness measured by SS-OCT is greater than that measured with non–swept source OCT instruments.\textsuperscript{51} Thus, the choroidal thickness data of our study should not be directly compared with studies using other OCT instruments. Second, our findings may only be applicable to the Chinese pediatric population, owing to strong population-dependent differences in choroidal thickness. Third, we cannot completely exclude the possibility that transverse magnification introduced systematic error in the measurements in our cohort with a wide range of axial lengths, although it is unlikely given that AL and SER were associated with the thickness of the subfoveal choroid, but not the retina, which serves as an internal control.

In future, we will repeat similar measurements in the same cohort in order to obtain longitudinal data. Furthermore, re-examination of the emmetropic and hyperopic groups, stratified by baseline choroidal thickness, may help elucidate the role of choroidal thickness as a marker for myopic progression.

In conclusion, myopic Chinese children have a thinner choroid in all areas, and thinner retina in the superior and inferior perifoveal regions, than do their emmetropic and hyperopic counterparts. Central foveal choroidal thickness was closely correlated with axial length and refractive diopters, while central foveal retinal thickness was related to age and intraocular pressure. There was no statistical relationship between central foveal choroidal and retinal thickness.

**REFERENCES**


39. Wu PC, Chen YJ, Chen CH, et al. Assessment of macular retinal thickness and volume in normal eyes and highly