



# Changes in Choroidal Thickness of Healthy **Children during Myopia Progression over 4** Years: Boramae Myopia Cohort Study Report 5

Jeong Hyun Lee, MD, MSc,<sup>1,\*</sup> Joo Young Shin, MD, PhD,<sup>1,\*</sup> Martha Kim, MD, PhD,<sup>2</sup> Kyoung Min Lee, MD, PhD,<sup>1</sup> Sohee Oh, PhD,<sup>3</sup> Seok Hwan Kim, MD, PhD,<sup>4</sup> Ho-Kyung Choung, MD, PhD,<sup>1</sup> Jeeyun Ahn, MD, PhD<sup>1</sup>

Objective: To investigate the relationship between choroidal thickness and myopia by analyzing change in choroidal thickness over time in children with myopia progression.

**Design:** Retrospective cohort study.

Participants: Children with myopia.

Methods: Spherical equivalent (SE), axial length, and choroidal thickness were measured every 2 years during course of 4 years in children with myopia enrolled in a prospective cohort study. Choroidal thickness was evaluated at 13 points on the ETDRS grid, and its longitudinal changes as myopia progresses were analyzed. Patients were categorized into 2 subgroups: progression group (SE change < -0.5 diopters [D] over 2 years) and stable group (SE change > -0.5D over 2 years).

Main Outcome Measures: Spherical equivalent of refractive errors, axial length, and choroidal thickness.

**Results:** A total of 46 eyes from 23 participants were included, with a mean baseline age of 9.6  $\pm$  1.7 years. The SE values at baseline, 2-year follow-up, and 4-year follow-up were  $-4.26 \pm 2.34$  D,  $-5.62 \pm 2.45$  D, and  $-8.67 \pm 2.47$  D, respectively, indicating an average myopia progression of 4.41 D over the 4-year period. During the initial 2 years, no significant thinning of choroidal thickness was observed at any of the 13 measured points. However, during the following 2 years, significant choroidal thinning was identified at 9 of the 13 points (P < 0.05). In the subgroup analysis of the subsequent 2 years, the progression group exhibited significant thinning at 8 points, while the stable group still showed no significant changes in choroidal thickness at any point.

Conclusions: In the early phase of myopia progression within moderate degree, choroidal thickness remained unchanged. However, when progressed to high myopia, significant choroidal thinning occurred, specifically in the progression group. In contrast, the stable group maintained consistent choroidal thickness throughout the study. These results suggest that choroidal thinning in children varies according to the degree of myopia that develops.

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Myopia has emerged as a significant global public health and socioeconomic concern, with its prevalence particularly high in East Asia.<sup>1,2</sup> Reports indicate an incidence of 49.7% to 62.0% in East Asian countries, markedly higher than that of non-Asian or other Asian regions, where it ranges between 6.0% and 20.0%.<sup>3</sup> Myopia typically develops during school years and tends to stabilize during adolescence.<sup>4</sup> In the Correction of Myopia Evaluation Trial (COMET) cohort, which included a large ethnically diverse group of children with myopia, the mean age at stabilization was 15.61 years, with a spherical equivalent (SE) of -4.87diopters (D).<sup>2</sup>

Although the pathogenesis of myopia progression is not fully understood, evidence suggests that the choroid plays an important role. Chemical signals initiating in the retina may influence the scleral extracellular matrix via the highly vascularized choroid, contributing to myopia development

a cross-sectional study and found significant increases in choroidal thickness in older children in both myopes and nonmyopes, whereas Jin et al<sup>10</sup> reported choroidal thinning during myopia progression in a 1-year longitudinal study, but with no significant changes among children without myopia progression. Similarly, Fontaine et al<sup>11</sup> found increasing choroidal thickness in children without myopia at baseline but thinning in those with myopia at baseline in a 15-month longitudinal study. These discrepancies may stem from differences in age, baseline refractive errors, or ethnic composition among the studies.

and progression.<sup>6</sup> Several studies using OCT have examined

choroidal thickness in children and adolescents. Cross-

sectional studies generally report an increase in choroidal

thickness with age, while longitudinal studies indicate varying relationships between choroidal thickness and

refractive changes.<sup>7-10</sup> For example, Read et al<sup>7</sup> performed

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Understanding the dynamic relationship between myopia progression and changes in choroidal thickness requires serial measurements over an extended period, ideally until myopia stabilizes. A recent study measured choroidal thickness of children (mean age of 9.3 years) annually over a 2-year period, revealing some insights.<sup>12</sup> However, given the prolonged time required for myopia to stabilize after onset, 2 years may not be sufficient to capture meaningful trends. Thus, in this study, we measured choroidal thickness every 2 years over a 4-year period in children with progressive myopia. By extending the observation period, we aimed to clarify the relationship between myopia progression and changes in choroidal thickness.

