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# Development of the retina and its relation with myopic shift varies from childhood to adolescence

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## ABSTRACT

**Aims** To elucidate the influence of age and myopic shift on retinal development.

**Methods** This 1-year longitudinal study included 769 participants aged 6–17 years. Cycloplegic refraction, axial length and swept-source optical coherence tomography were examined at baseline and follow-up. The thickness changes in the retina, ganglion cell complex (GCC) and outer retinal layers (ORL) in the macular region were calculated, and their relation with age and myopic shift was analysed with multiple linear regression analysis.

**Results** The thickness of the central foveal retinal layers was increased in children (<10 years) but unchanged or decreased in adolescents (>13 years). The thickness changes in the retina, GCC and ORL decreased with age ( $r=-0.24, -0.23, -0.15$ , respectively, all  $p<0.01$ ). Multiple regression analysis showed that the changes in central foveal retinal thickness (RT) and GCC thickness were independently associated with age and baseline spherical equivalent (SE), while the changes in ORL thickness were associated with age and SE changes. In children 8–9 years, a greater increase was observed in central foveal ORL thickness in those with no myopic shift ( $p<0.01$ ). The thickness of the most parafoveal and perifoveal retinal layers was less increased or more decreased in children <9 years with myopic shift ( $p<0.05$ ).

**Conclusions** Retinal development and its relation with myopic shift varies from childhood to adolescence. Myopia-related retinal thinning may result from less increase in the RT in childhood rather than a decrease in RT in adolescents. Children under 9 years old could be at a critical age for future myopia-related retinal thinning.

## INTRODUCTION

Myopia has become a global public health concern because of its soaring prevalence and severe complications.<sup>1,2</sup> The attenuated retina plays a critical role in several severe myopic complications, such as myopic maculopathy and rhegmatogenous retinal detachment.<sup>3</sup> Previous studies found that parafoveal and perifoveal retinal thickness (RT) decreases significantly with axial length (AL) in adults,<sup>4–8</sup> and some studies also reported similar findings in children.<sup>9–12</sup> However, so far, it is unclear when this thinning process begins and how it affects the development of the retina in childhood and adolescence.

Apart from refractive status, age is also closely related to RT in children and adolescents. Previous studies indicated that central foveal RT increases with age by approximately 1.8  $\mu\text{m}$  per year in

children 4–15 years old.<sup>13,14</sup> Thus, the direction and magnitude of RT change and its relation with myopic shift are very likely to be different in young people of different age groups and differ in the same person from childhood to adolescence. However, to date, previous studies have not reported the relation between myopia and retinal development in different age groups. Read *et al*<sup>15</sup> found that myopia was associated with a small decrease in parafoveal RT in 102 children aged 10–15 years (<2  $\mu\text{m}$  over 18 months). Our previous study<sup>16</sup> indicated that central foveal RT was unchanged, and most parafoveal and perifoveal subfields were increased or unchanged in 88 children with myopic shift. These inconsistent results may result from the participants' age differences.

This study aimed to elucidate the influence of myopia on retinal development in children and adolescents. The longitudinal changes in whole retina, ganglion cell complex (GCC), and outer retinal layer (ORL) thickness over 1 year were investigated in 769 participants from 6 to 17 years old, and the thickness change of each retinal layer and its relation with myopic shift were analysed in different age groups.

## METHODS

### Setting and participants

This 1-year longitudinal study was a part of our former cross-sectional study, which included participants randomly selected by cluster sampling from four primary and middle schools in Jiading District in Shanghai, China.<sup>16</sup> The baseline study was conducted in December 2015, and 1 year later, a total of 775 students from the same cohort participated in the follow-up study and received the same examinations. According to our previous study,<sup>17</sup> a total of 1244, 282 and 108 participants were required to detect the difference in RT changes between children with and without myopic shift in the central foveal, parafoveal and perifoveal regions, respectively ( $\alpha=0.05$ , power=0.9,  $n_1:n_2=1:1$ ). Thus, the number of participants in this study may not have been enough to reveal the difference in central foveal RT change between groups.

