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## Choroidal thickness profiles in myopic eyes of young adults in the Correction of Myopia Evaluation Trial cohort

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### Abstract

**Purpose**—To examine the relationship of choroidal thickness with axial length (AL) and myopia in young adult eyes in the ethnically diverse Correction of Myopia Evaluation Trial (COMET) cohort.

**Design**—Cross-sectional, multi-center, study

**Methods**—In addition to measures of myopia by cycloplegic autorefractometry and AL by A-scan ultrasonography, participants underwent optical coherence tomography imaging of the choroid (RTVue) in both eyes at their last visit (14 years after baseline). Using digital calipers, two independent readers measured choroidal thickness in the right eye (left eye if poor quality; n=37) at seven locations: fovea and 750, 1500, 2250 $\mu$ m nasal (N) and temporal (T) to the fovea.

**Results**—Choroidal thickness measurements were available from 294/346 (85%) of imaged participants (mean age: 24.3 $\pm$ 1.4 years; 44.9% male) with mean myopia of -5.3 $\pm$ 2.0D and mean AL of 25.5 $\pm$ 1.0mm. Overall, choroidal thickness varied by location (p<0.0001) and was thickest at the fovea (273.8 $\pm$ 70.9  $\mu$ m) and thinnest nasally (N2250, 191.5 $\pm$ 69.3  $\mu$ m). Multivariable analyses showed significantly thinner choroids in eyes with more myopia and longer AL at all locations except T2250 (p 0.001) and presence of peri-papillary crescent at all locations except T1500 and T2250 (p 0.0001). Choroidal thickness varied by ethnicity at N2250 (p<0.0001), with Asians having the thinnest and African Americans the thickest choroids.

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ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST.

**Conclusion**—Choroids are thinner in longer, more myopic young adult eyes. The thinning was most prominent nasally and in eyes with a crescent. In the furthest nasal location, ethnicity was associated with choroidal thickness. The findings suggest that choroidal thickness should be evaluated, especially in the nasal regions where myopic degenerations are most commonly seen clinically.

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## Introduction

The choroid, primarily a vascular structure, has several important functions in the eye including delivery of blood and nutrients to the outer retina, thermoregulation of the retina, and secretion of growth factors (for a recent review see <sup>1</sup>). If the choroid is compromised, a loss of blood flow and oxygen to the retina can occur and ultimately lead to a variety of visually debilitating ocular diseases.<sup>2</sup> In myopia, axial elongation of the eye can lead to choroidal degeneration and/or breaks in Bruch's membrane, clinically evident as lacquer cracks, chorioretinal atrophy, Fuch's spot<sup>3-4</sup> or myopic choroidal neovascularization.<sup>5</sup> Further, the prevalence of myopia in the United States has increased in recent years to 40% of the population aged 12-54 years<sup>6</sup> and is particularly high in Asian populations where it reached levels as high as 95.5% in a population of Chinese University students.<sup>7</sup> Given such ocular co-morbidities and increasing prevalence in both the US and Asia, a more complete characterization of the choroid in young adult myopic eyes is warranted.

The choroid has also been implicated in the modulation of eye growth in animals, due to its rapid thinning in response to hyperopic defocus (image plane behind the retina), which in coordination with increasing vitreous chamber depth, moves the retina toward the image plane.<sup>8-9</sup> Similarly, in human eyes the choroid thins rapidly in response to hyperopic defocus imposed by a negative-powered lens<sup>10</sup> or sustained accommodation.<sup>11</sup> These responses occur within hours after the imposition of stimuli that, over sustained periods, produce axial elongation, and eventually myopia. Given its unique position between the retina and sclera, the choroid may be a source of scleral growth regulators in response to such local visual stimuli, making it potentially important in emmetropization and axial elongation.<sup>12</sup>

The advent of high-resolution spectral domain optical coherence tomography (SD-OCT) allows for the evaluation of choroidal thickness *in vivo*, which may provide important information about the possible role of the choroid in human myopia and the increased susceptibility of the myopic eye to ocular disease. In fact, human studies have found that thinner choroids are associated with higher amounts of myopia in adults<sup>13-15</sup> and children.<sup>16-17</sup> Only a few studies have investigated the association of choroidal thickness and axial length and report thinner choroids in longer eyes.<sup>13,18-19</sup> Read et al. showed that the choroid of myopic children is thinner than that of nonmyopes and suggested that the magnitude of this difference is greater than would be expected simply from axial elongation.<sup>17</sup> However, many OCT studies have looked at choroidal thickness only centrally at the fovea, in older participants, in non-ethnically diverse populations, and/or did not investigate the relationship of choroidal thickness with both refractive error and axial length or the presence of peri-papillary crescent, typically an indicator of higher amounts of

myopia.<sup>3</sup> Therefore, a better understanding of the factors associated with choroidal thickness in young myopic eyes is needed.

