LONGITUDINAL CHANGES IN CHOROIDAL AND RETINAL THICKNESSES IN CHILDREN WITH MYOPIC SHIFT

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Purpose: To elucidate the development of the choroid and retina in children, and to explore changes in these during myopic shift.

Methods: A total of 118 children aged 7 to 12 years participated in this 1-year longitudinal study. Children underwent several examinations at baseline and follow-up, including cycloplegic refraction, axial length measurement, and swept-source optical coherence tomography. Thickness changes in the choroid and retina were compared among children with or without myopic shift.

Results: Eighty-eight children (74.6%) developed a myopic shift after 1 year, and their central foveal choroid was significantly attenuated ($P < 0.01$). No significant change was observed in choroids of children without myopic shift ($P = 0.83$). Choroidal thickness decreased in all subfields during myopic shift, whereas the thickness of the retinal layers increased or were unchanged in most subfields. Axial length increase and central foveal choroidal thinning were associated with myopic shift ($R^2 = 0.157$, $P < 0.01$), but axial length increase was not significantly related to choroidal thinning ($P > 0.05$).

Conclusion: Choroidal thinning occurs early in myopic progression. Axial length increase and choroidal thinning are independently associated with myopic shift.

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The increasing prevalence of myopia is a global public health concern.[1,2] Although the precise mechanisms underlying myopia development are unknown, growing evidence suggests that choroid may contribute to myopic pathogenesis. Recently, several studies have demonstrated that choroidal thinning is a significant structural change preceding the development of myopia.[3–7] Animal models of induced myopia or hyperopia confirm that changes in the choroid precede changes in axial length (AL) and scleral remodeling.[8,9] Furthermore, during active accommodation, the choroid thins and AL increases proportional to the accommodative effort.[10]

Few data are available to describe longitudinal changes in the choroid during childhood; so, its potential role in myopic pathogenesis is largely unexplored. A recent prospective study of white children showed that although myopes have significantly thinner choroid compared with others, choroidal thickness increases with age in myopic children. However, the potential relationship between changes in choroidal thickness over time and changes in refractive status were not described.[11] A cross-sectional study of healthy adults indicated that subfoveal choroidal thickness is strongly associated with age and refractive error.[12] Thus, refractive changes may affect choroidal thickness, and this should be weighed when studying pediatric choroidal changes during development.

We investigated longitudinal changes in choroidal thickness of school-age children over 1 year to elucidate the anatomical and topographic changes of the choroid and retinal layers over time, and to explore their relationship with refractive changes and AL growth.

Methods

Setting and Participants

This study was conducted according to the tenets of the Declaration of Helsinki and the study protocol was approved by the institutional review board of Shanghai General Hospital, Shanghai Jiao Tong University.

This longitudinal study was a follow-up study based on our former cross-sectional study.[13] In 2015,

a primary school located in Shanghai, China, was randomly selected using cluster sampling, and 299 students participated in a cross-sectional investigation of choroidal and retinal thicknesses using the swept-source optical coherence tomography (SS-OCT). One year later, the investigation site was again set up within the school, and 118 children of the same student cohort participated. Participants' loss was chiefly due to school graduation. Participants were excluded if the best corrected visual acuity was less than 20/25, or if a self-reported history of intraocular surgery or ocular comorbidities was documented. Before the study, informed consents were obtained from students and their guardians.

Research Methods

The participants' age and sex were recorded according to state-issued identification cards, and heights and weights were measured at the site. Each participant underwent a series of ophthalmic examinations, including tonometry, cycloplegic refraction, keratometry, AL measurements, and SS-OCT. Intraocular pressure was measured using a noncontact tonometer (model NT-4000; Nidek Inc, Fremont, CA) before cycloplegia. Cycloplegia was achieved by administering one dose of topical 0.5% proparacaine (Alcaine; Alcon, Fort Worth, TX), and 2 doses of 1% cyclopentolate (Cyclogyl; Alcon) applied 5 minutes apart. Corneal curvature radius (CR) and refraction were measured using a desk-mounted autorefractor (model KR-8900; Topcon, Tokyo, Japan) after full dilation was achieved. Axial length was measured using a noncontact optical biometry (IOLMaster, version 5.02; Carl Zeiss Meditec, Oberkochen, Germany). Detailed examination methods are described elsewhere.[13]