The inclusion criteria were best-corrected visual acuity  $\geq 20/25$ , no previous intraocular surgery history, and no severe eye diseases (including amblyopia, strabismus, ptosis, congenital cataracts, glaucoma and fundus diseases). Participants were excluded if they were unable to cooperate or if the optical coherence tomography (OCT) images were still unclear after being retaken (signal strength



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**Table 1** Characteristics of the participants at baseline and follow-up and the difference between sexes (mean±SD)

Parameters	Total (n=769)	Boys (n=409)	Girls (n=360)	P value†
Age (y)				
Baseline	10.90±3.10	10.81±3.04	11.00±3.17	0.39
SER (D)				
Baseline	-0.52±2.25	-0.35±2.06	-0.72±2.43	0.02
Follow-up	-0.95±2.41	-0.76±2.23	-1.16±2.58	0.02
Change	-0.43±0.47*	-0.42±0.47*	-0.44±0.47*	0.59
AL (mm)				
Baseline	23.75±1.23	23.93±1.17	23.56±1.27	<0.01
Follow-up	24.00±1.23	24.19±1.17	23.78±1.27	<0.01
Change	0.24±0.28*	0.26±0.27*	0.22±0.28*	0.08
RT (µm)				
Baseline	233±19	237±18	229±19	<0.01
Follow-up	236±21	239±19	232±22	<0.01
Change	2±13*	2±13*	3±13*	0.19
GCC (µm)				
Baseline	53±10	55±10	51±10	<0.01
Follow-up	53±12	55±11	51±12	<0.01
Change	0±10	-1±10	0±9	0.41
ORL (µm)				
Baseline	180±15	182±12	178±12	<0.01
Follow-up	183±12	184±11	181±13	<0.01
Change	3±6*	2±6*	3±7*	0.13

\*P<0.05 for comparison between baseline and follow-up using a paired t-test.  
†P for comparison between boys and girls using a t-test.  
AL, axial length; GCC, ganglion cell complex; ORL, outer retinal layer; RT, retinal thickness; SER, spherical equivalent refraction.

index <60). The research team consisted of one ophthalmologist, five optometrists, two public health physicians and two nurses. The investigation site was located within the schools.

All of the participants and their guardians understood the study protocol and signed informed consent forms.

## Research methods

Detailed examination procedures were described previously.<sup>16</sup> Briefly, the age and sex of the participants were recorded from state-issued identification cards, and their heights and weights were measured at the site. Each participant underwent a series of comprehensive ophthalmic examinations, including visual acuity, sensorimotor examination, slit-lamp biomicroscopy and fundus examination. These examinations were followed by several ancillary tests, including tonometry, cycloplegic refraction, corneal curvature, AL and OCT. Visual acuity was measured using a retro-illuminated Early Treatment of Diabetic Retinopathy Study (ETDRS) chart at a distance of 4 m. The intraocular pressure was measured by a non-contact tonometer (model NT-4000, Nidek, Fremont, California, USA) before dilation, and the AL was measured using noncontact optical biometry (IOL Master, V.5.02, Carl Zeiss Meditec, Oberkochen, Germany). Cycloplegia was achieved by administering one drop of topical 0.5% proparacaine (Alcaine, Alcon, Fribourg, Switzerland), followed by two doses of 1% cyclopentolate (Cyclogyl, Alcon, Fribourg, Switzerland), applied 5 min apart. After 30 min, 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 measurements were performed with a

desk-mounted autorefractor (model KR-8900, Topcon, Tokyo, Japan).