The purpose of this study is to determine whether choroidal thickness at several locations surrounding the fovea is related to ethnicity, gender, presence of peri-papillary crescent, axial length and amount of myopia in a large cohort of myopic young adults, from the Correction of Myopia Evaluation Trial (COMET), in which over one-quarter have high myopia (worse than -6.0 D).

## Subjects and Methods

The COMET study design<sup>20</sup> and main treatment outcomes<sup>21</sup> have been described previously. Briefly, the randomized multi-center clinical trial (clinicaltrials.gov identifier at each of the clinical centers: NCT00000113) evaluated two lens treatments, single vision and progressive addition lenses, in a large, multi-ethnic group who were aged 6 to < 12 years with low to moderate myopia when they enrolled, and reported a statistically, but not clinically significant treatment effect of 0.20 D after three years. COMET has continued as a longitudinal observational study of factors associated with myopia progression and stabilization. In the current analyses, data are combined for the two lens treatment groups. During the final study visit, the standard study protocol, including measurements of axial length and cycloplegic refractive error, was followed as described below and previously. In addition to these procedures, OCT imaging of the choroid was performed, as described below.

### Participants

346 young myopic adults, aged 20.4-27.5 (mean: 24.2±1.4) years old at their final study visit 14 years after baseline, had OCT imaging of the choroid performed at their respective clinical centers (Optometry Schools / Colleges in Birmingham, AL; Boston, MA; Houston, TX; and Philadelphia, PA). The study protocols were HIPAA compliant and conformed to the Declaration of Helsinki and the institutional review boards at each participating center approved the research protocols. At study enrollment, informed consent was obtained from parents and assent from their children, after a written and verbal explanation of the clinical procedures. Participants were re-consented as adults at age 18 years and for additional measurements, described below.

### Standard Study Procedures

As part of the COMET study protocol, refractive error and axial length were measured in all participants at each annual visit. Study optometrists who were certified on all procedures performed all measurements. Refractive error was measured 30 minutes after administration of a second drop of a cycloplegic agent (2 drops of 1% tropicamide, separated by 4-6 minutes), using an autorefractor (ARK-700A; Nidek, Japan). Five consecutive reliable measurements were taken in each eye and the mean cycloplegic refractive error, in terms of spherical equivalent, was calculated for each eye.

Axial length was measured by ultrasonography (A-2500; Sonomed, New York, USA) after a drop of anesthetic (1% proparacaine) was placed in each eye. Five consecutive

measurements were taken, either using the slit lamp (preferred technique) or handheld technique, in each eye. A standard deviation less than or equal to 0.10 mm between measurements was maintained for each eye. Mean axial length was then calculated for each eye from these measurements.

### OCT Imaging

The SD-OCT device (RTVue, Model RT-100, Optovue, Inc. Fremont, CA) used in this study can capture 26,000 A scans/second with a depth resolution of 5  $\mu\text{m}$  using a scanning laser diode at a wavelength of  $840\pm 10$  nm. In COMET, OCT imaging was initially performed beginning in the 11<sup>th</sup> study year by the study optometrist in each participant's right eye followed by the left eye, with natural pupils, unless the pupil size was smaller than 3 mm under dim illumination (n=5). For these few participants, OCT imaging was performed with dilated pupils after all other ocular measurements were taken. No optical correction was used when images were taken. To improve image quality, all participants received one drop of an artificial tear with mild viscosity in each eye prior to imaging. In addition, fixation and blinks were monitored during all scans.

After imaging, the en face and cross-sectional SLO images of the optic nerve (3D disc baseline registration scan) from all participants were evaluated by a trained study optometrist (EH or WMT) for the presence or absence of a peri-papillary crescent. A crescent, a common clinical observation in myopic patients, is defined as a retraction of the Bruch's membrane complex from the optic nerve head margin.<sup>3</sup> A crescent was graded as 'present' if two conditions were met: (1) the crescent was observable beyond the previously verified disc margin in any location around the nerve on the en face image and (2) a corresponding increase in signal intensity from the underlying sclera in the crescent area on the cross-sectional image was observed.