An SS-OCT (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 the choroid, retina, ganglion cell layer, and nerve fiber layer. Built-in software was used to segment layers and construct topographical maps. Choroidal thickness was measured as the distance between the Bruch membrane and the choroid–sclera interface. The whole retina was measured from the internal limiting membrane to the interface between photoreceptor outer segments and retinal pigment epithelium. Ganglion cell layer thickness was measured from the interface between nerve fiber layer and ganglion cell layer to the interface between inner plexiform layer and inner nuclear layer. Nerve fiber layer was measured from the internal limiting membrane to the interface between nerve fiber layer and ganglion cell layer. The Early Treatment Diabetic Retinopathy Study grid was applied once the tomography map was obtained, which divided the macula into three concentric circles centered in the fovea: central foveal circle (diameter = 1 mm), parafoveal circle (diameter = 3 mm), and perifoveal circle (diameter = 6 mm). The parafoveal and perifoveal regions were subdivided into superior, inferior, temporal, and nasal subfields. Detailed image acquisition and analysis procedures are described elsewhere.[13]

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Statistical Analyses

SAS (version 8.0; SAS Institute, Cary, NC) was used for statistical analyses. Only right-eye data were used for statistical analysis and spherical equivalent refraction (SER) information was used for analysis of refractive status. Myopic shift means the follow-up SER decreased compared with baseline SER, whereas hyperopic shift means follow-up SER increased compared with baseline SER. Considering that a minimal myopic shift has limited clinical meaning, a subgroup analysis of significant myopic shift was made in which only those with at least a -0.5 D myopic shift were evaluated. The AL-to-CR ratio (AL/CR) was the length of the axial divided by the radius of the corneal curvature. Characteristics are presented as mean ± SD for continuous variables, and as rates (proportions) for categorical data. Statistical significance was defined as $P < 0.05$ (two-tailed).

Data distribution was examined using a Kolmogorov–Smirnov test, and all SS-OCT measurements were normally distributed. Changes in SS-OCT

measurements between 2015 (baseline) and 2016 (follow-up) were compared using a paired Student's *t*-test. Intergroup differences were tested using a Student's *t*-test or variance analysis, and the *P* values were adjusted using Holm adjustment for multiple comparisons. Categorical variables were compared using a chi-square test. Comparisons among the OCT measurements of the perifoveal circle, parafoveal circle, and central regions of the same eye, and among the measurements of the four quadrants were made using repeated-measures analysis of variance and contrast analysis. A linear correlation test was used to assess the relationship between the changes of OCT measurements and ocular variants, and stepwise multiple regression analysis was performed to determine independent factors of a myopic shift.

Results

A total of 118 participants, including 52 boys and 66 girls, were enrolled in this study. The mean age of the participants at the time of the baseline examination was 10.14 ± 0.84 years (range: 7–12 years). At follow-up, 88 children developed a myopic shift, whereas 20 developed a hyperopic shift, and the remaining 10 participants had refraction unchanged from baseline. The myopic shift that occurred in the right eyes was matched by a similar shift in 97% of the left eyes. Among the children with myopic shift, 53 with a significant myopic shift (≤ -0.5 D) were included in the subgroup. No difference in age (t = -1.20, $P = 0.23$) or sex ($\chi^2 = 0.14$, $P = 0.70$) was found between the participants with or without myopic shift. At baseline, the participants with myopic shift had a lower mean SER and a higher AL/CR compared with the others, but their baseline AL was not statistically longer, and no difference was observed in the OCT measurements between the two groups (Table 1).

Comparing Longitudinal Changes in Participants With and Without Myopic Shift

For participants without myopic shift, increased AL and decreased ganglion cell layers were observed after follow-up; however, there was no significant change in the central foveal choroidal thickness over time. For participants with myopic shift, there was a significant decrease in the mean thickness of the central foveal choroid and ganglion cell layers, and increased mean AL and AL/CR at the end of the study period compared with baseline measurements 1 year before. Patients with significant myopic shift showed similar longitudinal changes except for no significant decrease in ganglion cell layer thickness. The increase of

AL/CR during the follow-up was significantly higher in children with myopic shift, whereas the longitudinal changes of the other measurements were not different between the two groups. No significant difference was observed in AL or OCT measurements between children with and without myopic shift after the follow-up (Table 1).