# Methods

## Subjects

This study reviewed medical records from the Boramae Myopia Cohort study, a prospective investigation of children with myopia.<sup>13–15</sup> Eligible participants were children <13 years of age with myopia, defined as an SE of  $\leq$ -0.75 D in cycloplegic refraction. Enrollment of participants occurred between February 2013 and September 2014. Exclusion criteria included a history of ocular surgery, significant ocular disease, poor OCT image quality, or lack of adherence to follow-up visits. All participants underwent comprehensive ophthalmic evaluations, including best-corrected visual acuity assessment, cycloplegic refraction testing, slit-lamp biomicroscopy, intraocular pressure measurement, dilated fundus

examination, keratometry (RKT-7700; Nidek), and axial length measurement (IOL Master version 5; Carl Zeiss Meditec). Choroid thickness was evaluated using spectral-domain OCT (Spectralis OCT; Heidelberg Engineering). OCT was performed between 10 AM to 3 PM to minimize the impact of diurnal variations in choroidal thickness. Cycloplegic refraction was performed  $\geq$ 30 minutes after the instillation of 1% cyclopentolate hydrochloride ophthalmic solution (Cyclogyl, Alcon).

Patients were initially examined every 6 months for 2 years, with an additional follow-up performed 2 years after the first 24 months. Participants were categorized into 2 subgroups (progression group and stable group) based on the degree of SE change over 2 years, with 0.5 D serving as the cutoff for myopia stabilization (> -0.5 D).<sup>5</sup> Changes in choroidal thickness were investigated in each subgroup. This study was approved by the institutional review board of Seoul National University Boramae Medical Center (No. 16-2013-6) and conformed to the Declaration of Helsinki. Informed consent to participate in the study was obtained from all participants' guardians.

#### Measurement of Choroidal Thickness

Macular choroidal thickness was measured using infrared imaging coupled with vertical and horizontal scans in enhanced depth imaging mode during each visit. An ETDRS grid was superimposed on the infrared images, and choroidal thickness was measured at 13 points: the fovea and at 1 mm, 3 mm, and 6 mm from the fovea in the temporal (T1, T3, T6), nasal (N1, N3, N6), superior (S1, S3, S6), and inferior (I1, I3, I6) regions (Fig 1). Thickness measurements were performed manually by drawing a perpendicular line from the outer border of the retinal pigment



Figure 1. Infrared images with horizontal (A) and vertical (B) OCT scans used to measure choroidal thickness at 13 points (yellow arrows) on the ETDRS 6-mm grid, which is overlaid on the IR images. IR = infrared.

Table 1. Baseline Characteristics

|                                           | Total = 46 Eyes      |
|-------------------------------------------|----------------------|
| Age (years)                               | 9.6 ± 1.7            |
| Male/female, n (%)                        | 9 (39.13)/14 (60.87) |
| Tonometer (mmHg)                          | $15.1 \pm 2.5$       |
| Spherical equivalent (diopters)           | $-4.26 \pm 2.34$     |
| BCVA (logMAR)                             | $0.01 \pm 0.02$      |
| Axial length (mm)                         | $24.80 \pm 1.28$     |
| Subfoveal choroidal thickness ( $\mu m$ ) | $262.74 \pm 63.23$   |

BCVA = best-corrected visual acuity; logMAR = logarithm of the minimal angle of resolution.

epithelial layer to the sclerochoroidal interface, using the Heidelberg Eye Explorer software (version 1.10.2.0). All measurements were performed by a single grader (J.H.L.) masked to the patient characteristics.

# Statistical Analysis

Spherical equivalent, axial length, and macular choroidal thickness at the 13 measurement points were compared between the initial 2 years and the subsequent 2 years using linear mixed-effects model analysis with random subject effects to account for (1) intereye correlations within the same subject, (2) intervisit correlations within the same eye, and (3) interregional correlations within the same eye. To identify factors associated with changes in subfoveal choroidal thickness, a multivariable linear mixed-effects model analysis with random intercepts and slopes was performed, including the following variables: age, sex, baseline axial length, baseline SE, and visit time. Continuous data were presented as mean  $\pm$  standard deviation and categorical data as frequency and percentage. All statistical analyses were performed with commercially available software (Stata V.16.0; StataCorp) and SAS V.9.4 (SAS Institute Inc). A P value <0.05 was considered statistically significant.

## Results

A total of 23 children with myopia (46 eyes) were included in the study, comprising of 9 males and 14 females. At baseline, the mean age was  $9.6 \pm 1.7$  years, the mean SE was  $-4.26 \pm 2.34$  D (indicative of moderate myopia), and the mean axial length was  $24.80 \pm 1.28$  mm (Table 1). Of the 46 eyes, 37 (80.43%) were classified into the progression group during the initial 2 years, increasing to 39 eyes (84.78%) in the subsequent 2 years. None of the patients showed increase in SE during the study period.