At the final visit (14<sup>th</sup> study year), to investigate choroidal thickness, a 6 mm line scan (average of 25 B scans), centered on the fovea, was taken in each eye. All scans were individually inspected at the time of measurement to ensure good image quality (Signal Strength Index (SSI) > 50, with no breaks or shearing in the images) and were re-taken, if necessary. The 'auto-all focus' feature of the RTVue was utilized during all image acquisition in an attempt to minimize any retinal magnification effects that might have occurred due to differences in participants' axial lengths. This feature automatically estimates the participant's refraction, in diopters, and accordingly adjusts the system's configuration to minimize magnification errors. In addition, a previous report using the same instrument<sup>22</sup> and pilot testing of our data (n=33) showed that no correction was necessary for possible magnification effects associated with increased axial length.

### Measurement of Choroidal Thickness

Two masked independent readers at the IDEA Reading Center manually measured choroidal thickness (using the chorio-scleral border) in the right eye (left eye if poor right eye quality (n=37)). Choroidal thickness was measured with digital calipers available with RTVue software (version 6.10.100.22) at seven locations; fovea and 750, 1500, 2250  $\mu\text{m}$  nasal (N) and temporal (T) to the fovea (**Figure 1**). If at any one location the chorio-scleral border was

not visible to the grader the remaining locations were still graded, if possible. For each location, the average of the two readers' measurements was used or the consensus value, if necessary. Consensus grading occurred if the two readers' choroidal thickness differed by either 15%<sup>23-24</sup> or 30  $\mu\text{m}$ . This method of manual choroidal thickness measurement using digital calipers has been shown to be highly repeatable.<sup>22,25</sup>

## Statistical Analysis

All statistical analyses were performed using SAS version 9.3 (the SAS institute, Cary, NC). Participant demographic characteristics including gender and self-reported ethnicity, as well as ocular components were each evaluated for associations with choroidal thickness measurements in all 7 locations using t-tests (gender, axial length (median split), presence/absence high myopia (worse than -6.0 D), presence/absence of crescent) and ANOVA tests (ethnicity). Pearson correlation coefficients were used to evaluate the relationship between choroidal thickness and axial length/spherical equivalent refraction as a continuous variable at each location. To account for the correlations among all the regions within the same participant, linear mixed models were then used to assess the effects of potential risk factors when the choroidal thickness of all regions were included as the outcome in the same model. Covariates under consideration for inclusion in the linear mixed models included gender, ethnicity, axial length (continuous), presence/absence of crescent, and spherical equivalent refraction. Due to the collinearity between axial length and refraction, they were included separately in two different models. To achieve the most parsimonious model, final models were selected to include only the statistically significant factors (ethnicity, axial length or spherical equivalent refraction, presence/absence of crescent; p-value < 0.05) and adjusted for multiple comparisons using Bonferroni's correction. The adjusted parameter estimates and their standard errors from the models are presented along with the corresponding p-values. Visual acuity and participant age were not evaluated for associations with choroidal thickness given the narrow ranges in the cohort.

## Results

### Overall

Analyses were based on the 294/346 (85%) (n=3 excluded due to refractive surgery/ missing data, n=49 not gradable at any location) scans that were gradable at least at one location in one eye. The mean ( $\pm$  s.d.) refractive error of the participants with usable data was -5.3 (2.0) D and the mean axial length was 25.5 ( $\pm$ 1.0) mm. As shown in **Table 1**, significant differences were found between the gradable and not gradable group by ethnicity, refractive error and axial length with the not gradable group generally having a higher percentage of African Americans (p< 0.01), less myopia (mean difference=0.8D, p=0.01), and shorter eyes (mean difference= 0.4mm, p=0.01). The percentage of scans needing adjudication in at least one location based on the previously defined criteria was 29% with the majority of adjudications occurring in the outer retinal locations. After adjudication, the inter-class coefficients of choroidal thickness measurements between graders were >0.98 in all measured retinal locations (range= 0.98 to 0.99).