For participants with myopic shift, stepwise multiple regression analysis indicated that the degree of myopic shift was independently associated with increased AL and decreased central foveal choroidal thickness ($P < 0.01$, $R^2 = 0.1567$), and the parameter estimate for AL is -0.29 ± 0.09 ($P < 0.01$), the parameter estimate for choroidal thickness is 0.003 ± 0.001 ($P = 0.02$), whereas other factors such as age, sex, and the thickness change of ganglion cell layers were not related to myopic shift. However, linear correlation test suggested that changes in central foveal choroidal thickness were not associated with changes of AL or AL/CR. No factor was found related to the degree of myopic shift in the subgroup of significant myopia shift.

Longitudinal Changes in Participants With Myopic Shift Stratified by Final Refraction

Among the 88 participants who developed a myopic shift during the 1-year study period, there were 24 myopes, 17 emmetropes, and 47 hyperopes at the baseline. At the end of the 1-year follow-up, seven emmetropes and two hyperopes developed myopic refraction, and 14 hyperopes became emmetropic. Thus, at the end of the study, 33 participants were myopic, 24 emmetropic, and 31 hyperopic with the mean age of 10.31 ± 0.72, 10.33 ± 0.78, and 9.70 ± 0.84 years, respectively, whereas among the 53 children with significant myopic shift, there were 28 myopes, 19 emmetropes, and 6 hyperopes after 1-year follow-up. Hyperopes were younger than the others (F = 6.75, $P < 0.01$). There were no differences in sex ($\chi^2 = 0.71$, $P = 0.70$) among participants of different final refractive statuses. The baseline and follow-up ocular characteristics of these children are described in Table 2.

Participants who were emmetropic or myopic at the end of the follow-up showed a significant decrease in central foveal choroidal thickness but had no changes in the ganglion cell layer. The same results were shown in the subgroup of significant myopic shift. Regression tests suggested that the decrease of the central foveal retina and choroid, and the increase of AL were associated with the degree of myopic shift in myopes ($P < 0.01$, $R^2 = 0.3518$). The parameter estimate for AL is -0.35 ± 0.16 ($P = 0.04$), the parameter

Table 1. The Characteristics of the Participants in the Baseline and Follow-up Study

	Total (n = 118)			Myopic Shift (n = 88) [Significant Myopic Shift (n = 53)]			Nonmyopic Shift (n = 30)			P Between Groups		
	Baseline	Follow-up	P	Baseline	Follow-up	P	Baseline	Follow-up	P	Baseline	Follow-up	Longitudinal Changes
SER (diopter)	0.20 ± 1.39	−0.17 ± 1.61	<0.01	−1.63 ± 1.42 [−0.34 ± 1.61]	−2.45 ± 1.46 [−1.12 ± 1.72]	<0.01 [<0.01]	0.53 ± 0.78	0.77 ± 0.76	<0.01	0.04	<0.01	<0.01
AL/CR*	2.96 ± 0.10	3.00 ± 0.11	<0.01	3.07 ± 0.08 [3.00 ± 0.10]	3.14 ± 0.08 [3.06 ± 0.10]	<0.01 [<0.01]	2.92 ± 0.07	2.95 ± 0.08	<0.01	<0.01	0.02	0.03
AL (mm)	23.18 ± 0.92	23.47 ± 0.98	<0.01	24.08 ± 0.96 [23.44 ± 1.06]	24.55 ± 1.02 [23.87 ± 1.11]	<0.01 [<0.01]	23.01 ± 0.71	23.20 ± 0.69	<0.01	0.26	0.09	0.09
Choroid (μm)	251 ± 62	243 ± 63	<0.01	215 ± 51 [230 ± 52]	203 ± 52 [214 ± 52]	<0.01 [<0.01]	262 ± 70	263 ± 65	0.83	0.31	0.10	0.31
Retina (μm)	239 ± 29	234 ± 18	0.08	240 ± 21 [239 ± 28]	239 ± 17 [237 ± 19]	0.36 [0.59]	239 ± 31	230 ± 19	0.05	0.95	0.35	0.47
Ganglion cell layer (μm)	49 ± 15	45 ± 8	<0.01	49 ± 13 [48 ± 14]	48 ± 6 [46 ± 8]	0.01 [0.32]	50 ± 15	43 ± 9	0.02	0.80	0.78	0.70
Nerve fiber layer (μm)	11 ± 9	9 ± 3	0.05	11 ± 8 [12 ± 9]	10 ± 2 [9 ± 3]	0.08 [0.07]	10 ± 9	8 ± 2	0.24	1	0.54	0.99

Statistical significance was tested using paired *t*-test.
*P was adjusted using Holm adjustment for multiple comparisons.