At 2-year and 4-year follow-up, the mean SE was  $-5.62 \pm 2.45$  D and  $-8.67 \pm 2.47$  D, respectively, reaching high myopia at the 4-year follow-up. Over the entire 4-year follow-up, the mean amount of myopia progression was 4.41 D. Both SE and axial length showed significant changes toward myopia progression during the initial 2 years (SE:  $-4.26 \pm 2.34$  D to  $-5.62 \pm 2.45$  D, P < 0.001; axial length:  $24.80 \pm 1.28$  mm to  $25.39 \pm 1.35$  mm, P < 0.001) and the subsequent 2 years (SE:  $-5.62 \pm 2.45$  D to  $-8.67 \pm 2.47$  D, P < 0.001; axial length:  $25.39 \pm 1.35$  mm to  $25.94 \pm 0.84$  mm, P = 0.015).

During the initial 2 years, when myopia remained within moderate degree, there were no significant thinning in choroidal thickness at any of the 13 measurement points (Table 2). Subgroup analysis further showed that even within the progression group (SE change: -1.65 D), no significant choroidal thinning was detected at any point (Table 3). The stable group (SE change: -0.41 D) also demonstrated no significant change in choroidal thickness.

In the following 2 years, as myopia progressed to high degree, significant thinning in choroidal thickness was observed at 9 of the 13 measurement points (P < 0.05) (Table 2). The 4 points without significant change (T6, S6, N6, and I6) were all located at most outer circle of ETDRS grid (Fig 2). In the progression group (SE change: -2.70

| Parameters                      | Baseline           | 2-Year Follow-Up   | 4-Year Follow-Up   | $P^{\mathrm{a}}$ | $\mathbf{P}^{\mathbf{b}}$ |
|---------------------------------|--------------------|--------------------|--------------------|------------------|---------------------------|
| Spherical equivalent (diopters) | $-4.26 \pm 2.34$   | $-5.62 \pm 2.45$   | $-8.67 \pm 2.47$   | <0.001           | < 0.001                   |
| Axial length (mm)               | $24.80 \pm 1.28$   | $25.39 \pm 1.35$   | $25.94 \pm 0.84$   | < 0.001          | 0.015                     |
| Choroidal thickness (µm)        |                    |                    |                    |                  |                           |
| Center                          | $262.74 \pm 63.23$ | $265.65 \pm 64.99$ | $218.89 \pm 51.27$ | 0.696            | 0.001                     |
| Temporal 1                      | $274.91 \pm 61.12$ | $274.91 \pm 62.97$ | $233.44 \pm 42.96$ | 0.955            | 0.016                     |
| Superior 1                      | $267.52 \pm 54.82$ | $272.30 \pm 62.17$ | $229.11 \pm 52.25$ | 0.496            | 0.005                     |
| Nasal 1                         | $249.98 \pm 62.85$ | $251.48 \pm 66.00$ | $203.56 \pm 51.22$ | 0.770            | 0.005                     |
| Inferior 1                      | $267.63 \pm 59.35$ | $268.76 \pm 62.21$ | $219.94 \pm 53.08$ | 0.980            | 0.001                     |
| Temporal 3                      | $287.15 \pm 55.51$ | $288.91 \pm 55.59$ | $237.50 \pm 56.81$ | 0.793            | 0.001                     |
| Superior 3                      | $278.78 \pm 49.25$ | $286.74 \pm 56.75$ | $245.61 \pm 40.46$ | 0.262            | 0.037                     |
| Nasal 3                         | $204.76 \pm 67.70$ | $210.87 \pm 70.40$ | $158.22 \pm 44.11$ | 0.184            | 0.001                     |
| Inferior 3                      | $276.50 \pm 56.03$ | $275.11 \pm 58.51$ | $235.17 \pm 41.90$ | 0.615            | 0.024                     |
| Temporal 6                      | $291.80 \pm 58.84$ | $297.78 \pm 63.29$ | $271.61 \pm 77.52$ | 0.490            | 0.144                     |
| Superior 6                      | $279.65 \pm 54.22$ | $299.96 \pm 59.52$ | $268.17 \pm 64.81$ | 0.011            | 0.082                     |
| Nasal 6                         | $146.39 \pm 65.09$ | $144.70 \pm 56.23$ | $114.39 \pm 30.19$ | 0.654            | 0.097                     |
| Inferior 6                      | $258.37 \pm 49.75$ | $271.37 \pm 77.82$ | $260.17 \pm 65.00$ | 0.139            | 0.109                     |
|                                 |                    |                    |                    |                  |                           |

Table 2. Longitudinal Changes in Spherical Equivalent, Axial Length, and Choroidal Thickness

 $P^{a}$  = baseline vs. 2-year follow-up,  $P^{b}$  = 2-year follow-up vs. 4-year follow-up.