Swept source-OCT (SS-OCT, model DRI OCT-1 Atlantis, Topcon, Tokyo, Japan) with a lateral resolution of 20 µm and an in-depth resolution of 8 µm was used to measure the thickness of macular retinal layers. A radial scan with 12 lines centred on the fovea and separated by 30° was used to capture OCT images. Multiple B-scan averaging was used to improve the image details, and each OCT image was the overlapping of 48 B-scans. Each OCT image took 1–2 min to acquire. To ensure that the scan location was the same as in the baseline examination, the follow-up mode was used when performing the examinations at the follow-up visit. One experienced technician performed both baseline and follow-up visits between 10:00 and 15:00 hours to ensure the repeatability of OCT measurements. Scans were retaken if poor alignment, low signal strength (signal strength index <60), blinks (black lines across the image) or motion artefacts (shearing or breaks of the vessel pattern) took place. To determine the repeatability of the measurements, 21 participants were randomly selected and examined by the specific technician twice, and the Bland-Altman plot showed good repeatability of the RT, GCC and ORL measurements, with a mean differences between 0.03 and 1.53, and the biggest 95% limits of agreement (95% LoA) smaller than 11 µm (online supplemental figures 1–3).

Built-in software was used to segment the layers and construct topographic maps. All acquired images were inspected, and manual segmentation and adjustment were performed if necessary. The personnel who performed the manual segmentation were masked to the participants' other information. RT was defined as the distance from the internal limiting membrane to the interface between the retinal pigment epithelium and the Bruch membrane. GCC was defined as the distance from the internal limiting membrane to the interface between the inner plexiform layer and inner nuclear layer. ORL was defined as the distance from the interface between the inner plexiform layer and inner nuclear layer to the interface between the retinal pigment epithelium and the Bruch membrane. The ETDRS grid was applied accordingly, which divided the macula into three concentric circles centred 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 divided into superior, inferior, temporal and nasal subfields. The average thickness of the retina, GCC and ORL within each subfield was calculated automatically. Detailed image acquisition and analysis procedures are described elsewhere.<sup>16–18</sup>

## Statistical analysis

All data were doubly entered independently by two research associates, and the discrepancies were adjudicated. SAS (V.8.0, SAS Institute) was used for all statistical analyses. Only the right-eye data were used in the analysis to avoid intereye dependencies. Spherical equivalent refraction (SER) was used to classify the refractive status, SER=sphere power+(cylinder power)/2. Myopia was defined as SER≤-0.5 diopter (D), and hyperopia was defined as SER≥0.5 D. Myopic shift was defined as a SER decrease of more than 0.5 D from baseline to follow-up measurement.

The data distribution was examined using the Kolmogorov-Smirnov test. All of the SS-OCT measurements were normally distributed. The required sample size was