Table 2. The Characteristics of the Participants With Myopic Shift/Significant Myopic Shift in the Baseline and the Follow-up Study

Myopic Shift / Significant Shift	Myopes (n = 33) / Myopes (n = 28)			Emmetropes (n = 24) / Emmetropes (n = 19)			Hyperopes (n = 31) / Hyperopes (n = 6)			P^* Between Groups		
	Baseline	Follow-up	P	Baseline	Follow-up	P	Baseline	Follow-up	P	Baseline	Follow-up	Longitudinal Changes
SER (diopter)	−1.40 ± 1.47	−2.22 ± 1.51	<0.01	0.53 ± 0.24	−0.03 ± 0.26	<0.01	1.29 ± 0.58	0.98 ± 0.51	<0.01	<0.01	<0.01	<0.01
	−1.37 ± 1.51	−2.27 ± 1.56	<0.01	0.51 ± 0.26	−0.11 ± 0.21	<0.01	1.75 ± 0.74	1.08 ± 0.70	<0.01	<0.01	<0.01	<0.01
AL/CR	3.06 ± 0.08	3.13 ± 0.08	<0.01	2.94 ± 0.08	3.00 ± 0.05	<0.01	2.91 ± 0.07	2.94 ± 0.06	<0.01	<0.01	<0.01	<0.01
	3.05 ± 0.08	3.12 ± 0.09	<0.01	2.94 ± 0.09	3.00 ± 0.06	<0.01	2.90 ± 0.07	2.94 ± 0.08	0.07	<0.01	<0.01	0.43
AL (mm)	23.94 ± 0.99	24.40 ± 1.05	<0.01	22.84 ± 0.75	23.21 ± 0.67	<0.01	22.78 ± 0.69	22.97 ± 0.70	<0.01	<0.01	<0.01	0.01
	23.96 ± 0.97	24.43 ± 1.06	<0.01	22.82 ± 0.80	23.22 ± 0.71	<0.01	23.02 ± 1.05	23.33 ± 1.08	0.03	<0.01	<0.01	0.66
Choroid (μm)	216 ± 52	203 ± 52	0.01	256 ± 49	237 ± 57	0.02	276 ± 61	271 ± 55	0.44	<0.01	<0.01	0.19
	212 ± 53	198 ± 53	<0.01	244 ± 41	221 ± 42	<0.01	273 ± 54	264 ± 49	0.18	0.03	0.03	0.38
Retina (μm)	240 ± 22	240 ± 17	0.95	227 ± 29	231 ± 16	0.44	247 ± 33	236 ± 19	0.05	0.11	0.21	0.15
	243 ± 22	242 ± 17	0.76	230 ± 32	231 ± 18	0.93	250 ± 36	237 ± 23	0.32	0.38	0.48	0.50
Ganglion cell layer (μm)	49 ± 13	48 ± 7	0.60	44 ± 12	44 ± 7	0.89	53 ± 18	44 ± 8	<0.01	0.16	0.08	0.04
	50 ± 14	48 ± 7	0.59	45 ± 12	45 ± 8	0.84	53 ± 23	41 ± 8	0.19	0.43	0.25	0.30
Nerve fiber layer (μm)	12 ± 9	10 ± 2	0.22	10 ± 9	8 ± 4	0.30	11 ± 9	9 ± 3	0.37	1.70	0.91	0.97
	12 ± 9	10 ± 3	0.15	11 ± 10	8 ± 4	0.31	11 ± 7	10 ± 3	0.70	1.70	0.99	0.96

Paired t-test was used to test statistical significance for longitudinal changes in each group, and analysis of variance was used to compare the values among the three groups. Myopes, emmetropes, and hyperopes were according to the refractive status at the end of the study.
*P was adjusted using Holm adjustment for multiple comparisons.