| Parameters                      | Progression Group ( $n = 37$ Eyes) |                    |         | Stable Group $(n = 9 \text{ Eyes})$ |                     |       |
|---------------------------------|------------------------------------|--------------------|---------|-------------------------------------|---------------------|-------|
|                                 | Baseline                           | 2-Year Follow-Up   | P*      | Baseline                            | 2-Year Follow-Up    | P*    |
| Spherical equivalent (diopters) | $-4.03 \pm 2.44$                   | $-5.68 \pm 2.52$   | < 0.001 | $-4.95 \pm 1.57$                    | $-5.36 \pm 1.56$    | 0.001 |
| Axial length (mm)               | $24.78 \pm 1.19$                   | $25.48 \pm 1.24$   | < 0.001 | $24.84 \pm 1.62$                    | $25.18 \pm 1.62$    | 0.006 |
| Choroidal thickness (µm)        |                                    |                    |         |                                     |                     |       |
| Center                          | $268.62 \pm 55.37$                 | $268.92 \pm 57.19$ | 0.414   | $238.56 \pm 88.73$                  | $252.22 \pm 93.72$  | 0.584 |
| Temporal 1                      | $278.19 \pm 50.12$                 | $275.32 \pm 57.17$ | 0.869   | $261.44 \pm 97.23$                  | $273.22 \pm 87.12$  | 0.745 |
| Superior 1                      | $272.62 \pm 49.00$                 | $273.73 \pm 53.35$ | 0.285   | $246.56 \pm 74.07$                  | $266.44 \pm 94.25$  | 0.349 |
| Nasal 1                         | $250.08 \pm 54.77$                 | $250.97 \pm 59.57$ | 0.397   | $249.56 \pm 104.69$                 | $253.56 \pm 92.35$  | 0.928 |
| Inferior 1                      | $269.38 \pm 53.81$                 | $269.10 \pm 59.65$ | 0.461   | $260.44 \pm 81.93$                  | $267.33 \pm 88.88$  | 0.528 |
| Temporal 3                      | $294.68 \pm 54.00$                 | $290.32 \pm 56.64$ | 0.699   | $256.22 \pm 53.61$                  | $283.11 \pm 53.87$  | 0.285 |
| Superior 3                      | $281.76 \pm 47.92$                 | $286.16 \pm 53.66$ | 0.137   | $266.56 \pm 55.70$                  | $289.11 \pm 71.77$  | 0.188 |
| Nasal 3                         | $203.68 \pm 51.30$                 | $211.81 \pm 61.79$ | 0.063   | $209.22 \pm 117.95$                 | $207.00 \pm 103.35$ | 0.764 |
| Inferior 3                      | $278.78 \pm 55.76$                 | $276.54 \pm 57.20$ | 0.584   | $267.11 \pm 59.52$                  | $269.22 \pm 66.95$  | 0.724 |
| Temporal 6                      | $298.97 \pm 56.74$                 | $298.24 \pm 66.68$ | 0.889   | $262.33 \pm 61.42$                  | $295.89 \pm 50.18$  | 0.169 |
| Superior 6                      | $282.35 \pm 54.54$                 | $297.59 \pm 54.71$ | 0.004   | $268.56 \pm 54.60$                  | $309.67 \pm 79.57$  | 0.157 |
| Nasal 6                         | $144.19 \pm 47.52$                 | $145.03 \pm 43.10$ | 0.371   | $155.44 \pm 116.43$                 | $143.33 \pm 97.08$  | 0.589 |
| Inferior 6                      | $258.35 \pm 52.50$                 | $269.27 \pm 82.41$ | 0.093   | $258.44 \pm 39.02$                  | $280.00\pm58.29$    | 0.290 |

Table 3. Longitudinal Changes in Spherical Equivalent, Axial Length, and Choroidal Thickness during the First 2 Years

n = number.

\*Linear mixed-effects model analysis.

D), significant choroidal thinning occurred at 8 of the 13 points, while no significant thinning was observed in the stable group (SE change: -0.13 D). The 5 points (S3, T6, S6, N6, and I6) remained unaffected in the progression group (Table 4).

Topographic variations in choroidal thickness within the ETDRS grid are shown in Figure 3. Vertically, the S point tended to be thicker than the I point, while horizontally, the T point tended to be thicker than the N point. These differences were more pronounced at larger ETDRS circle.

The multivariable linear mixed-effects model analysis identified baseline longer axial length as the significant factor associated with thinning in subfoveal choroidal thickness over the 4-year period (P = 0.007), while age, sex, and baseline SE were not significant (Table 5). Change of subfoveal choroidal thickness was  $-14.98 \ \mu$ m/year (P = 0.003) during the following 2 years.

## Discussion

This study demonstrates that choroidal thickness generally decreased as myopia progresses in school-age children, aligning with the findings of Xiong et al and Xu et al.<sup>12,16</sup> Xiong et al<sup>16</sup> conducted a 1-year longitudinal study involving 756 children and adolescents and reported that central foveal choroidal thinning occurred in children with a myopic shift, which significantly differed from those without myopia progression ( $-8 \ \mu m \ vs. +2 \ \mu m$ ). Similarly, Xu et al<sup>12</sup> followed 168 children over 2 years, observing a reduction of 24.63  $\ \mu m$  in central choroid thickness in conjunction with a -1.50 D myopic shift.

