# Longitudinal Changes in Choroidal Thickness Varied With Refractive Progression in Myopic and Non-Myopic Children: A Two-Year Cohort Study

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**Purpose.** To evaluate the longitudinal changes in subfoveal choroidal thickness (SFCT) in children with different refractive status.

**Methods.** A total of 2290 children 3 to 14 years old who attended the first year of kindergarten (G0), first year of primary school (G1), fourth year of primary school (G4), or first year of junior high school (G7) in Guangzhou, China, were recruited and followed up for 2 years. All participants received cycloplegic autorefraction, axial length measurement and SFCT measurement using a CIRRUS HD-OCT device. Children were divided into groups of persistent non-myopia (PNM), persistent myopia (PM), or newly developed myopia (NDM). Children in the PNM and PM groups were further divided into subgroups of stable refraction (absolute mean annual spherical equivalent refraction [SER] change $< 0.5$ D) and refractive progression (absolute mean annual SER change $\geq 0.5$ D).

**Results.** The mean $\pm$ SD ages for the G1 to G7 cohorts were $3.89 \pm 0.30$, $6.79 \pm 0.47$, $9.71 \pm 0.34$, and $12.54 \pm 0.38$, years, respectively. SFCT consistently decreased in the NDM group across the G1 to G7 cohorts (all $P < 0.001$) and exhibited variability across different age cohorts in the PNM and PM groups. Further subgroup analysis revealed significant thickening of SFCT in the PNM-stable group among the G0, G1, and G7 cohorts (all $P < 0.05$), whereas it remained stable among all cohorts in the PM-stable group (all $P > 0.05$). Conversely, SFCT exhibited thinning in the G4 and G7 cohorts in the PM-progressive group (both $P < 0.01$) and for the entire cohort of children in the PNM-progressive group ($P = 0.012$).

**Conclusions.** SFCT increased in nonmyopic children with stable refraction, remained stable in myopic children maintained stable refraction, and decreased in those with refractive progression, whether they were myopic or not.

Keywords: choroidal thickness, OCT, refractive errors, childhood

The recent surging prevalence of myopia globally has raised significant concerns, particularly in Asian countries.[1–3] Although the physiologic mechanisms of myopia remain unclear, increasing attention has been focused on the role of the choroid in the processes of emmetropization and myopization.[4] Located in the middle layer of the eye wall, the choroid is sensitive to retinal defocus signals and thins in response to hyperopic defocus, which is considered a risk factor for myopia.[5–7] Furthermore, the choroid may also play a role in the modulation of scleral growth by synthesizing signaling molecules or regulating blood perfusion.[4,8] Choroidal thickness (ChT) is closely related to eye length and typically decreases with axial elongation. Generally, non-myopic children have thicker choroids than their myopic counterparts.[9,10]

Another key factor influencing ChT is age. Previous animal studies on the natural rhythm of choroidal growth have suggested that the choroid thickens from infancy to maturity in primates reared with unrestricted vision.[11,12] However, the process of choroidal change in human eyes remains uncertain. Existing studies have yielded conflicting results. Cross-sectional observations on ChT typically show thickening with age among children from Western countries[10,13] and thinning with age among Asian children.[14,15] This inconsistency extends to longitudinal observations when considering myopia. ChT was reported to

increase,[9,16] remain unchanged,[17] or decrease[18] in nonmyopic eyes and to increase slightly[9] or decrease[16,19] in myopic eyes during follow-up. Given that age and myopia both affect ChT in children, the selection of age range and myopic proportion significantly influences the study of intrinsic choroidal changes. Consequently, the purposes of this study were to investigate the longitudinal changes in ChT among children with varying degrees of myopia progression.

## Methods

### Study Population

This research was conducted as part of the Zengcheng School Myopia Study (ZOOM).[20,21] Briefly, 7050 children in four different grades (first-year kindergarten, grade 0 [G0]; first-year primary school, grade 1 [G1]; fourth-year primary school, grade 4 [G4]; and first-year junior high school, grade 7 [G7]) were recruited from Guangzhou, China. Ocular examinations were performed on all participating children. Due to time constraints in the mass screening programs implemented within schools, the evaluation of subfoveal choroidal thickness (SFCT) was conducted on 3554 children from these four grades using stratification sampling. Written informed consent was obtained from all children and their parents or guardians before each visit. This study was conducted according to the tenets of the Declaration of Helsinki and has been registered on clinicaltrial.gov (NCT03589937). This study was approved by the Institutional Review Board of Zhongshan Ophthalmic Center, Guangzhou, China (2018KYPJ079).

Among the 3554 participants involved in the SFCT measurements within the ZOOM study, children exhibiting the following conditions were excluded from the current research: (1) absence of baseline or follow-up ocular assessments; (2) best-corrected visual acuity (BCVA) below 20/40 for children ages 3 to 5 years and below 20/25 for those 6 years and older; (3) history of systemic abnormalities or ocular diseases (e.g., amblyopia, strabismus, cataract, glaucoma, retinal disease); (4) prior exposure to atropine eye drops, orthokeratology treatment, myopia control spectacles, or multifocal soft contact lenses during both baseline and follow-up; (5) poor choroidal imaging quality; or (6) inadequate follow-up optical coherence tomography (OCT) data. Basic information on sex, age, and grade was recorded. Ocular examinations and OCT measurements were primarily conducted in the months of October and November, with a few instances in December, both during the baseline assessment in 2018 and throughout the subsequent follow-ups in 2019 and 2020. All OCT data were consistently collected between 10 AM and 4 PM. At each follow-up visit, all participants underwent examination using the same equipment and protocol as in the baseline measurement.