Table 3. The Development of Choroid and Retinal Layers in Children With Myopic Shift Over 1 Year

Structure	Region	Baseline	Follow-up	Longitudinal Changes	P
Choroid (μm)	Central fovea	248 ± 60	236 ± 61	−11 ± 30	<0.01†
	Parafoveal nasal	221 ± 59	210 ± 60	−11 ± 27	<0.01
	Parafoveal temporal	261 ± 57	248 ± 59	−13 ± 30	<0.01
	Parafoveal superior	250 ± 58	240 ± 59	−10 ± 27	<0.01
	Parafoveal inferior	246 ± 58	235 ± 59	−11 ± 30	<0.01
	Perifoveal nasal	177 ± 55	167 ± 53	−10 ± 26	<0.01
	Perifoveal temporal	265 ± 54	252 ± 53	−13 ± 29	<0.01
	Perifoveal superior	236 ± 52	236 ± 54	−7 ± 24	0.01
	Perifoveal inferior	241 ± 53	224 ± 54	−12 ± 26	<0.01
Retina (μm)	Central fovea	238 ± 29	236 ± 18	−3 ± 26	0.36
	Parafoveal nasal	307 ± 22	312 ± 14	5 ± 18	<0.01
	Parafoveal temporal	293 ± 21	302 ± 13	9 ± 19	<0.01
	Parafoveal superior	309 ± 22	311 ± 14	2 ± 20	0.39
	Parafoveal inferior	302 ± 23	313 ± 13	11 ± 22	<0.01
	Perifoveal nasal	293 ± 20	297 ± 15	4 ± 16	0.03
	Perifoveal temporal	264 ± 19	267 ± 13	3 ± 16	0.11
	Perifoveal superior	278 ± 22	285 ± 13	6 ± 21	<0.01
	Perifoveal inferior	274 ± 21	267 ± 14	−7 ± 17	<0.01
Ganglion cell layer (μm)	Central fovea	49 ± 15	45 ± 8	−4 ± 14	0.01
	Parafoveal nasal	92 ± 9	94 ± 5	2 ± 7	<0.01
	Parafoveal temporal	87 ± 9	90 ± 5	4 ± 9	<0.01
	Parafoveal superior	91 ± 10	94 ± 6	3 ± 11	<0.01
	Parafoveal inferior	89 ± 11	95 ± 5	6 ± 11	<0.01
	Perifoveal nasal	72 ± 8	75 ± 6	3 ± 7	<0.01
	Perifoveal temporal	74 ± 8	74 ± 5	0 ± 6	0.88
	Perifoveal superior	65 ± 8	70 ± 6	5 ± 8	<0.01
	Perifoveal inferior	67 ± 9	63 ± 6	−4 ± 8	<0.01
Nerve fiber layer (μm)	Central fovea	11 ± 9	9 ± 3	−2 ± 9	0.08
	Parafoveal nasal	25 ± 6	24 ± 3	−1 ± 7	0.06
	Parafoveal temporal	20 ± 7	21 ± 5	2 ± 8	0.05
	Parafoveal superior	31 ± 12	24 ± 3	−7 ± 12	<0.01
	Parafoveal inferior	27 ± 10	30 ± 3	3 ± 10	<0.01
	Perifoveal nasal	51 ± 10	51 ± 5	0 ± 10	0.91
	Perifoveal temporal	23 ± 5	25 ± 4	2 ± 6	<0.01
	Perifoveal superior	45 ± 12	43 ± 4	−2 ± 11	0.17
	Perifoveal inferior	44 ± 12	46 ± 5	2 ± 12	0.22

estimate for choroidal thickness is 0.005 ± 0.002 ($P = 0.02$), and the parameter estimate for retinal thickness is 0.007 ± 0.003 ($P = 0.01$). In children of significant myopic shift, the thickness decrease of the choroid and ganglion cell layers were associated with the degree of myopic shift in myopes ($P < 0.01$, $R^2 = 0.3888$). The parameter estimate for choroidal thickness is 0.006 ± 0.002 ($P < 0.01$) and the parameter estimate for ganglion cell layer thickness is 0.01 ± 0.003 ($P < 0.01$). By contrast, participants who were hyperopic at the end of the follow-up had no change in choroidal thickness but had a significantly decreased central foveal ganglion cell layer thickness. Only increased AL was associated with myopic shift for those who were hyperopes after the follow-up ($P < 0.01$, $R^2 = 0.2956$), and the parameter estimate for AL is −0.74 ± 0.21, $P < 0.01$. No significant change of OCT measurements was shown in hyperopes with significant myopic shift.

During the follow-up, AL and AL/CR increased less, whereas ganglion cell layer attenuated more in hyperopes compared with other groups. However, no difference between groups was shown in children with significant myopic shift (Table 2).