Although the sample size of our study was relatively small, the extended 4-year follow-up with biennial examinations provided valuable insights into the relationship between choroidal thickness and myopia progression. Over the study period, we observed a decrease of 43.85  $\mu$ m in



Figure 2. Change of choroidal thickness is demonstrated with gray scale. Bold blue circle indicates significant thickening and bold red circle indicates significant thinning compared with the previous visit. I = inferior; N = nasal; S = superior; T = temporal.

| Parameters                      | Progression Group ( $n = 39$ Eyes) |                    |       | Stable Group $(n = 7 \text{ Eyes})$ |                    |                |
|---------------------------------|------------------------------------|--------------------|-------|-------------------------------------|--------------------|----------------|
|                                 | 2-Year Follow-Up                   | 4-Year Follow-Up   | P*    | 2-Year Follow-Up                    | 4-Year Follow-Up   | $\mathbf{P}^*$ |
| Spherical equivalent (diopters) | $-6.61 \pm 2.46$                   | $-9.31 \pm 2.15$   | 0.001 | $-5.33 \pm 0.80$                    | $-5.46 \pm 1.01$   | 0.777          |
| Axial length (mm)               | $25.78 \pm 0.88$                   | $26.11 \pm 0.80$   | 0.084 | $24.89 \pm 0.63$                    | $25.11 \pm 0.51$   | 0.275          |
| Choroidal thickness (µm)        |                                    |                    |       |                                     |                    |                |
| Center                          | $243.64 \pm 45.78$                 | $211.50 \pm 46.82$ | 0.021 | $258.25 \pm 66.11$                  | $244.75 \pm 65.18$ | 0.650          |
| Temporal 1                      | $253.21 \pm 46.70$                 | $226.93 \pm 39.60$ | 0.023 | $287.75 \pm 42.84$                  | $256.25 \pm 52.63$ | 0.604          |
| Superior 1                      | $248.93 \pm 44.52$                 | $220.14 \pm 49.46$ | 0.035 | $268.00 \pm 57.79$                  | $260.50 \pm 56.37$ | 0.573          |
| Nasal 1                         | $217.93 \pm 40.45$                 | $195.36 \pm 51.12$ | 0.042 | $244.75 \pm 31.99$                  | $232.25 \pm 46.19$ | 0.920          |
| Inferior 1                      | $244.57 \pm 43.46$                 | $209.29 \pm 42.85$ | 0.009 | $274.75 \pm 60.99$                  | $257.25 \pm 74.97$ | 0.840          |
| Temporal 3                      | $271.21 \pm 47.37$                 | $236.00 \pm 58.35$ | 0.042 | $295.50 \pm 35.09$                  | $242.75 \pm 59.04$ | 0.182          |
| Superior 3                      | $254.64 \pm 36.05$                 | $240.50 \pm 35.56$ | 0.085 | $283.50 \pm 31.27$                  | $263.50 \pm 57.00$ | 0.648          |
| Nasal 3                         | $127.36 \pm 35.11$                 | $115.12 \pm 26.50$ | 0.045 | $201.25 \pm 23.47$                  | $189.25 \pm 24.39$ | 0.892          |
| Inferior 3                      | $252.71 \pm 51.00$                 | $223.86 \pm 38.02$ | 0.007 | $281.75 \pm 45.51$                  | $274.75 \pm 31.60$ | 0.789          |
| Temporal 6                      | $281.93 \pm 57.48$                 | $271.64 \pm 84.80$ | 0.396 | $318.00 \pm 64.95$                  | $271.50 \pm 53.81$ | 0.585          |
| Superior 6                      | $272.71 \pm 63.51$                 | $262.43 \pm 70.74$ | 0.576 | $305.00 \pm 41.90$                  | $288.25 \pm 37.82$ | 0.526          |
| Nasal 6                         | $127.36 \pm 35.11$                 | $118.41 \pm 33.07$ | 0.247 | $125.00 \pm 11.94$                  | $101.25 \pm 11.32$ | 0.283          |
| Inferior 6                      | $257.29 \pm 96.27$                 | $235.14 \pm 66.69$ | 0.060 | $246.25 \pm 16.17$                  | $239.75 \pm 28.06$ | 0.656          |

Table 4. Longitudinal Changes in Spherical Equivalent, Axial Length, and Choroidal Thickness during the Subsequent 2 Years

n=number.