### Ocular Examinations

Ocular examinations including BCVA, refractive error, slit-lamp examination, and axial length (AL) measurements were performed. The BCVA was measured at a distance of 5 meters using an Early Treatment Diabetic Retinopathy Study chart with optimal correction. AL was measured using swept-source OCT-based biometry (ZEISS IOLMaster 700; Carl Zeiss Meditec, Oberkochen, Germany) before cycloplegia. Five readings with the lowest standard deviation (SD), not exceeding 0.1 mm, were averaged and recorded for each eye. Three drops of 1% cyclopentolate hydrochloride (Alcon, Fort Worth, TX, USA) were used to induce cycloplegia, with one drop being administered at 0, 5, and 25 minutes.[22] Successful cycloplegia was achieved when the pupil diameter was at least 6 mm and the pupillary light reflex was absent. Otherwise, an additional drop of cyclopentolate was administered and cycloplegic status was re-examined 20 minutes later. Cycloplegic autorefraction was examined using a close-field autorefractor with measurement accuracy of 0.12 diopter (D) for power and 1° for axis (KR-8800; Topcon, Tokyo, Japan).

### Measurement of Choroidal Thickness

The OCT analysis of SFCT was conducted on the right eye after cycloplegia using a CIRRUS HD-OCT device (Carl Zeiss Meditec) with a transverse resolution of 15 µm and an axial resolution of 5 µm. Both a 512 × 128 macular cube protocol and high-definition (HD) radial macular scan were performed for all participants. The HD radial macular scan, comprised of 12 radial lines separated by 15° and covering a 6-mm-diameter circular area centered on the fovea, was utilized for choroidal imaging, along with an enhanced depth imaging modality (Fig. 1 *Left*). Each radial line scan included 1024 A-scans and was averaged by eight B-scans. The automatic eye-tracking feature was employed during OCT scanning, and the follow-up function was used for all participants at every follow-up scan. The fovea was defined as the thinnest central point of the macular. The SFCT was defined as the perpendicular distance between the Bruch membrane and the choroid–scleral interface at the fovea (Fig. 1 *Right*). The horizontal section of the HD radial macular scan was chosen for further manual measurement of SFCT using the built-in linear measurement tool. Each image was evaluated by two independent technicians, and their measurements of SFCT were averaged and included in the final analysis. Images with signal strengths of less than 7, motion artifacts, foveal misalignment, or unclear choroidoscleral boundaries were excluded. A total of 50 images were randomly selected to test the interrater reliability and within-rater repeatability of SFCT measurements before formal measuring. The mean interrater difference was −1.68 µm (95% confidence interval [CI], −7.59 to 4.23), with 96% of the measurement points located inside the 95% limits of agreement (LoA), indicating good interrater reliability. The mean within-rater difference was −0.68 µm (95% CI, −8.16 to 6.80), with 98% of measurement points falling within the 95% LoA, indicating strong within-rater reliability (Supplementary Figs. S1, S2).

### Statistical Analysis

Only data from the right eyes were analyzed. The longitudinal changes in the acquired parameters during the 2-year follow-up were calculated as annual average changes. Myopia was defined as a cycloplegic spherical equivalent refraction (SER) $\leq -0.50$ D. Children were divided into three different refractive status groups: persistent nonmyopia (PNM; SER $> -0.5$ D at baseline and during follow-up), persistent myopia (PM; SER $\leq -0.5$ D at baseline and during follow-up), or newly developed myopia (NDM; SER $> -0.5$ D at baseline and $\leq -0.5$ D during follow-up). Given that children in the PNM or PM groups still exhibited different rates of SER progression, they were further catego-

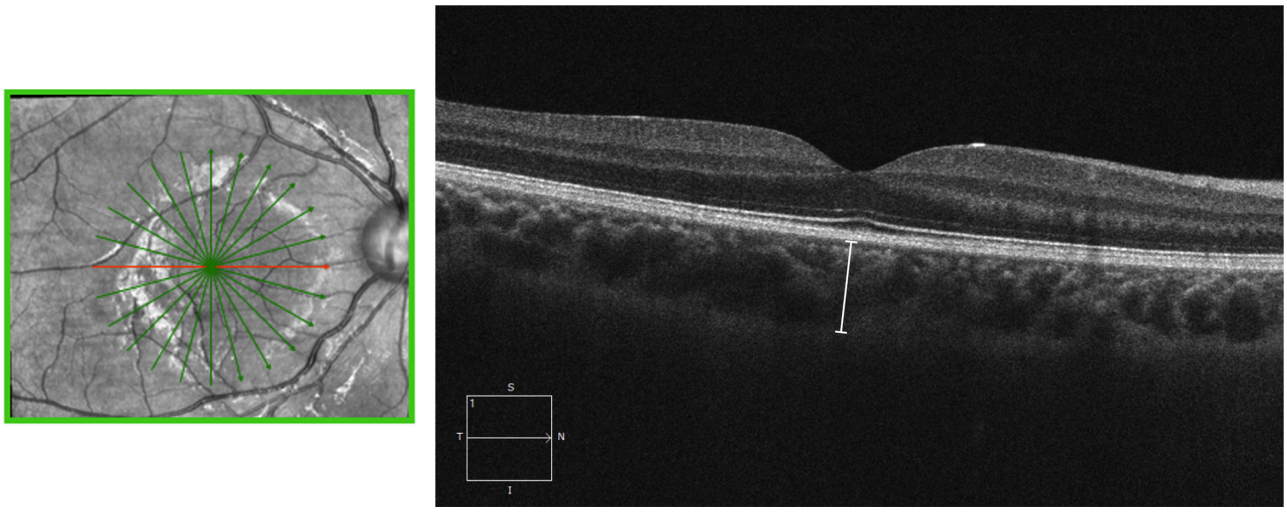


**Figure 1.** (*Left*) An example of the HD radial macular scan using the CIRRUS HD-OCT device. (*Right*) Illustration of choroidal thickness measurement at the fovea; a perpendicular line was drawn from the posterior edge of the retinal pigment epithelium to the choroid–sclera junction using the built-in caliper tool.

rized into stable (absolute mean annual SER change < 0.5 D) or progressive (absolute mean annual SER change ≥ 0.5 D) subgroups.