Overall, choroidal thickness varied across the seven locations ( $p < 0.0001$ ) and was thickest at the fovea (mean  $\pm$  s.d.:  $273.8 \pm 70.9 \mu\text{m}$ ) and thinnest at N2250 ( $191.5 \pm 69.3 \mu\text{m}$ ), as demonstrated by the choroidal thickness profile diagram in **Figure 2**. These data show significant nasal-temporal asymmetries in choroidal thickness in these young myopic eyes. On average, the nasal choroid thinned more rapidly than the temporal choroid at locations peripheral to the fovea. The difference between the choroidal thickness at the fovea and N2250 was  $62.3 \mu\text{m}$ , which is about twice the difference in choroidal thickness between the fovea and T2250, a difference of  $30.1 \mu\text{m}$ . The largest nasal-temporal difference in choroidal thickness was between N2250 ( $191.5 \mu\text{m}$ ) and T750 ( $271.3 \mu\text{m}$ ) (mean difference =  $79.3 \mu\text{m}$ ,  $p < 0.0001$ ).

### Ethnicity and Gender

Overall, African Americans had the thickest choroids and Asians had the thinnest at all locations. However, ethnicity was only significantly associated with choroidal thickness in the furthest nasal locations (N1500,  $p = 0.05$  and N2250,  $p = 0.01$ , **Figure 3**). In these locations, compared to African Americans, Asians had significantly thinner choroids (Mean  $\pm$  s.e. at N1500 =  $50.1 \pm 15.7 \mu\text{m}$  thinner,  $p < 0.01$  at N2250 =  $66.4 \pm 14.7 \mu\text{m}$  thinner,  $p < 0.01$ ). In addition, compared to African Americans, Whites had significantly thinner choroids at N1500 ( $33.0 \pm 10.5 \mu\text{m}$  thinner,  $p = 0.01$ ) and at N2250 Hispanics and Whites had significantly thinner choroids ( $\sim 32$ - $51 \mu\text{m}$  thinner,  $p = 0.01$ ). There were no gender differences in choroidal thickness at any of the seven measured locations (range of mean difference between males and females:  $-5$  to  $5 \mu\text{m}$ ,  $p = 0.47$  at each location).

### Axial Length and Presence of High Myopia

Longer eyes, based on a median split of participants' axial length ( $25.5 \text{ mm}$ ), had significantly thinner choroids at all retinal locations ( $p = 0.01$  at all locations except  $p < 0.05$  at T2250, **Figure 4**). Likewise, those participants with high myopia worse than  $-6.0\text{D}$  ( $n = 86$ , mean  $\pm$  s.d. =  $-7.8 \pm 1.4\text{D}$ ) had significantly thinner choroids at all retinal locations ( $p = 0.01$ , **Figure 4**), in comparison to those participants with lower amounts of myopia ( $n = 208$ , mean  $\pm$  s.d. =  $-4.2 \pm 1.1\text{D}$ ). The mean differences in choroidal thickness were similar in longer vs. shorter eyes (range:  $19$ - $36 \mu\text{m}$  thinner) and high vs. low myopia ( $22$ - $40 \mu\text{m}$  thinner). These differences were generally more pronounced in the nasal vs. temporal locations as shown in **Figure 4**.

### Presence of Crescent

As mentioned earlier, each participant was evaluated for the presence or absence of crescent. The mean axial length and amount of myopia of participants who did have a crescent were longer/worse ( $25.7 \text{ mm} / -5.7 \text{ D}$ ) than those who did not have a crescent ( $25.2 \text{ mm} / -4.8 \text{ D}$ ). Therefore, participants with a crescent had significantly longer eyes ( $0.5 \text{ mm}$  longer) and were more myopic by  $0.9\text{D}$  ( $p < 0.0001$  for both). The presence of a peri-papillary crescent was also highly associated with thinner choroids. Specifically, eyes with a crescent had significantly thinner choroids compared to eyes without a crescent at all retinal locations measured ( $27$ - $45 \mu\text{m}$  thinner,  $p < 0.0003$ ), except the T2250 location, as shown in **Figure 5**. Similar to the differences seen in choroidal thickness with and presence of high myopia, the

largest differences between presence and absence of crescent were noted in the nasal locations.

### Multivariable Analysis

A multivariable analysis (linear mixed model using axial length, presence or absence of crescent, and ethnicity as covariates) of the possible factors associated with choroidal thickness showed that longer axial length was significantly associated with thinner choroids ( $p = 0.001$ ) at all except the furthest temporal location (T2250). In general, choroids were approximately 10-16  $\mu\text{m}$  thinner per 1mm increase in axial length, with the greatest slope occurring at the N1500 location ( $16.4 \pm 4.0 \mu\text{m}$  thinner / 1mm increase,  $p < 0.0001$ ). Similarly, the presence of crescent was significantly associated with thinner choroids ( $p = 0.0001$ ) at all except the furthest temporal locations (T1500, T2250) (**Table 2**). In this model, choroids were estimated to be 8 to 35  $\mu\text{m}$  thinner in eyes with than without a crescent. When myopia was used instead of axial length as a covariate (data not shown), the findings were similar, with more myopia associated with thinner choroids ( $p = 0.004$ ) at all locations.