\*Linear mixed-effects model analysis.

central choroidal thickness along with a substantial magnitude of myopia progression (-4.41 D). Given the longer follow-up duration, larger changes in both SE and choroidal thickness were expected. During the following 2 years, subfoveal choroidal thickness change was -46.76 µm (average of -23.38 µm/year, -14.99 µm/year on multivariate analysis), which is larger amount than previous studies where average of choroidal thinning was  $-12 \,\mu\text{m/}$ year in children aged 6 to 9 with myopic shift of -0.66 D in one study and  $-12.32 \,\mu$ m/year along with  $-1.50 \,\text{D}$  myopic shift in another study.<sup>12,16</sup> This may be due to large amount of myopic shift (-3.05 D) during the following 2 years in the current study. Notably, compared with previous studies, choroidal thinning became significant only when myopia progressed to high degree.<sup>12,16</sup> This suggests that changes in choroidal thickness may serve as a predictive factor for progression to high myopia.

The pronounced thinning in choroidal thickness observed in children with high myopia may reflect differences in eyeball growth patterns. In eyes with high myopia, global scleral expansion occurs with preferential equatorial growth to maintain the posterior pole's position.<sup>17</sup> This equatorial expansion may explain the absence of significant choroidal changes during the relatively earlier stages of myopia. Furthermore, staphyloma, an outpouching of scleral tissue, is a hallmark of pathologic myopia, one of many factors contributing to the choroidal thinning observed in advanced stages of myopia.<sup>18</sup>

Interestingly, no significant change in choroidal thickness was observed during the initial 2 years even in the progression group. This may be due to variations in age and refractive status among participants. Xiong et al<sup>16</sup> found that choroidal thinning was less pronounced in children aged 10 to 13 years than those aged 6 to 9 years with myopia progression. As the average age in our study was  $9.6 \pm 1.7$  years, many participants were nearing the 10 to

13 age group, potentially explaining the limited choroidal thinning observed initially. The baseline moderate myopia of participants may have influenced the results. Previous studies suggest that physiologic choroidal thickening may offer protection against axial elongation in early stages of myopia but not in more advanced stages.<sup>8</sup>

Several hypotheses have been proposed to explain the compensatory thickening of the choroid. One theory suggests that the choroid acts as a physical barrier, resisting scleral expansion and limiting the effects of retinal growth factors.<sup>19</sup> Another theory is related to the optical emmetropization process, where myopic defocus induces choroidal thickening and reduces axial length, while hyperopic defocus results in choroidal thinning and axial elongation.<sup>20</sup> In fact, the S6 point in the initial 2 years showed significant thickening.

Findings from the low-concentration atropine for myopia progression study indicate that long-term choroidal thickening occurs as atropine eyedrops inhibit the choroidal thinning effect caused by hyperopic defocus, thereby slowing axial elongation.<sup>21</sup> Recently, the 5-year dose-dependent efficacy of low-concentration atropine in preventing myopia progression, as measured by SE and axial length, has been reported.<sup>22</sup> While thinning of the choroidal thickness may predict myopic progression, thickening could also serve as an indicator of the treatment efficacy of low-concentration atropine in preventing myopic progression.

In terms of topographic distribution, our study found that the S and T sectors of the choroid were thicker than the I and N sectors, consistent with previous studies.<sup>8,23-26</sup> However, unlike earlier studies, we observed that parafoveal choroidal thickness was not greater than perifoveal thickness, particularly in the S and T regions.<sup>8,23,26</sup> This discrepancy may be due to our use of single-point measurements rather than quadrant-averaged values.



Figure 3. Locational comparison of choroidal thickness within same ETDRS circle at each visit. Comparisons were performed using the linear mixed-effects model. The asterisks indicate significant differences in choroidal thickness across sectors within the same ETDRS circle. I = inferior; N = nasal; S = superior; T = temporal.

Longer baseline axial length was the only significant factor associated with thinning of subfoveal choroidal thickness over the study period. This finding aligns with a previous study reporting a negative correlation between baseline axial length and choroidal thickness change.<sup>12</sup> Neither sex nor age significantly influenced choroidal thickness changes, consistent with the majority of prior research.<sup>26–28</sup> However, Xu et al<sup>12</sup> noted that female children experienced more pronounced choroidal thinning than males.

According to the COMET study, the mean age at myopia stabilization was 15.61 years, with a corresponding SE of -4.87 D at stabilization.<sup>5</sup> In our study, the mean baseline age was 9.13 years, and the 4-year follow-up brought participants close to the typical stabilization age. The baseline SE of  $-4.26 \pm 2.34$  D was also relatively high. However, considering that the COMET study included various ethnicities and that the degree of myopia at stabilization was highest among Asians (-5.45 D), our findings are reasonable. As our study population is composed of children with existing refractive errors who were receiving clinical care, their baseline degree of myopia was inherently greater than other studies.

In a longitudinal study involving a larger cohort of healthy young adults (395 eyes of 198 participants), baseline median refractive error of +0.38 D decreased to +0.13 D over an 8-year period and subfoveal choroidal thickness increased by 1.3  $\mu$ m/year.<sup>29</sup> However, choroidal thinning was observed in eyes showing myopic progression (defined as a change in SE  $\leq -0.5$  D over 8 years), even in the earlier stages of myopia, which contrasts with the findings of our study. Differences in baseline age, baseline SE, and ethnicity might have contributed to these similar yet distinct results.