Continuous data are presented as mean ± SD or as median (interquartile range [IQR]), and their normality was tested using the Kolmogorov–Smirnov test. Categorical data were presented as absolute and relative frequencies. The baseline distributions among the three refractive status groups were compared by the $\chi^2$ test, ANOVA, or Kruskal–Wallis test. Tests for linear trend were performed for annual changes in SER, AL, and SFCT among the three refractive status groups. Student's *t*-test or Mann–Whitney *U* test was used to compare the differences between the stable and progressive groups. Additionally, differences between baseline and follow-up data were compared using either the paired *t*-test or Wilcoxon signed-rank test. The locally weighted scatterplot smoothing (LOWESS) plots were constructed to show the changes in SFCT with AL growth in both the PNM and PM groups. Linear regression models were fitted to assess potential factors associated with SFCT in different refractive status groups. The LOWESS regression was performed using RStudio 1.3.1093 (R Foundation for Statistical Computing, Vienna, Austria). Statistical analysis was performed using SPSS Statistics 24.0 (IBM, Chicago, IL, USA). A two-sided *P* value < 0.05 was considered statistically significant. The *P* values for multiple comparisons were adjusted using the Bonferroni adjustment method.

## Results

Of the 3554 children involved in baseline OCT measurements, 20 were excluded due to poor BCVA; 836 were excluded for missing follow-up OCT data or initiation of interventions such as atropine, orthokeratology, myopia control spectacles, or multifocal soft contact lenses during the follow-up period; 336 were excluded due to poor signal strength in OCT imaging or unrecognized choroidoscleral boundaries; and 72 were excluded due to missing baseline or follow-up ocular parameters. Finally, data from 2290 children were included in the final analysis. The distribution of age, gender, and SER was comparable among the four age groups between the final sample and the baseline sample (Supplementary Table S1). Baseline and follow-up characteristics of children excluded due to image quality issues are outlined in Supplementary Table S2. Notably, no significant differences in SER or AL were found between the excluded and final samples in the G0 and G1 cohorts. However, children excluded in the G4 ($n = 93$) and G7 ($n = 81$) cohorts exhibited more hyperopia in SER: G4 baseline, 0.46 ± 1.36 D versus 0.50 D (IQR, −0.50 to 0.88; $P = 0.027$); G4 follow-up, −0.27 ± 1.69 D versus −0.63 D (IQR, −2.25 to 0.38; $P = 0.001$); G7 baseline: −0.13 D (IQR, −1.57 to 0.50) versus −0.75 D (IQR, −2.38 to 0.38; $P = 0.028$); G7 follow-up: −1.21 ± 1.98 D versus −1.79 ± 2.12 D ($P = 0.038$). Furthermore, excluded children in the G4 cohort had a significantly shorter AL (baseline: 23.27 ± 0.98 vs. 23.53 ± 0.80 mm, $P = 0.019$; follow-up: 23.76 ± 1.12 vs. 24.13 ± 0.90 mm, $P = 0.004$).

The baseline characteristics of the study participants are shown in Table 1. The mean ± SD ages of children were 3.89 ± 0.30 years in the G0 cohort, 6.79 ± 0.47 years in the G1 cohort, 9.71 ± 0.34 years in the G4 cohort, and 12.54 ± 0.38 years in the G7 cohort. The number of children classified into the PNM, PM, or NDM groups was 1543, 476, and 271, respectively. Within each refractive group, sex distribution was comparable across different age cohorts (all $P > 0.05$, data not tabulated). Additionally, there was a decreasing trend in SER and an increasing trend in AL with age across different age cohorts (all $P < 0.05$, data not tabulated). In terms of variations among subgroups, children in the PNM group had the thickest SFCT, followed by the NDM and PM groups in G4 and G7 (both $P < 0.001$). No significant differences were observed for SFCT distribution among the three groups in G1 ($P = 0.253$). The distributions of SER and AL were significantly different among the PNM, NDM, and PM groups in G1, G4, and G7 (all $P < 0.001$).

The mean annual changes of SER, AL, and SFCT for children with PNM, PM, or NDM in each cohort are shown in Table 2. Among the G1 to G7 groups, children in the NDM group demonstrated the fastest progression rate in both SER

**Table 1.** Baseline Characteristics of the Study Participants

| | Mean ± SD | | | | |
|---|---|---|---|---|---|
| | **Total ($n$ = 2290)** | **PNM ($n$ = 1543)** | **PM ($n$ = 476)** | **NDM ($n$ = 271)** | ***P*** |
| G0 | | | | | |
| *n* | 140 | 138 | — | 2 | — |
| Male, *n* (%) | 72 (51.06) | 71 (51.45) | — | 0 | — |
| Age (y) | 3.89 ± 0.30 | 3.89 ± 0.30 | — | 3.94 ± 0.21 | — |
| SER (D)* | 1.44 ± 0.59 | 1.47 ± 0.54 | — | 0.63 ± 0.53 | — |
| AL (mm) | 22.07 ± 0.61 | 22.07 ± 0.61 | — | 21.66 ± 0.74 | — |
| SFCT (µm) | 363.09 ± 57.20 | 363.43 ± 57.54 | — | 365.00 ± 44.55 | — |
| G1 | | | | | |
| *n* | 1043 | 972 | 8 | 63 | — |
| Male, *n* (%) | 583 (55.84) | 546 (56.17) | 4 (50.00) | 32 (50.79) | 0.685† |
| Age (y) | 6.79 ± 0.47 | 6.79 ± 0.42 | 6.95 ± 0.27 | 6.73 ± 0.93 | 0.407‡ |
| SER (D)* | 1.24 ± 0.66 | 1.32 ± 0.59 | −1.11 ± 0.63 | 0.37 ± 0.38 | <0.001‡ |
| AL (mm) | 22.62 ± 0.67 | 22.59 ± 0.67 | 23.19 ± 0.70 | 22.94 ± 0.58 | <0.001‡ |
| SFCT (µm) | 346.18 ± 59.38 | 347.02 ± 59.07 | 336.38 ± 65.31 | 334.74 ± 63.50 | 0.253‡ |
| G4 | | | | | |
| *n* | 517 | 248 | 139 | 130 | — |
| Male, *n* (%) | 279 (53.97) | 145 (58.47) | 75 (53.96) | 59 (45.38) | 0.053† |
| Age (y) | 9.71 ± 0.34 | 9.68 ± 0.36 | 9.72 ± 0.32 | 9.75 ± 0.29 | 0.146‡ |
| SER (D)* | 0.50 (−0.50, 0.88) | 0.93 ± 0.50 | −1.76 ± 1.02 | 0.26 ± 0.37 | <0.001§ |
| AL (mm) | 23.53 ± 0.80 | 23.22 ± 0.69 | 24.19 ± 0.72 | 23.40 ± 0.66 | <0.001‡ |
| SFCT (µm) | 322.15 ± 58.33 | 335.54 ± 54.72 | 293.26 ± 55.78 | 327.57 ± 57.19 | <0.001‡ |
| G7 | | | | | |
| *n* | 590 | 185 | 329 | 76 | — |
| Male, *n* (%) | 310 (52.54) | 117 (63.24) | 149 (45.29) | 44 (57.89) | <0.001† |
| Age (y) | 12.54 ± 0.38 | 12.50 ± 0.40 | 12.56 ± 0.38 | 12.54 ± 0.37 | 0.230‡ |
| SER (D)* | −0.75 (−2.38, 0.38) | 0.79 ± 0.85 | −2.37 ± 1.44 | 0.00 (−0.25, 0.13) | <0.001§ |
| AL (mm) | 24.12 ± 1.02 | 23.37 ± 0.70 | 24.63 ± 0.95 | 23.73 ± 0.54 | <0.001‡ |
| SFCT (µm) | 309.95 ± 68.37 | 352.37 ± 63.12 | 284.39 ± 61.22 | 317.44 ± 56.46 | <0.001‡ |