**Table 2** Longitudinal changes in participants with or without myopic shift across the age groups (mean±SD)

Parameters	Total (n=769)	Age 6–7 years (n=154)	Age 8–9 years (n=238)	Age 10–11 years (n=97)	Age 12–13 years (n=120)	Age 14–15 years (n=101)	Age 16–17 years (n=59)	P value
<b>SER (D)</b>								
Total	-0.43±0.47*‡	-0.37±0.53*‡	-0.46±0.52*‡	-0.52±0.48*‡	-0.44±0.41*‡	-0.36±0.32*‡	-0.36±0.33*‡	0.04
Myopic shift	-0.85±0.33*‡	-0.92±0.39*‡	-0.91±0.35*‡	-0.92±0.33*‡	-0.79±0.24*‡	-0.67±0.18*‡	-0.67±0.19*‡	<0.01
Non-myopic shift	-0.09±0.23*‡	-0.03±0.25	-0.05±0.25†	-0.13±0.21*‡	-0.09±0.19*‡	-0.16±0.21*‡	-0.16±0.23*‡	<0.01
P value	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	
<b>AL (mm)</b>								
Total	0.24±0.28*‡	0.33±0.30*‡	0.27±0.33*‡	0.28±0.23*‡	0.21±0.17*‡	0.13±0.20*‡	0.08±0.10*‡	<0.01
Myopic shift	0.36±0.31*‡	0.54±0.33*‡	0.40±0.39*‡	0.40±0.15*‡	0.28±0.16*‡	0.19±0.25*‡	0.12±0.09†	<0.01
Non-myopic shift	0.15±0.20*‡	0.20±0.20*‡	0.16±0.23*‡	0.17±0.25*‡	0.13±0.15*‡	0.09±0.15*‡	0.05±0.11†	<0.01
P value	<0.01	<0.01	<0.01	<0.01	<0.01	0.02	0.01	
<b>RT (µm)</b>								
Total	2±13*‡	7±15*‡	4±14*‡	1±9	0±12	-2±11	-2±10	<0.01
Myopic shift	2±12*‡	8±17*‡	2±12	0±11	1±8	-1±11	-2±10	<0.01
Non-myopic shift	3±14*‡	7±14*‡	6±15*‡	1±8	0±15	-2±11	-2±11	<0.01
P value	0.34	0.80	0.05	0.43	0.57	0.58	0.76	
<b>GCC (µm)</b>								
Total	0±10	3±12*‡	0±9	-1±8	-2±9*‡	-3±8*‡	-3±8*‡	<0.01
Myopic shift	0±9	5±14†	0±8	-2±9	-2±7†	-3±8†	-4±5*‡	<0.01
Non-myopic shift	0±10	3±10†	1±10	-1±6	-3±11	-3±8*‡	-3±9	<0.01
P value	0.79	0.29	0.49	0.31	0.70	0.96	0.57	
<b>ORL (µm)</b>								
Total	3±6*‡	4±5*‡	3±8*‡	2±5*‡	3±6*‡	1±5	1±5	<0.01
Myopic shift	2±6*‡	3±5*‡	2±6*‡	2±5†	3±5*‡	2±5†	2±7	0.81
Non-myopic shift	3±7*‡	4±5*‡	5±9*‡	2±4*‡	2±6*‡	1±5	0±4	<0.01
P value	0.07	0.11	<0.01	0.98	0.56	0.51	0.25	

\*P&lt;0.01.

†P&lt;0.05.

‡P&lt;0.05 after Bonferroni correction.

AL, axial length; GCC, ganglion cell complex; ORL, outer retinal layer; RT, retinal thickness; SER, spherical equivalent refraction.

calculated using two-sample t-test power analysis. 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. Categorical variables were compared using the  $\chi^2$  test. Linear correlation analysis was used to analyse the factors related to the changes in RT, GCC thickness and ORL thickness; subsequently, the factors with significant correlations were further analysed using stepwise multiple linear regression analysis to explore the independent factors associated with the changes in the RT, GCC thickness and ORL thickness.

Statistical significance was defined as  $p < 0.05$  (two tailed). Bonferroni correction was used to adjust for multiple comparisons. The characteristics are presented as the mean±SD for normally distributed continuous variables and as the number (percentage) for categorical data.