Despite the insights provided by this study, there are some limitations. First, the relatively small sample size may have introduced variability, which could have been mitigated by including a more diverse population in terms of age and refractive status. Second, our study's focus on children with moderate myopia limited the ability to explore correlations with milder degree of myopia. Third, the absence of OCT angiography was another limitation, as OCT angiography could have provided valuable information on blood flow, which is often reduced in high myopia.<sup>30</sup> Fourth,

Table 5. Multivariable Linear Mixed-Effects Model with Random Intercept and Slope for Analysis of Factors Associated with Changes in Subfoveal Choroidal Thickness

| Variables                                 | Estimate | Standard Error | 95% Confidence Interval | Р     |
|-------------------------------------------|----------|----------------|-------------------------|-------|
| Age (yrs)                                 | 5.08     | 5.43           | -5.82 to 15.98          | 0.354 |
| Sex (female)                              | 21.49    | 18.12          | -14.86 to 57.83         | 0.241 |
| Baseline axial length (mm)                | -24.65   | 8.94           | -42.58 to $-6.73$       | 0.007 |
| Baseline spherical equivalent (diopters)  | 4.08     | 4.39           | -4.72 to 12.89          | 0.357 |
| Visit                                     |          |                |                         | 0.011 |
| Baseline vs. 2-year follow-up*            | -2.94    | 6.26           | (-15.71, 9.84)          | 0.642 |
| Four-year follow-up vs. 2-year follow-up* | -29.97   | 9.26           | (-48.88, -11.05)        | 0.003 |

\*Two-year follow-up was the reference time point.

transverse scaling correction was not applied when measuring choroidal thickness, which might have provided more accurate measurements. However, as the baseline axial length in our study (24.80 mm) is similar to the default axial length of Spectralis OCT (24.385 mm), the potential difference is expected to be minimal. Future studies with larger cohorts, longer follow-up periods, and OCT angiography assessments will further elucidate the

# **Footnotes and Disclosures**

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<sup>1</sup> Department of Ophthalmology, Seoul National University College of Medicine, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, South Korea.

<sup>2</sup> Department of Ophthalmology, Sensory Organ Research Institute, Dongguk University Ilsan Hospital, Goyang, South Korea.

<sup>3</sup> Medical Research Collaborating Center, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, South Korea.

<sup>4</sup> The One Seoul Eye Clinic, Seoul, South Korea.

\*J.H.L. and J.Y.S. contributed equally to this study.

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References

- 1. Dolgin E. The myopia boom. Nature. 2015;519:276-278.
- Liang YB, Wong TY, Sun LP, et al. Refractive errors in a rural Chinese adult population: the handan eye study. *Ophthalmology*. 2009;116:2119–2127.
- Matsumura S, Ching-Yu C, Saw SM. Global epidemiology of myopia. In: Ang M, Wong TY, eds. Updates on Myopia: A Clinical Perspective. Singapore: Springer Singapore; 2020: 27–51.
- 4. Goss DA, Winkler RL. Progression of myopia in youth: age of cessation. *Am J Optom Physiol Opt.* 1983;60:651–658.
- Myopia stabilization and associated factors among participants in the Correction of Myopia Evaluation Trial (COMET). *Invest Ophthalmol Vis Sci.* 2013;54:7871–7884.
- 6. Summers JA. The choroid as a sclera growth regulator. *Exp Eye Res.* 2013;114:120–127.
- Read SA, Collins MJ, Vincent SJ, Alonso-Caneiro D. Choroidal thickness in childhood. *Invest Ophthalmol Vis Sci.* 2013;54:3586–3593.
- 8. Xiong S, He X, Deng J, et al. Choroidal thickness in 3001 Chinese children aged 6 to 19 Years using swept-source OCT. *Sci Rep.* 2017;7:45059.

relationship between myopia progression and choroidal thickness.

In conclusion, the change in choroidal thickness is closely associated with the degree of myopia that develops. Significant thinning occurred only after progression to high myopia, highlighting the complexity of the relationship between choroidal thickness and myopia development.

No animal subjects were used in this study.

Author Contributions:

Conception and design: Shin, M. Kim, K.M. Lee, Oh, S.H. Kim, Choung, Ahn

Data collection: J.H. Lee, Shin, M. Kim, Oh

Analysis and interpretation: J.H. Lee, Shin, M. Kim, K.M. Lee, S.H. Kim, Choung, Ahn

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Correspondence:

Jeeyun Ahn, MD, PhD, Department of Ophthalmology, SMG-SNU Boramae Medical Center, 20, Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, South Korea. E-mail: autre24@gmail.com; and Ho-Kyung Choung, MD, PhD, Department of Ophthalmology, SMG-SNU Boramae Medical Center, 20, Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, South Korea. E-mail: hokyung214@gmail.com.