* SER is represented as either the mean ± SD or median (IQR).
† $\chi^2$ test.
‡ One-way ANOVA test.
§ Kruskal–Wallis test.

and AL changes, followed by those in the PM and PNM groups (all $P < 0.001$). With regard to the changes in SFCT, children in the PNM group exhibited close-to-significant SFCT thickening in G0 ($P = 0.055$) and significant thickening in G1 and G7 (both $P < 0.001$). Children in the NDM group, in contrast, had consistent SFCT thinning from G1 to G7 (all $P < 0.001$). SFCT thinned in G4 ($P < 0.001$) and remained unchanged in G1 and G7 (both $P > 0.05$) in the PM group. AL growth was consistently negatively correlated with SFCT changes across age groups and refractive groups (all $P < 0.05$).

Table 3 and Figure 2 show the mean annual changes in AL, SER, and SFCT for children with stable or progressive SER. AL increased and SER myopic shifted in all four subgroups, with the PM-progressive group having the largest magnitude, followed by the PNM-progressive, PM-stable, and PNM-stable groups ($P < 0.001$). The increase in AL was consistently larger in the G4 cohort across all refractive groups compared with children in G7 (all $P < 0.05$, data not tabulated). For SFCT, significant thickening was observed in the PNM-stable group in the G0, G1, and G7 cohorts (all $P < 0.05$), but not in the G4 cohort ($P = 0.407$). SFCT changes were comparable between boys and girls from G0 to G4, except in G7, where a larger thickening was observed in boys ($P = 0.017$, data not tabulated). In the PM-stable group, SFCT variations were not significant from G1 to G7 (all $P > 0.05$). The average rate of SFCT thickening was significantly faster in the PNM-stable group, measuring 4.54 ± 19.07 µm/y, compared to 1.22 ± 16.08 µm/y in the PM-stable group among all children overall ($P = 0.006$). The two progressive groups showed a close-to-significant decrease in SFCT in G4 in PNM children and a significant decrease in G4 and G7 in PM children. Additionally, the decrease of SFCT was larger in PM-progressive girls in the G7 cohort ($P = 0.024$, data not tabulated). The rate of SFCT thinning was comparable between two progressive groups among children overall (−6.59 ± 23.17 vs. −6.92 ± 16.41 µm/y; $P = 0.907$), as well as within the G4 cohort (−8.86 ± 23.07 vs. −9.53 ± 14.65 µm/y; $P = 0.884$).

Annual AL growth was negatively correlated with SFCT thickening among the four groups of children with different rates of SER progression (all $P < 0.05$) (Supplementary Tables S3, S4). Baseline AL was significantly associated with annual SFCT change in the PNM-stable and PNM-progressive groups (both $P < 0.05$), but not in two subgroups of PM children (both $P > 0.05$). The increase in SFCT was most prominent in PNM-stable children of the G7 cohort ($P < 0.001$). Furthermore, compared to children in the G4 cohort, PM-progressive children in G7 also exhibited a lesser decrease in SFCT ($P = 0.012$). Sex was not a significant impactor on annual SFCT change, except in the PNM-progressive group ($P = 0.048$).

Figure 3 shows the mean annual changes in SFCT with regard to axial elongation. In PNM children, SFCT thick-

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**Table 2.** Baseline and Follow-Up Characteristics of SER, AL, and SFCT in Three Refractive Groups