With respect to ethnicity, after adjustment for multiple comparisons choroidal thickness varied only at the furthest nasal retinal location (N2250,  $p < 0.0001$ ). At this location, Asians and Whites had significantly thinner choroids compared to African Americans ( $55.2 \pm 13.9$  and  $45.7 \pm 9.3 \mu\text{m}$  thinner, respectively,  $p < 0.0001$ ). In addition, the Hispanic and Mixed ethnic groups also had thinner choroids, compared to African Americans (32 and 46  $\mu\text{m}$  thinner, respectively), but these differences were not significant after adjustment for multiple comparisons ( $p = 0.25$ ).

### Discussion

The mean subfoveal choroidal thickness values reported in the COMET cohort are similar to those reported in other studies that have also investigated choroidal thickness in young adult myopic eyes (**Table 3**).

One of the interesting findings in the COMET cohort was the nasal-temporal asymmetry in choroidal thickness. This phenomenon ( $\sim 100 \mu\text{m}$  thinner nasally) has been reported in children with non-significant refractive error<sup>16,28</sup> and in adults with a range of refractive errors.<sup>19,29-30</sup> In myopic children, these nasal-temporal asymmetries were larger compared to that of non-myopic children and larger than what would be predicted purely due to stretching of the eye during axial elongation.<sup>17</sup> This asymmetry is supported by animal studies investigating eye growth that suggest that defocus is spatially weighted<sup>31-32</sup> and by human studies that report nasal-temporal asymmetries in peripheral eye length (nasal retina longer than temporal retina) in myopes.<sup>33-34</sup> The reason why the nasal choroid is thinner than the temporal choroid is not fully understood, but may be related to the anatomical positioning of the ciliary arteries and nerves.<sup>28</sup> This asymmetry, which appears to be more pronounced in the myopic eye, suggests that the nasal choroid may be more vulnerable to further thinning and degeneration with increased axial elongation, a concept that holds clinical significance, as discussed below.



The relationship between ethnicity and choroidal thickness has not been well characterized (**Table 3**). To our knowledge no previous study has investigated choroidal thickness in a large ethnically diverse population or with a cohort of African Americans. In the COMET cohort, there was a difference in choroidal thickness, especially nasally, with African Americans having the thickest choroids and Asians the thinnest. Although one small study<sup>35</sup> found that Asian myopic anisometropes had a greater interocular difference in choroidal thickness (more myopic eye thinner) and less nasal-temporal asymmetry compared to Caucasians, another small study (n= 30 participants)<sup>36</sup> did not find any difference in choroidal thickness between their Asian and Caucasian myopic participants. Therefore, even with the inability to visualize some of the thicker choroids of our African American participants, the novel observation regarding ethnic variation in choroidal thickness in the nasal quadrant of the eye is of interest and may be related to differences in eye shape between ethnic groups. This observation, which needs confirmation from other studies, may also be helpful in identifying myopic subgroups that are at high risk for future retinal and choroidal degenerations.

The finding that there are differences in choroidal thickness with ethnicity, particularly in the delicate nasal region of the posterior pole, holds some clinical significance, especially for Asians, the ethnicity group in the COMET cohort that had the thinnest choroids. The combination of thinner nasal choroids and a higher incidence of high myopia in Asian populations<sup>37</sup> may provide a greater risk for myopic retinal and choroidal degenerations. Given that a recent systematic review of population studies suggests that pathologic myopia may be more prevalent in Asian populations<sup>38</sup>, ethnically diverse, longitudinal, prospective studies should be undertaken to determine if in fact Asians are more prone to such myopic degenerations.

The relationship between choroidal thickness and gender is not clear. While COMET did not find a relationship with gender, earlier studies in young adults (mean age 24.9 years)<sup>18</sup> and older adults (50 years or older)<sup>39-40</sup> found that males had thicker choroids. However, studies investigating pediatric populations have not found a gender difference.<sup>28,36</sup> Further work is therefore warranted to determine if there are gender differences in choroidal thickness that only emerge as we age.