## RESULTS

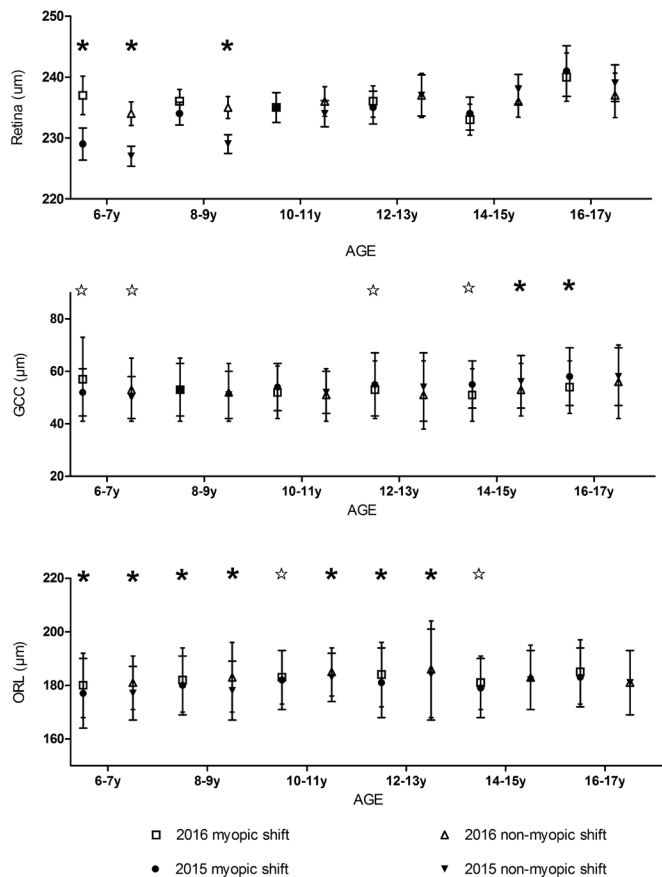
Among the 775 participants, six were excluded for unclear OCT images or poor cooperation; thus, a total of 769 participants with a mean age of  $10.90 \pm 3.10$  years old were enrolled in this study, and 53.18% of the participants were boys. The baseline thickness of the participants' central fovea retinal layers and SER, AL are shown in table 1. There was no significant difference in age between sexes. Although girls tended to be more myopic, their AL was shorter than that of boys. Boys had significantly thicker central fovea RT, GCC and ORL than girls at baseline (all  $p < 0.01$ ).

After 1 year of follow-up, an average myopic shift of  $-0.43 \pm 0.47$  D and an increased AL of  $0.24 \pm 0.28$  mm were observed in the participants. A mean increase of  $2 \pm 13$  µm and  $3 \pm 6$  µm was observed in the central foveal RT and ORL, respectively, while GCC thickness was unchanged. There was no significant difference in the changes in SER, AL, RT, GCC or ORL between sexes (table 1). A total of 344 (44.73%) participants developed myopic shift. No difference in the incidence of myopic shift was found between sexes (girls 47.98% vs boys 42.17%,  $p = 0.17$ ).

### Changes in the thickness of the central fovea RT, GCC and ORL with age and myopic shift

The changes in SER and AL and the changes in central fovea RT, GCC thickness and ORL thickness of each age group are listed in table 2. The extent of AL growth decreased with increasing age, especially in those with myopic shift ( $r = -0.40$ ,  $p < 0.01$ ). Meanwhile, in children with myopic shift, the extent of the SER decrease was also reduced with age ( $r = -0.30$ ,  $p < 0.01$ ). Those under 12 years old had the most significant myopic shift and AL growth ( $p < 0.01$ ).

In all participants, both with and without myopic shift, the central fovea RT was increased in children under 10 years old, and a mean increase of  $7 \pm 15$  µm and  $4 \pm 14$  µm was observed in those 6–7 and 8–9 years old, respectively. However, in adolescents over 13 years old, a decreasing trend was observed, although the thinning was not statistically significant. Similar to the changes in RT, the GCC



**Figure 1** The central fovea RT, GCC and ORL in participants with and without myopic shift in each age group at baseline and after the follow-up. \* $P < 0.01$  and  $p < 0.05$  after Bonferroni correction, ☆ $p < 0.05$ . GCC, ganglion cell complex; RT, retinal thickness; ORL, outer retinal layers.

thickness was increased during the follow-up in children under 8 years old, with a mean change of  $3 \pm 12 \mu\text{m}$ , but decreased in the older participants, with a mean change of  $-2 \pm 9 \mu\text{m}$  in those 12–13 years old and a mean decrease of  $-3 \pm 8 \mu\text{m}$  in those over 13. Unlike RT and GCC, the central fovea ORL was thickened during the follow-up in all age groups, but the thickening was not statistically significant in those over 14 years old (table 2, figure 1).