| | PNM | | | | PM | | | | NDM | | | | *P* Between Groups* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline, Mean ± SD | Follow-Up, Mean ± SD | Annual Change, Mean ± SD | *P*† | Baseline, Mean ± SD | Follow-Up, Mean ± SD | Annual Change, Mean ± SD | *P*† | Baseline, Mean ± SD | Follow-Up, Mean ± SD | Annual Change, Mean ± SD | *P*† | Annual Change, Mean ± SD |
| G0 | | | | | | | | | | | | | |
| *n* | 138 | 138 | 138 | — | — | — | — | — | 2 | 2 | 2 | — | — |
| SER (D)‡ | 1.47 ± 0.54 | 1.43 ± 0.54 | −0.02 ± 0.18 | 0.052 | — | — | — | — | 0.63 ± 0.53 | −1.25 ± 0.35 | −0.94 ± 0.09 | — | — |
| AL (mm) | 22.07 ± 0.61 | 22.46 ± 0.61 | 0.19 ± 0.10 | <0.001 | — | — | — | — | 21.66 ± 0.74 | 22.62 ± 0.73 | 0.48 ± 0.01 | — | — |
| SFCT (μm) | 363.43 ± 57.54 | 369.86 ± 56.47 | 3.22 ± 19.48 | 0.055 | — | — | — | — | 365.00 ± 44.55 | 358.00 ± 39.60 | −3.50 ± 2.47 | — | — |
| G1 | | | | | | | | | | | | | |
| *n* | 972 | 972 | 972 | — | 8 | 8 | 8 | — | 63 | 63 | 63 | — | — |
| SER (D)‡ | 1.32 ± 0.59 | 1.05 ± 0.61 | −0.13 ± 0.19 | <0.001 | −1.11 ± 0.63 | −2.33 ± 1.12 | −0.60 ± 0.50 | 0.012 | 0.37 ± 0.38 | −1.00 (−1.63, −0.63) | −0.79 ± 0.31 | <0.001 | <0.001 |
| AL (mm) | 22.59 ± 0.67 | 22.87 ± 0.67 | 0.14 ± 0.12 | <0.001 | 23.19 ± 0.70 | 23.91 ± 0.89 | 0.35 ± 0.19 | 0.005 | 22.94 ± 0.58 | 23.78 ± 0.65 | 0.42 ± 0.15 | <0.001 | <0.001 |
| SFCT (μm) | 347.02 ± 59.07 | 354.95 ± 64.53 | 3.97 ± 18.17 | <0.001 | 336.38 ± 65.31 | 340.44 ± 94.24 | 2.06 ± 25.18 | 0.826 | 334.74 ± 63.50 | 303.41 ± 67.80 | −15.66 ± 21.82 | <0.001 | <0.001 |
| G4 | | | | | | | | | | | | | |
| *n* | 248 | 248 | 248 | — | 139 | 139 | 139 | — | 130 | 130 | 130 | — | — |
| SER (D)‡ | 0.93 ± 0.50 | 0.48 ± 0.56 | −0.22 ± 0.22 | <0.001 | −1.76 ± 1.02 | −3.26 ± 1.09 | −0.75 ± 0.32 | <0.001 | 0.26 ± 0.37 | −1.36 ± 0.64 | −0.81 ± 0.31 | <0.001 | <0.001 |
| AL (mm) | 23.22 ± 0.69 | 23.56 ± 0.69 | 0.16 ± 0.14 | <0.001 | 24.19 ± 0.72 | 24.96 ± 0.72 | 0.39 ± 0.14 | <0.001 | 23.40 ± 0.66 | 24.25 ± 0.69 | 0.43 ± 0.13 | <0.001 | <0.001 |
| SFCT (μm) | 335.54 ± 54.72 | 335.68 ± 66.23 | 0.07 ± 21.91 | 0.958 | 293.26 ± 55.78 | 276.31 ± 52.87 | −8.47 ± 14.82 | <0.001 | 327.57 ± 57.19 | 300.67 ± 57.01 | −13.45 ± 20.98 | <0.001 | <0.001 |
| G7 | | | | | | | | | | | | | |
| *n* | 185 | 185 | 185 | — | 329 | 329 | 329 | — | 76 | 76 | 76 | — | — |
| SER (D)‡ | 0.79 ± 0.85 | 0.55 ± 0.92 | −0.11 ± 0.18 | <0.001 | −2.37 ± 1.44 | −3.23 ± 1.53 | −0.43 ± 0.27 | <0.001 | 0.00 (−0.25, 0.13) | −1.13 (−1.50, −0.75) | −0.56 (−0.75, −0.38) | <0.001 | <0.001 |
| AL (mm) | 23.37 ± 0.70 | 23.56 ± 0.73 | 0.09 ± 0.09 | <0.001 | 24.63 ± 0.95 | 25.05 ± 0.98 | 0.22 ± 0.11 | <0.001 | 23.73 ± 0.54 | 24.32 ± 0.63 | 0.29 ± 0.12 | <0.001 | <0.001 |
| SFCT (μm) | 352.37 ± 63.12 | 371.62 ± 73.50 | 9.63 ± 21.25 | <0.001 | 284.39 ± 61.22 | 282.31 ± 64.18 | −1.03 ± 16.82 | 0.264 | 317.44 ± 56.46 | 298.99 ± 66.69 | −9.22 ± 20.04 | <0.001 | <0.001 |

* *P* for trend was calculated by the linear regression model.
† The *P* values were computed using the Wilcoxon signed-rank test for non-normally distributed data and paired *t*-test for normally distributed variables.
‡ SER is represented as either the mean ± SD or median (IQR).

ened and then thinned, with a turning point in annual axial elongation at approximately 0.20 mm. Similarly, in PM children, SFCT started to thin when annual axial elongation was around 0.18 mm. This observed pattern of choroidal changes with AL elongation aligns with the above results, indicating that the SFCT thinning occurred when AL progressed rapidly.

## Discussion

In this prospective longitudinal study, we have, for the first time, to the best of our knowledge, shown that changes in SFCT differ, as they increased among the nonmyopic children with stable refraction, remained stable among the myopic children with stable refraction, and decreased in both nonmyopic and myopic children with refractive progression. Many studies have investigated the development of the choroid. Unlike the choroidal thickening observed from birth to puberty in normally reared animals,[12] the change in ChT with age in children varies—typically showing an increase in Western studies[9,13,23,24] and a decrease in Asian studies.[14,25,26] Racial differences in ChT development might exist; for example, Read et al.[27] demonstrated a thicker choroid in Australian indigenous children compared to Caucasian children. However, the onset of myopia also plays an important role in the process of choroidal change. In a longitudinal study, Fontaine et al.[16] reported that the SFCT increased in nonmyopic eyes but decreased in myopic eyes during a 15-month follow-up. Jin et al.[17] found that the central foveal choroid remained unchanged in children maintaining persistent nonmyopia and decreased when children experienced myopic shifts after 1-year follow-up. Xiong et al.[19] reported an increase in ChT in nonmyopic shift children 10 to 13 years old, but it remained unchanged in children of other ages. The inconsistencies observed among these studies may be attributed to the varying refractive progressions in children of school age.