One association that appears to be clear from this and several previous studies is that thinner choroids are associated with longer or more myopic eyes (**See Table 3**). However, only a few studies have reported this finding at multiple retinal locations surrounding the fovea in children (<18 years)<sup>16</sup> and older adults (~54 years).<sup>22,41</sup>

The current study found that the presence of crescent, an indicator of elongated axial lengths<sup>3</sup> and the most common retinal finding in highly myopic children<sup>42</sup>, was associated with a thinner choroid, especially nasally. These results agree with those from a small retrospective study of highly myopic eyes.<sup>43</sup> Given that the nasal choroid (area between the optic nerve and fovea) is already thinner in childhood, regardless of presence of myopia<sup>28</sup>, it is potentially more vulnerable to further thinning and subsequent degeneration if the eye becomes myopic or more myopic. This suggestion is supported by the fact that myopic degeneration tends to be observed clinically in the nasal retina between the optic nerve and

fovea. In fact, choroidal thickness has been considered a higher predictor than retinal thickness of posterior staphyloma height in myopic eyes.<sup>15</sup>

The current study has some strengths and limitations. It is strengthened by its large, ethnically diverse, young myopic cohort with a range of myopia. Findings from this cohort have clinical implications and may help us to better understand the role of the choroid in myopia development and progression. A potential limitation of this study is that a small percentage of participants had choroids that were difficult to visualize. These participants tended to be African American and have shorter, less myopic eyes, which is not surprising since the chorio-scleral boundary is more difficult to visualize in thicker choroids.<sup>22, 25</sup> Therefore, the inclusion of these excluded scans may have increased the range of choroidal thickness and perhaps led to even larger ethnic variations. However, the overall conclusions would likely be similar. Another limitation of this study is that although the COMET study was longitudinal over 14 years, choroid measures were only taken at the participants' last study visit, when the participants were on average 24 years old. Future studies may benefit from longitudinal choroidal thickness measures starting earlier or even before the onset of myopia so potential changes can be monitored and better understood during myopia development and progression. In addition, the availability of an age- gender- ethnicity-matched emmetropic control group would have offered an interesting comparison to our myopic cohort.

In summary, in the furthest nasal location choroidal thickness varied by ethnicity, with Asians having the thinnest choroids and African Americans the thickest. Choroids were thinner in longer, more myopic eyes, especially nasally. The presence of a peripapillary crescent was significantly associated with thinner choroids compared to eyes without crescent. Currently, the measurement of choroidal thickness via OCT is not routinely performed clinically. However, with future imaging and automated diagnostic capabilities, clinicians might be able to utilize choroidal thickness measures to understand the relationship between thin choroids and retinal complications of the elongated myopic eye. Additional longitudinal research using high-resolution imaging of the choroid is needed to determine whether myopic young adults with thin choroids are at risk of future ocular sequelae.

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## Appendix

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## Biography



**Elise Harb, OD, MS, FAAO**

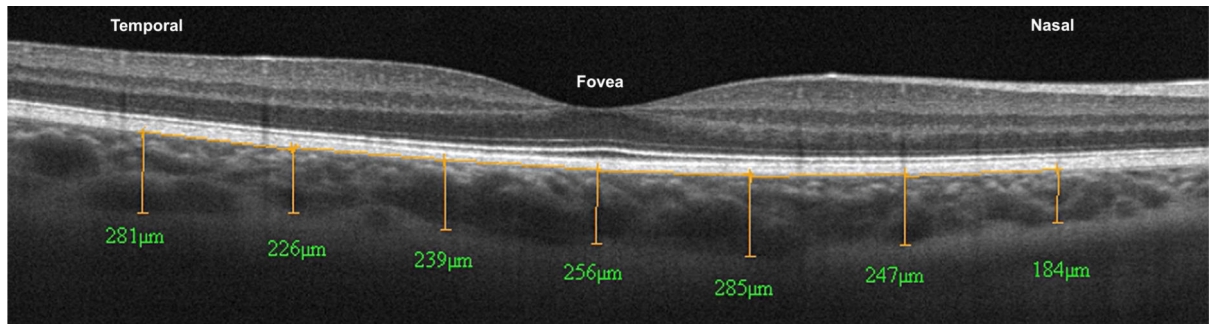
Elise Harb received her Doctorate in Optometry in 2004 and her Masters in Vision Science in 2005 from the New England College of Optometry in Boston, Massachusetts (USA) where she also completed a residency in pediatric optometry. She currently is a clinician scientist at the University of California at Berkeley School of Optometry, where her research is focused on the objective measurement of human visual behaviors and their relationship to refractive error development.