No significant difference was observed in the longitudinal changes in central foveal RT and GCC thickness between participants with and without myopic shift; however, the

**Table 3** Correlation coefficients between changes in ocular components and baseline characteristics (r value)

	RT change	GCC change	ORL change
Baseline age	-0.24*†	-0.23*†	-0.15*†
Sex	0.05	0.03	0.05
Baseline BMI	-0.15*†	-0.14*†	-0.12*†
BMI change	0.03	0.05	-0.01
Baseline AL	-0.21*†	-0.18*†	-0.18*†
AL change	0.06	0.10*†	-0.02
Baseline SER	0.22*†	0.21*†	0.16*†
SER change	0.04	-0.01	0.09†

\* $P < 0.01$ .

† $P < 0.05$ .

‡ $P < 0.05$  after Bonferroni correction.

AL, axial length; BMI, body mass index; GCC, ganglion cell complex; ORL, outer retinal layer; RT, retinal thickness; SER, spherical equivalent refraction.

increase in the central fovea ORL was more significant in those without myopic shift ( $5 \pm 9 \mu\text{m}$ ) than in those with myopic shift ( $2 \pm 6 \mu\text{m}$ ) in children 8–9 years old ( $p < 0.01$ ) (table 2).

**Factors associated with the thickness changes of the central fovea RT, GCC and ORL**

Linear correlation analysis showed that the longitudinal thickness changes in the RT, GCC and ORL decreased with age, baseline body mass index, and baseline AL and increased with baseline SER. Moreover, the changes in the GCC increased with the changes in AL, and the changes in ORL increased with the changes in the SER. The correlation coefficient and the corresponding p value of each factor are listed in table 3.

The factors related to the changes in RT, GCC thickness and ORL thickness were selected to further enter the multiple linear regression stepwise analysis. The changes in central foveal RT and GCC thickness were independently associated with age and baseline SER, while the changes in ORL were independently associated with age and SER changes. The regression coefficients of each factor are listed in table 4. The determination coefficients ( $R^2$ ) of the models were 0.0657, 0.0587 and 0.0323 for RT, GCC and ORL, respectively. According to the models, younger age and a higher baseline SER were related to a greater increase in the central foveal RT and GCC thickness, and a younger age and a less myopic shift were related to a greater central foveal ORL increase.

**The changes in the parafoveal and perifoveal RT, GCC thickness and ORL thickness with age and myopic shift**

The changes in parafoveal and perifoveal RT, GCC thickness and ORL thickness are shown in figure 2 and online supplemental tables 1–3. RT and GCC thickness were significantly decreased in the perifoveal superior and parafoveal inferior subfields and increased in the parafoveal superior and perifoveal inferior subfields. The ORL thickness was decreased in the superior quadrant and increased in the inferior quadrant. The changes in the horizontal quadrants were relatively small, but in adolescents 16–17 years old, a significant decrease in temporal ORL and nasal GCC and a significant increase in temporal GCC and nasal ORL thickness were observed.

Moreover, in all subfields except for the parafoveal inferior region, those with myopic shift showed less increased or more decreased RT, GCC thickness and ORL thickness than those with no myopic shift, but the difference was only statistically significant in several regions in children under 9 years old ( $p < 0.05$ ). The differences in parafoveal and perifoveal RT, GCC thickness and ORL thickness between children with and without myopia were smallest in those 14–15 years old (figure 2, online supplemental tables 1–3).

**DISCUSSION**

This longitudinal study indicated that the direction and magnitude of the changes in RT, GCC thickness and ORL thickness are different in children and adolescents. Moreover, myopia-related retinal thinning may result from a less increased RT in childhood rather than a decreased RT in adolescence. Children under 9 years old may be at a critical age for myopia-related retinal thinning.