Targeting children with a relatively low myopia rate (21.4%, lower than those previously reported in Chinese studies [2,28]) and making fine divisions based on SER progression, we found that the SFCT increased by 4.54 μm/y (mean value of all four cohorts) in nonmyopic children with stable refraction. Hansen et al.[24] reported a 5-year cumulative increase of 33 μm in SFCT among children with mean SER around zero. They also found that the increase of SFCT was less pronounced in girls undergoing early sexual maturation. In our study, children exhibited negligible thickening of SFCT in the G4 cohort (9 to 10 years old), followed by more substantial thickening in the G7 cohort (11 to 13 years old) within the PNM-stable group. Additionally, we observed less choroidal thinning in the G7 cohort among PM-progressive children. The observed greater choroidal thickening and less choroidal thinning in the G7 cohort were both more pronounced in boys. Xiong et al.[29] reported a lesser ChT thinning in children 11 years of age and older, which they speculated was mediated by pubertal growth spurts. In another longitudinal study, Xiong et al.[19] found that the choroidal increase occurred solely in nonmyopic shift children between the ages of 10 and 13 years. There is a possibility that children in different pubertal stages may experience differences in ChT development, but the precise relationship between them requires further examination through longer follow-up studies that include puberty stage evaluations and

**Table 3.** Baseline and Follow-Up Characteristics in SER, AL, and SFCT Among Children With Different Rates of SER Progression

| | Stable Group | | | | | | | | *P* Between Groups* | Progressive Group | | | | | | | | *P* Between Groups* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PNM | | | | PM | | | | Annual Change, Mean ± SD | PNM | | | | PM | | | | Annual Change, Mean ± SD |
| | Baseline, Mean ± SD | Follow-Up, Mean ± SD | Annual Change, Mean ± SD | *P*† | Baseline, Mean ± SD | Follow-Up, Mean ± SD | Annual Change, Mean ± SD | *P*† | | Baseline, Mean ± SD | Follow-Up, Mean ± SD | Annual Change, Mean ± SD | *P*† | Baseline, Mean ± SD | Follow-Up, Mean ± SD | Annual Change, Mean ± SD | *P*† | |
| Total | | | | | | | | | | | | | | | | | | |
| *n* | 1461 | 1461 | 1461 | — | 220 | 220 | 220 | — | — | 82 | 82 | 82 | — | 256 | 256 | 256 | — | — |
| SER (D)‡ | 1.19 ± 0.64 | 0.94 ± 0.69 | −0.13 ± 0.16 | <0.001 | −2.34 ± 1.52 | −2.84 ± 1.56 | −0.25 ± 0.15 | <0.001 | <0.001 | 1.19 (0.97, 1.88) | 0.06 (−0.25, 0.75) | −0.56 (−0.63, −0.50) | <0.001 | −2.04 ± 1.18 | −3.55 ± 1.17 | −0.76 ± 0.24 | <0.001 | <0.001 |
| AL (mm) | 22.75 ± 0.77 | 23.06 ± 0.76 | 0.16 ± 0.07 | <0.001 | 24.58 ± 0.94 | 24.90 ± 0.97 | 0.16 ± 0.08 | <0.001 | 0.313 | 22.57 ± 0.77 | 23.16 ± 0.78 | 0.29 ± 0.08 | <0.001 | 24.39 ± 0.89 | 25.10 ± 0.87 | 0.36 ± 0.12 | <0.001 | <0.001 |
| SFCT (μm) | 346.99 ± 58.88 | 356.07 ± 66.26 | 4.54 ± 19.07 | <0.001 | 285.28 ± 62.33 | 287.71 ± 67.08 | 1.22 ± 16.08 | 0.264 | 0.006 | 352.59 ± 63.43 | 339.41 ± 60.90 | −6.59 ± 23.17 | 0.012 | 290.05 ± 58.14 | 276.23 ± 57.05 | −6.92 ± 16.41 | <0.001 | 0.907 |
| G0 | | | | | | | | | | | | | | | | | | |
| *n* | 137 | 137 | 137 | — | — | — | — | — | — | 1 | 1 | 1 | — | — | — | — | — | — |
| SER (D)‡ | 1.46 ± 0.53 | 1.42 ± 0.54 | −0.02 ± 0.17 | 0.079 | — | — | — | — | — | 2.13 | 1.13 | −0.50 | — | — | — | — | — | — |
| AL (mm) | 22.08 ± 0.59 | 22.47 ± 0.60 | 0.20 ± 0.09 | <0.001 | — | — | — | — | — | 21.23 | 21.86 | 0.32 | — | — | — | — | — | — |
| SFCT (μm) | 363.24 ± 57.71 | 370.02 ± 56.63 | 3.39 ± 19.45 | 0.043 | — | — | — | — | — | 388 | 347 | −20.50 | — | — | — | — | — | — |
| G1 | | | | | | | | | | | | | | | | | | |
| *n* | 927 | 927 | 927 | — | 4 | 4 | 4 | — | — | 45 | 45 | 45 | — | 4 | 4 | 4 | — | — |
| SER (D)‡ | 1.30 ± 0.57 | 1.04 ± 0.58 | −0.13 ± 0.15 | <0.001 | −1.28 ± 0.84 | −1.66 ± 1.01 | −0.19 ± 0.18 | 0.134 | — | 1.38 (1.00, 2.25) | 0.38 (−0.13, 1.13) | −0.56 (−0.59, −0.50) | <0.001 | −1.03 ± 0.43 | −3.06 ± 0.94 | −1.02 ± 0.30 | 0.008 | — |
| AL (mm) | 22.60 ± 0.66 | 22.91 ± 0.66 | 0.16 ± 0.07 | <0.001 | 23.37 ± 0.57 | 23.69 ± 0.67 | 0.21 ± 0.08 | 0.013 | — | 22.26 ± 0.68 | 22.85 ± 0.71 | 0.29 ± 0.09 | <0.001 | 23.14 ± 0.92 | 24.14 ± 1.12 | 0.50 ± 0.15 | 0.007 | — |
| SFCT (μm) | 347.23 ± 58.94 | 355.87 ± 64.65 | 4.32 ± 17.87 | <0.001 | 345.00 ± 92.08 | 355.13 ± 109.32 | 5.06 ± 11.94 | 0.459 | — | 342.41 ± 62.03 | 335,71 ± 59.48 | −3.35 ± 22.55 | 0.324 | 327.63 ± 35.67 | 325.75 ± 90.54 | −0.94 ± 36.23 | 0.950 | — |
| G4 | | | | | | | | | | | | | | | | | | |
| *n* | 220 | 220 | 220 | — | 23 | 23 | 23 | — | — | 28 | 28 | 28 | — | 116 | 116 | 116 | — | — |
| SER (D)‡ | 0.89 ± 0.47 | 0.48 ± 0.54 | −0.20 ± 0.15 | <0.001 | −1.99 ± 1.00 | −2.60 ± 1.02 | −0.38 (−0.44, −0.25) | <0.001 | 0.001 | 1.13 (0.88, 1.56) | −0.13 (−0.25, 0.22) | −0.56 (−0.63, −0.50) | <0.001 | −1.71 ± 1.02 | −3.40 ± 1.07 | −0.84 ± 0.26 | <0.001 | <0.001 |
| AL (mm) | 23.25 ± 0.68 | 23.61 ± 0.71 | 0.18 ± 0.07 | <0.001 | 24.33 ± 0.67 | 24.77 ± 0.75 | 0.22 ± 0.12 | <0.001 | <0.013 | 23.00 ± 0.60 | 23.62 ± 0.62 | 0.31 ± 0.06 | <0.001 | 24.16 ± 0.72 | 25.00 ± 0.70 | 0.42 ± 0.12 | <0.001 | <0.001 |
| SFCT (μm) | 332.83 ± 52.75 | 335.25 ± 67.05 | 1.21 ± 21.54 | 0.407 | 274.98 ± 51.39 | 268.63 ± 49.63 | −3.17 ± 14.81 | 0.313 | 0.342 | 356.66 ± 65.56 | 338.95 ± 60.32 | −8.86 ± 23.07 | 0.053 | 296.87 ± 56.12 | 277.82 ± 53.55 | −9.53 ± 14.65 | <0.001 | 0.884 |
| G7 | | | | | | | | | | | | | | | | | | |
| *n* | 177 | 177 | 177 | — | 193 | 193 | 193 | — | — | 8 | 8 | 8 | — | 136 | 136 | 136 | — | — |
| SER (D)‡ | 0.77 ± 0.86 | 0.55 ± 0.92 | −0.11 ± 0.15 | <0.001 | −2.39 ± 1.58 | −2.89 ± 1.61 | −0.25 ± 0.15 | <0.001 | <0.001 | 0.69 (0.63, 1.53) | −0.31 (−0.38, 0.44) | −0.50 (−0.55, −0.50) | 0.008 | −2.33 ± 1.22 | −3.70 ± 1.25 | −0.69 ± 0.18 | <0.001 | 0.001 |
| AL (mm) | 23.39 ± 0.70 | 23.60 ± 0.71 | 0.10 ± 0.06 | <0.001 | 24.64 ± 0.95 | 24.94 ± 0.97 | 0.15 ± 0.07 | <0.001 | <0.001 | 22.92 ± 0.85 | 23.35 ± 0.91 | 0.21 ± 0.08 | <0.001 | 24.60 ± 0.94 | 25.22 ± 0.98 | 0.31 ± 0.09 | <0.001 | 0.005 |
| SFCT (μm) | 350.60 ± 62.98 | 372.10 ± 73.51 | 10.75 ± 20.31 | <0.001 | 285.26 ± 62.51 | 288.58 ± 67.26 | 1.66 ± 16.27 | 0.159 | <0.001 | 391.13 ± 56.46 | 360.81 ± 77.53 | −15.16 ± 27.65 | 0.165 | 283.12 ± 59.52 | 273.39 ± 58.63 | −4.86 ± 16.90 | 0.001 | 0.331 |