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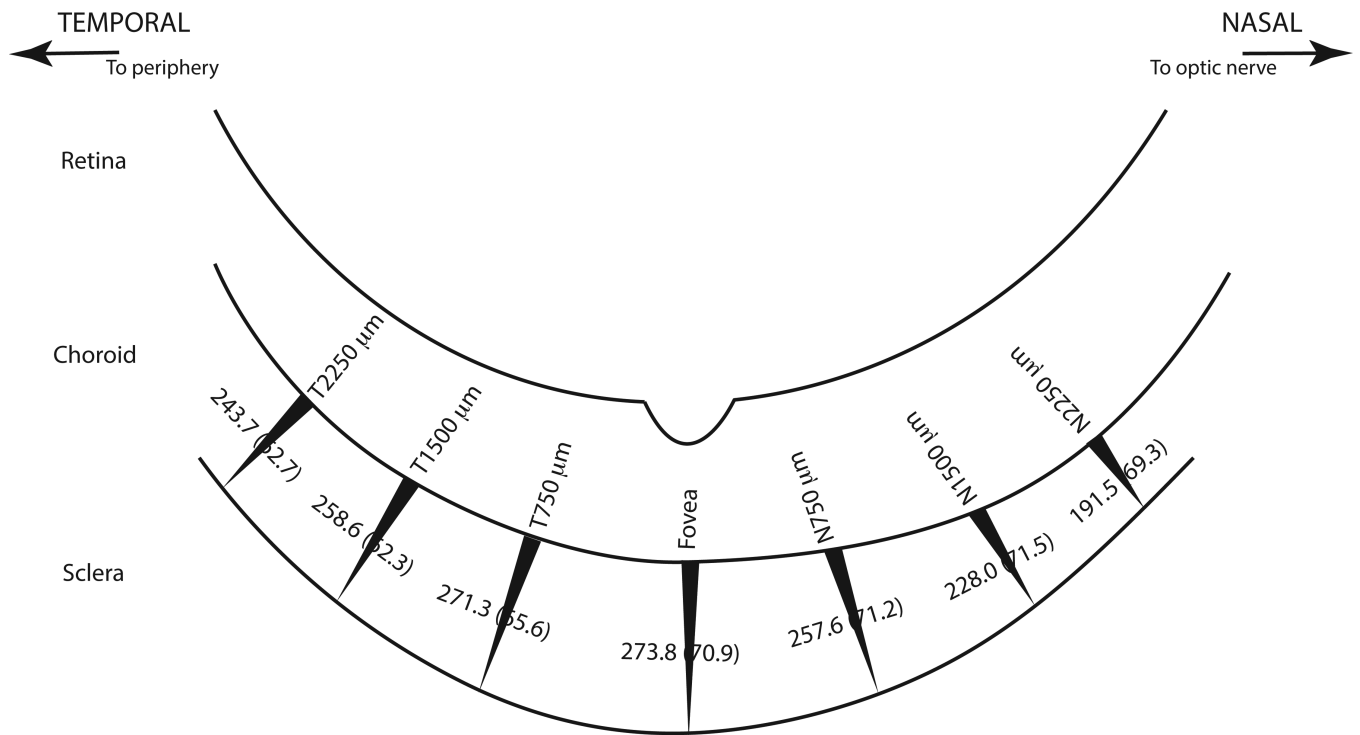
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**Figure 1. Measurement of choroidal thickness in myopic eyes**