**Table 4** Multiple regression analysis of factors associated with retinal layer thickness changes

	RT			GCC			ORL		
	coefficient	Standard coefficient	P value	coefficient	Standard coefficient	P value	coefficient	Standard coefficient	P value
Intercept	10.07±2.03	0	<0.01*	5.26±1.47	0	<0.01*	6.67±0.83	0	<0.01*
Baseline age	-0.67±0.19	-0.16	<0.01*	-0.50±0.14	-0.16	<0.01*	-0.31±0.07	-0.16	<0.01*
Baseline SER	0.75±0.26	0.13	<0.01*	0.45±0.19	0.11	0.02	/	/	/
SER change	/	/	/	/	/	/	1.22±0.47	0.09	<0.01*

R<sup>2</sup> for the RT model=0.0657; R<sup>2</sup> for the GCC model=0.0587; R<sup>2</sup> for the ORL model=0.0323.

\*P<0.05 after Bonferroni correction.

GCC, ganglion cell complex; ORL, outer retinal layer; RT, retinal thickness; SER, spherical equivalent refraction.

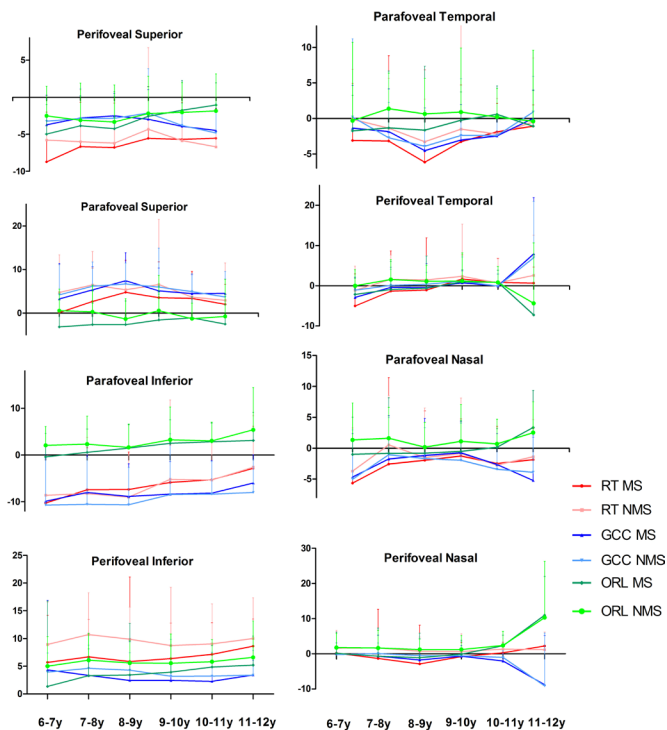
First, our results revealed that the central fovea RT, GCC thickness and ORL thickness were increased in children (<10 years) but unchanged or even decreased in adolescents (>13 years), and the longitudinal changes in the central fovea RT, GCC thickness and ORL thickness decreased with age. This was consistent with a former study, which observed a large increase in RT occurring throughout infancy and early childhood that stabilised to adult levels by approximately the age of 12.<sup>19</sup> Moreover, our study further suggested that the development of the GCC stops earlier at the age of 8, and the development of the ORL stops later, at the age of 14. We observed that the central fovea GCC thickness increased in children under 8 years old but decreased in older participants, while the central fovea ORL thickened in those under 14 years old but remained unchanged afterwards. Two former cross-sectional studies indicated that central foveal RT increases with age by approximately 1.8 µm per year in children 4–15 years old,<sup>13 14</sup> while in our study, the increase in RT only occurred in those under 10 years old (7 µm for the 6–7 years age group and 4 µm for the 8–9 years age group). This inconsistency may result from different study designs. These studies did not take the participants' refractive status into analysis; thus, they

only revealed a relation between age and RT, which could be caused by other factors such as refractive status. Our results were consistent with a former longitudinal study<sup>15</sup> of children 10–15 years old, which found no retinal layer thickness change during the 18 months follow-up. Thus, the current study provided a better understanding of children's RT changes over time.