* The intergroup *P* values were computed using the Mann–Whitney *U* test for non-normally distributed data and Student's *t*-test for normally distributed variables.
† The *P* values were computed using the Wilcoxon signed-rank test for non-normally distributed data and the paired *t*-test for normally distributed variables.
‡ SER is represented as either the mean ± SD or median (IQR).

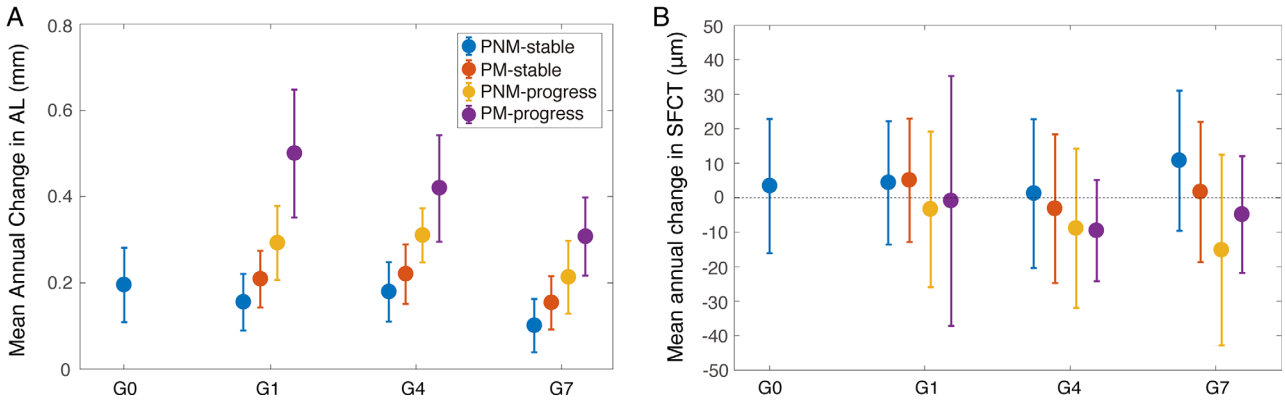


**Figure 2.** Mean annual changes in AL (**A**) and SFCT (**B**) across different age cohorts among children within the PNM-stable, PM-stable, PNM-progressive, and PM-progressive groups.