- 9. Read SA, Alonso-Caneiro D, Vincent SJ, Collins MJ. Longitudinal changes in choroidal thickness and eye growth in childhood. *Invest Ophthalmol Vis Sci.* 2015;56:3103–3112.
- **10.** Jin P, Zou H, Xu X, et al. Longitudinal changes in choroidal and retinal thicknesses in children with myopic shift. *Retina*. 2019;39:1091–1099.
- Fontaine M, Gaucher D, Sauer A, Speeg-Schatz C. Choroidal thickness and ametropia in children: a longitudinal study. *Eur J Ophthalmol.* 2017;27:730–734.
- Xu M, Yu X, Wan M, et al. Two-year longitudinal change in choroidal and retinal thickness in school-aged myopic children: exploratory analysis of clinical trials for myopia progression. *Eye Vis.* 2022;9:5.
- Kim M, Choung HK, Lee KM, et al. Longitudinal changes of optic nerve head and peripapillary structure during childhood myopia progression on OCT: Boramae myopia cohort study report 1. *Ophthalmology*. 2018;125:1215–1223.
- Lee KM, Choung HK, Kim M, et al. Positional change of optic nerve head vasculature during axial elongation as evidence of lamina cribrosa shifting: Boramae myopia cohort study report 2. *Ophthalmology*. 2018;125:1224–1233.

- Lee KM, Choung HK, Kim M, et al. Change of β-zone parapapillary atrophy during axial elongation: Boramae myopia cohort study report 3. *Invest Ophthalmol Vis Sci.* 2018;59: 4020–4030.
- 16. Xiong S, He X, Zhang B, et al. Changes in choroidal thickness varied by age and refraction in children and adolescents: a 1-year longitudinal study. *Am J Ophthalmol.* 2020;213:46–56.
- Lee KM, Park SW, Kim M, et al. Relationship between threedimensional magnetic resonance imaging eyeball shape and optic nerve head morphology. *Ophthalmology*. 2021;128: 532–544.
- Ruiz-Medrano J, Montero JA, Flores-Moreno I, et al. Myopic maculopathy: current status and proposal for a new classification and grading system (ATN). *Prog Retin Eye Res.* 2019;69:80–115.
- 19. Troilo D, Nickla DL, Wildsoet CF. Choroidal thickness changes during altered eye growth and refractive state in a primate. *Invest Ophthalmol Vis Sci.* 2000;41:1249–1258.
- 20. Read SA, Collins MJ, Sander BP. Human optical axial length and defocus. *Invest Ophthalmol Vis Sci.* 2010;51: 6262–6269.
- 21. Yam JC, Jiang Y, Lee J, et al. The association of choroidal thickening by atropine with treatment effects for myopia: two-year clinical trial of the low-concentration atropine for myopia progression (LAMP) study. *Am J Ophthalmol.* 2022;237: 130–138.
- 22. Zhang XJ, Zhang Y, Yip BHK, et al. Five-year clinical trial of the low-concentration atropine for myopia progression

(LAMP) study: phase 4 report. *Ophthalmology*. 2024;131: 1011–1020.

- Read SA, Collins MJ, Vincent SJ, Alonso-Caneiro D. Choroidal thickness in myopic and nonmyopic children assessed with enhanced depth imaging optical coherence tomography. *Invest Ophthalmol Vis Sci.* 2013;54:7578–7586.
- Zhang JM, Wu JF, Chen JH, et al. Macular choroidal thickness in children: the shandong children eye study. *Invest Ophthalmol Vis Sci.* 2015;56:7646–7652.
- Xu J, Zheng J, Yu S, et al. Macular choroidal thickness in unilateral amblyopic children. *Invest Ophthalmol Vis Sci.* 2014;55:7361–7368.
- 26. Jin P, Zou H, Zhu J, et al. Choroidal and retinal thickness in children with different refractive status measured by sweptsource optical coherence tomography. *Am J Ophthalmol.* 2016;168:164–176.
- Bidaut-Garnier M, Schwartz C, Puyraveau M, et al. Choroidal thickness measurement in children using optical coherence tomography. *Retina*. 2014;34:768–774.
- He X, Jin P, Zou H, et al. CHOROIDAL thickness in healthy Chinese children aged 6 to 12: the Shanghai children eye study. *Retina*. 2017;37:368–375.
- **29.** Lee SS, Alonso-Caneiro D, Lingham G, et al. Choroidal thickening during young adulthood and baseline choroidal thickness predicts refractive error change. *Invest Ophthalmol Vis Sci.* 2022;63:34.
- Shimada N, Ohno-Matsui K, Harino S, et al. Reduction of retinal blood flow in high myopia. *Graefes Arch Clin Exp Ophthalmol.* 2004;242:284–288.