Moreover, our results also indicated an increased superior (2–5 µm) and a decreased inferior (-3 to -10 µm) RT in the parafoveal region and an increased inferior (6–9 µm) and a decreased superior (-6 to -9 µm) RT in the perifoveal region. Compared with our study, a former longitudinal study<sup>15</sup> reported smaller thickness changes in retinal layers in the parafoveal and perifoveal regions (<2 µm in 18 months). This might result from differences in the data analysis methods. The previous study only reported the mean thickness change of the four quadrants in the parafoveal and perifoveal regions, which could cause the counteraction of the RT changes between superior and inferior regions, thus resulting in a smaller mean change.

Second, we compared the thickness change between participants with and without myopic shift, and found that in children 8–9 years old, the increase in the central fovea ORL was more significant in those without myopic shift, and the regression analysis showed that the changes in ORL thickness were independently associated with age and SER changes. Moreover, in children under 10 years old, the retinal layers of most parafoveal and perifoveal regions were less increased or more decreased in those with myopic shift. This was consistent with a former study,<sup>15</sup> which reported a significantly greater increase in nerve fibre layer in non-myopic children than in myopic children. Our results not only revealed that the effect of myopia on retinal development is age-specific but also suggest a critical age range for myopia development. This implies that the thinner retinal layers observed in myopic children and adolescents are not from attenuation in the developed retina in adolescence but from interference with retinal development in childhood. Thus, patients with an early onset (<10 years) of myopia may be more likely to have a thinner retina in early adulthood, which leads to the early occurrence of severe myopic complications. Moreover, this finding also implies that myopia-related retinal thinning probably starts from peripheral regions and the ORL.

It should be noted that although the RT changes observed during the follow-up were statistically significant in several regions and age groups, the change magnitude was generally small (<8 µm). Considering the 8 µm in-depth resolution of the SS-OCT used in the current study and the repeatability of the OCT measurements (95% LoA=(-9.19, 10.89) in central foveal macular retina), the longitudinal changes could result from system error. This may also explain the inconsistency between the current study and our previous one.<sup>16</sup> Some parafoveal and perifoveal regions showed a small magnitude of RT increase in



**Figure 2** Changes in parafoveal and perifoveal RT, GCC and ORL in participants with and without myopic shift in each age group. GCC, ganglion cell complex; RT, retinal thickness; ORL, outer retinal layers.

our previous study<sup>16</sup> but were decreased in the current study. Similarly, the difference in the longitudinal changes between participants with and without myopic shift was of small magnitude. Thus, the difference only showed a tendency towards retinal thinning in children under 10 with myopic shift, but the difference is unlikely to be of clinical significance. This indicated that for children above 6, the changes in RT, GCC thickness and ORL thickness related to myopic shift are relatively subtle.

The biggest limitation of this study was the relatively short follow-up period. Although myopic shift occurs fast and very often in Chinese children, the structure of the retina changes slowly because it mostly consists of neurons. This limitation is partly addressed by the wide age range of our participants, yet a longer observation period may reveal more important findings about the relation between retinal development and myopia. Moreover, the sample size of the current study was not large enough to detect the difference in central foveal RT changes between children with and without myopic shift. Furthermore, the magnification was not corrected before image capture in our study, which could impact the results. However, our previous study (not yet published), which enrolled 149 children with a mean age of 12.51 and mean AL and spherical equivalent of 24.74 mm (range: -9.63 to 2.25) and -2.64 D (range: 22.09 to 29.30), respectively, showed no significant difference in RT before and after magnification correction in all nine sectors of the ETDRS grid, especially in the central fovea (the difference was  $-0.054\ \mu\text{m}$ ,  $t=-0.08$ ,  $p=0.940$ ). Therefore, the current results are expected to be credible. We will perform magnification correction before image capture in future studies, thus we expect more accurate results. Finally, our findings may only apply to Chinese children because of racial differences.

In conclusion, this study indicated that the development of the retina and its relationship with myopia varies from childhood to adolescence. Children under 9 years old could be susceptible to myopia-related retinal thinning.

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