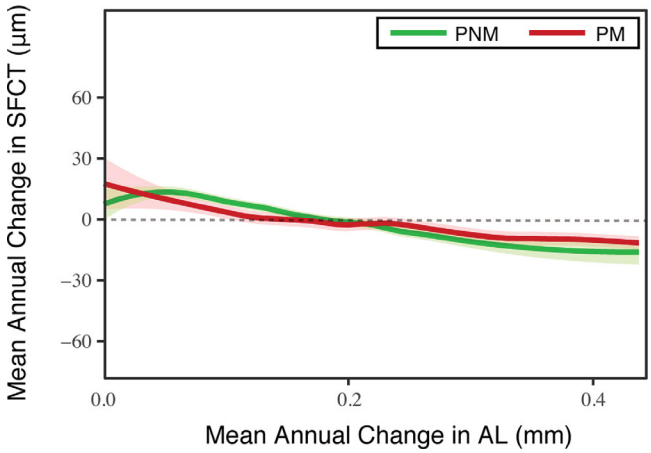


**Figure 3.** Changes in SFCT with AL growth in PNM and PM children. The curves were fitted with LOWESS plots with a span of 0.50.

involve the same sample of participants with similar refractive states.

With regard to children undergoing refractive progression, the choroid thinned in both nonmyopic (−6.59 µm/y) and myopic (−6.92 µm/y) eyes. Xiong et al.[19] reported a choroidal thinning of −4 µm/y in PNM children and −5 µm/y in PM children. However, in their study, children in these two groups were not differentiated based on SER progression. In this study, we also observed a slight, though nonsignificant, increase in SFCT in children with stable myopia. Read et al.[9] found that ChT could increase in myopic children when AL progression is slow. Moreover, studies on myopia control have reported SFCT increases when myopia progression is impeded by atropine eye drops and/or orthokeratology.[30,31] These outcomes indicate that, at least during the pediatric period, the choroid may remain stable or thicken in myopic eyes showing relatively slow axial eye growth.

As previously mentioned and confirmed in our study, the rate of AL growth has an important impact on ChT change; however, the extent to which AL growth leads to choroidal thinning remains uncertain. Read et al.[9] reported a negative relationship between SFCT change and AL growth. It can be inferred from their graphical representation that the thickening of SFCT disappeared in both nonmyopic and myopic eyes when AL growth reached around 0.20 mm. Jin et al.[17] documented a mean AL growth of 0.19 mm in nonmyopic children whose ChT remained unchanged during a 1-year follow-up. In our study, we observed that the SFCT began to decrease when the mean annual increase in AL was approximately 0.20 mm in the PNM group and 0.18 mm in the PM group. Previous proposals suggest that the developmental increase of the choroid serves as compensation to slow axial eye growth during the juvenile period.[12] Mutti et al.[32] reported an average elongation of AL about 0.1 mm/y in emmetropic children 6 to 14 years old. Additionally, Tideman et al.[33] observed an AL growth of 0.19 mm/y in emmetropic children 9 years old. It is plausible that choroidal thinning occurs when AL extends beyond the compensatory adjustment capacity of the choroid. However, the influence of other factors, including age, sex, baseline ocular status, and more, in the progression of ChT thinning driven by fast AL elongation requires further examination and discussion. Furthermore, the rate of AL growth and the variation in ChT serve as primary indicators for assessing the efficacy of myopic treatment. Elucidating their relationship will provide further insights into the effects of current myopic control therapies.

The current study has the merit of being the first longitudinal examination, to the best of our knowledge, of choroidal changes in children characterized by a refined division based on stable or progressive refractive statuses. These findings have enriched our comprehension of choroidal development during childhood, providing insights that contribute to addressing inconsistencies observed in previous studies. Furthermore, these results could offer valuable information regarding the role of the choroid in myopia control. Nevertheless, several limitations should be acknowledged. First, the study included Chinese children exclusively; thus, further exploration of ethnic variations in ChT changes with different rates of refractive progression is warranted. Second, this study focused on choroidal changes in children 3 to 14 years old. Recent research by Lee et al.[34] revealed that the choroid continued to thicken in young adults without myopic progression during the third decade of life. Extended observations covering a wider age range would provide further insights into the continuous evolution of the choroid throughout life. Third, the low prevalence of myopia, which resulted in uneven subgroup distribution, particularly in the PM-stable

and PNM-progressive groups, as well as the exclusion of children in the G4 cohort due to poor image quality, may have introduced bias to our observations within these groups. Future endeavors will involve a larger participant pool to delve deeper into SFCT changes within these refractive and age groups. Fourth, the timing of OCT imaging during follow-up was not standardized, as scans were conducted between 10 AM and 4 PM. Additionally, caffeine intake, body mass index, and birth weight were not controlled for in this study. Although we believe caffeine consumption should be limited in Chinese children of our studied age cohorts, and BMI has been reported as not being correlated with choroidal changes,[24] these variables require better control in future studies. Fifth, some of the differences we observed were smaller than the interrater repeatability. This further reminds us of the need for tighter control of possible choroid-related influencing factors in future research, as well as more accurate automated measurement in ChT. Finally, in our study, baseline and follow-up SFCT was obtained after achieving complete cycloplegia induced by 1% cyclopentolate hydrochloride. This approach was adopted to optimize image quality and eliminate the potential influence of accommodation on ChT. However, previous reports have indicated that cycloplegic agents can influence ChT.[35–38] The consistency of choroidal changes measured before and after cycloplegia during longitudinal studies requires further discussion.

In conclusion, our study revealed that the development of SFCT was influenced by the combination of age and refractive state. Specifically, SFCT increased in nonmyopic children with stable refraction, remained stable in myopic children with stable refraction, and decreased in those suffering rapid refractive progression, irrespective of whether they were myopic or nonmyopic.

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