Longitudinal Changes of Parafoveal and Perifoveal Choroid and Retinal Layers in Participants With Myopic Shift

For participants who developed a myopic shift during the study period, choroidal thickness decreased in all quadrants in the parafoveal and perifoveal circles. The perifoveal choroid attenuated most compared with parafoveal and central choroids, and the superior quadrant attenuated the least in both parafoveal and perifoveal circles (Table 3 and Figure 1). However, apart from the correlation between thickness changes in the superior parafoveal choroid changes in
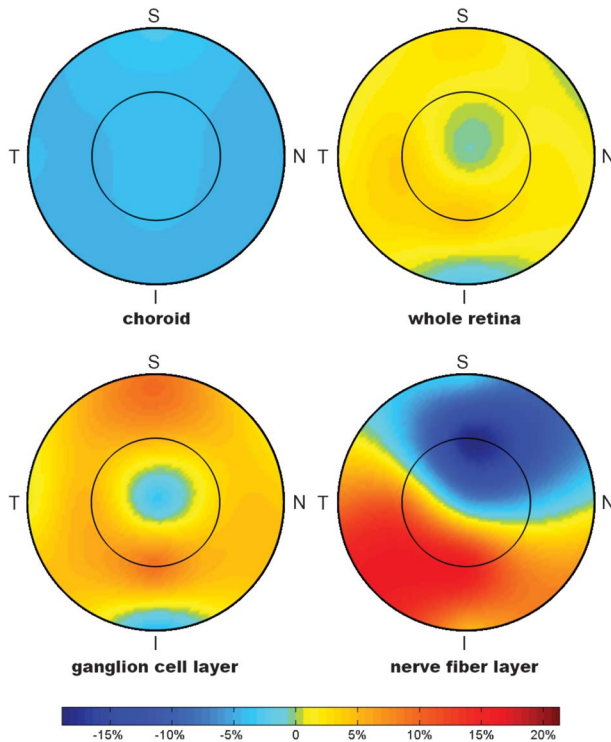
Fig. 1. Longitudinal changes of choroid and retinal layers in children with myopic shift. The colors denote percent changes in the thickness of each layer between the baseline examination and the 1-year follow-up. No thickness change is shown in green, whereas cold colors (blue to purple) denote interim thinning and warm colors (yellow to red) denote interim thickening.

SER (r = 0.25, P = 0.02), no other association was found between changes of parafoveal/perifoveal choroidal thickness and changes in SER or AL (P > 0.05 for all comparisons).

During the study period, most subfields of the whole retina, the ganglion cell layer, and the nerve fiber layer were thickened, except for the inferior perifoveal retina and ganglion cell layer, and the superior parafoveal nerve fiber layer was attenuated compared with baseline (Table 3 and Figure 1). Thickness changes of the inferior perifoveal retina were the sole factor correlated with changes in SER (r = 0.23, P = 0.03). No other changes in the parafoveal or perifoveal retinal layers were related to changes in AL.

Discussion

To the best of the authors' knowledge, this is the first longitudinal study to investigate the changes in pediatric choroid and retinal layers and to explore their relationship with myopic shift. Our results suggested that children with myopic shift concurrently had decreasing choroidal thickness in all regions, but the retinal thickness in most subfields were stable or

increasing. Both AL and choroidal thickness were independently associated with the myopic shift, but increased AL was not related to decreases in choroidal thickness.

Compared with children without myopic shift, children with myopic shift had smaller SER and higher AL/CR at baseline, indicating the potential for using AL/CR as a predictor of myopic shift. All children had increased AL and decreased ganglion cell layer at follow-up. Children with myopic shift had a more rapid AL increase compared with the others, but the speed of ganglion cell layer thinning was similar between the two groups.

Contradictory data have been obtained for changes in the choroid during development. Some cross-sectional studies reported increased subfoveal choroidal thickness with age,[5,14–16] whereas others reported the opposite findings.[17,18] Changes in choroidal thickness during development in each participant may be relatively small compared with the thickness differences between individuals, which may skew data. In our longitudinal study, decreased choroidal thickness was observed in children with myopic shift, but no choroidal changes occurred for those without myopic shift. These data contradict the findings of a previous prospective study of Australian children,[11] which indicated significant increases of average choroidal thickness in both myopic and nonmyopic children; however, this study also described that participants with faster AL growth had less choroidal thickening, and some even showed choroidal thinning, which is similar to our findings. Aside from population differences,[19] such inconsistency may be due to differences in study design. The previous study stratified based on baseline refractive status, whereas our study correlated refractive changes with choroidal changes. Evidence suggests that AL elongation and other biometric changes occur most rapidly within 12 months before and after the onset of myopia;[20,21] so, using baseline refractive status to stratify participants may not be sufficiently sensitive for detecting decreased choroidal thickness.

Our data showed that AL growth and central foveal choroidal thinning were independently associated with myopic shift, which is consistent with findings of previous studies in children and adults[4–7] However, a longer AL was not related to choroidal thinning in our study. Former studies indicate that the choroid may facilitate axial growth by modulating remodeling of the scleral extracellular matrix.[8,9] The absence of an association between AL increases and choroid thickness decreases in our study implies that these changes may be governed by different mechanisms during the development of myopia, and that choroidal thinning in

myopia may not simply be a mechanical sequela of globe elongation. However, our study was small and may not be of sufficient power to capture an association between AL increase and choroidal thinning.

Among children with myopic shift, differences were noticed when participants were stratified based on finial refractive status. For hyperopes, significant thinning of the central foveal ganglion cell layer was observed, but no choroidal changes occurred. Decreasing SER was related to AL elongation. But for myopes with a myopic shift, a significant decrease in choroidal thickness was observed, and no change occurred to the ganglion cell layer. Furthermore, choroidal thinning, retinal thinning, and AL increases were all independently related to myopic shift. Although the accuracy of the regression analysis was limited by the small sample size, these differences suggested that distinctive mechanisms may exist between emmetropization and myopia development. Emmetropization is a normal process during eye development, during which the AL in a hyperopic eye increases until the eye becomes emmetropic. By contrast, development of myopia may be viewed as a pathologic process where the myopic shift during emmetropization fails to halt once the eye is emmetropic. In summary, our data suggest that central foveal ganglion cell layer thinning may be a physiologic finding, whereas choroidal thinning may be a pathologic finding of uncontrolled myopic shift during development.

Topographically, during myopic shift, the thickness of the choroid decreased in all regions, and the thinning of central foveal and superior parafoveal choroid correlated with decreased SER. By contrast, although the central foveal ganglion cell layer thickness decreased, showed a decreased thickness, no longitudinal changes was observed in the central foveal whole retina and nerve fiber layer thickness, and most subfields of retinal layers were unchanged or thickened. Only the inferior perifoveal retinal thickness decreased with SER changes. These findings suggest that during myopic shift, choroidal thinning may occur before retinal thinning. To confirm this, we would need to study the same population for years to observe changes of the choroid and retinal layers over time.

The perifoveal choroid circle was attenuated more than the parafoveal and central choroid, suggesting that choroidal thinning probably starts peripherally during early myopia development, and may result in a subtle relative peripheral hyperopia, which is recognized as a predictor of myopia progression by former studies.[22] Our study implies that peripheral choroidal thinning might occur first in the process of peripheral hyperopia, and could be a potential sensitive predictor of myopia development.

The main limitation of our study is the small sample size, especially for subgroups with myopic shift divided by follow-up refraction status, which may be insufficiently powered to elucidate subtle relationships between different biometric and anatomical measurements. Also, because the number of children with hyperopic shift was small, we combined them with those with no refractive shift as children with no myopic shift; thus, the characteristics of children with hyperopic shift were not discussed in this article. We will repeat this study with more participants in the future to confirm our findings, and to explore the effect of different myopia treatments on retinal and choroidal thicknesses.

In conclusion, our study demonstrates that during pediatric myopic shift, choroidal thickness decreased in all regions, but the retina thickened or was unchanged in most areas, indicating that choroidal thinning may occur before retinal thinning during early myopic progression. Myopic shift was independently associated with AL growth and choroidal thinning, whereas AL increase was not related to decreases in choroidal thickness; thus, a thinning choroid may not simply be secondary stretching effects of eye elongation. Different mechanisms may underlie physiological and pathologic myopic shifts. Ganglion cell layer thinning may be a physiological process in emmetropization, whereas choroidal thinning may relate to the development of myopia.

Key words: choroid, children, myopia, retina, swept-source optical coherence tomography (SS-OCT).

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