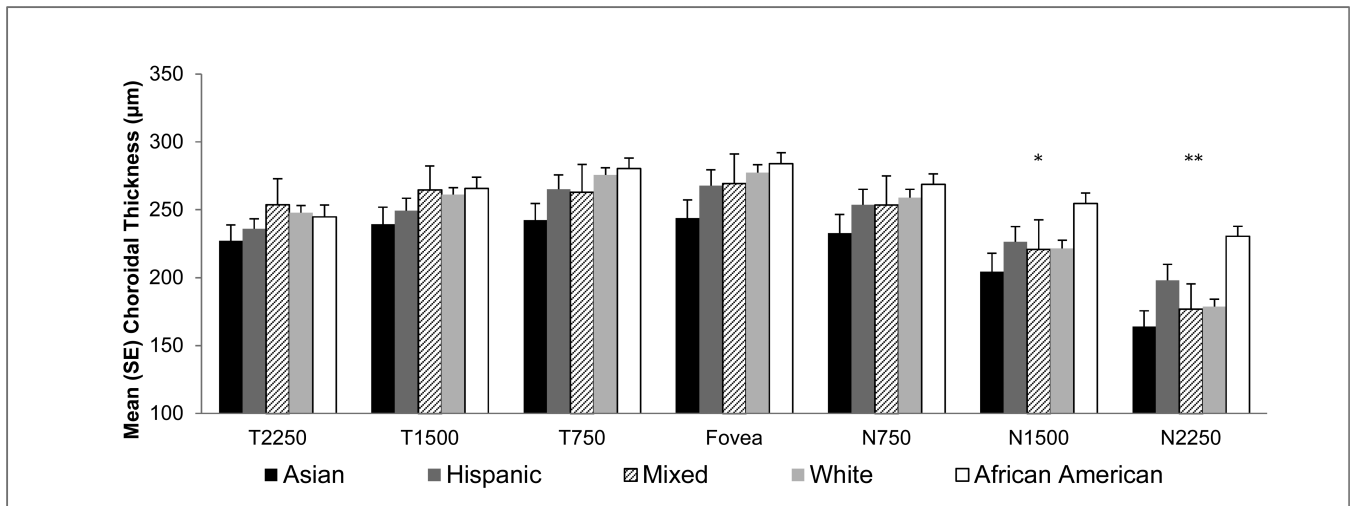
Digital calipers (yellow lines) were used to measure the choroidal thickness from the posterior edge of the retinal pigment epithelium to the chorio-scleral junction at seven locations surrounding the fovea (subfoveal and 750, 1500 and 2250  $\mu\text{m}$  temporal and nasal to the fovea). The image and mean choroidal thickness at each location shown here is from a typical myopic participant.





**Figure 2. Nasal-temporal asymmetries in choroidal thickness in myopic eyes**

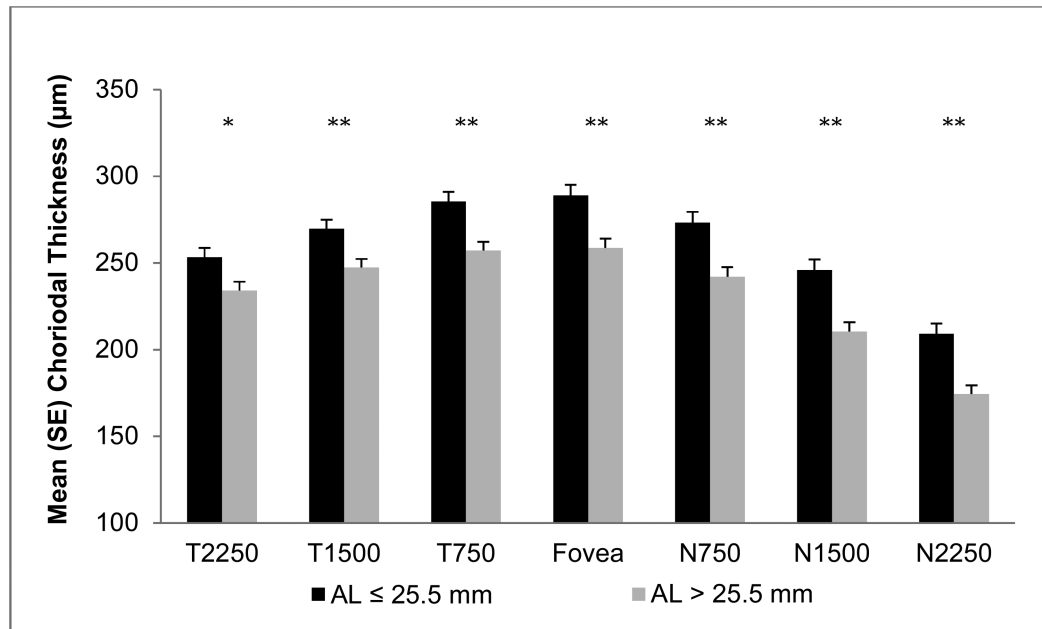
Mean (SD) choroidal thickness at each of the seven measured locations surrounding the fovea (subfoveal and 750, 1500 and 2250 μm temporal (T) and nasal (N) to the fovea) in the myopic participants of the Correction of Myopia Evaluation Trial demonstrates nasal-temporal asymmetries.



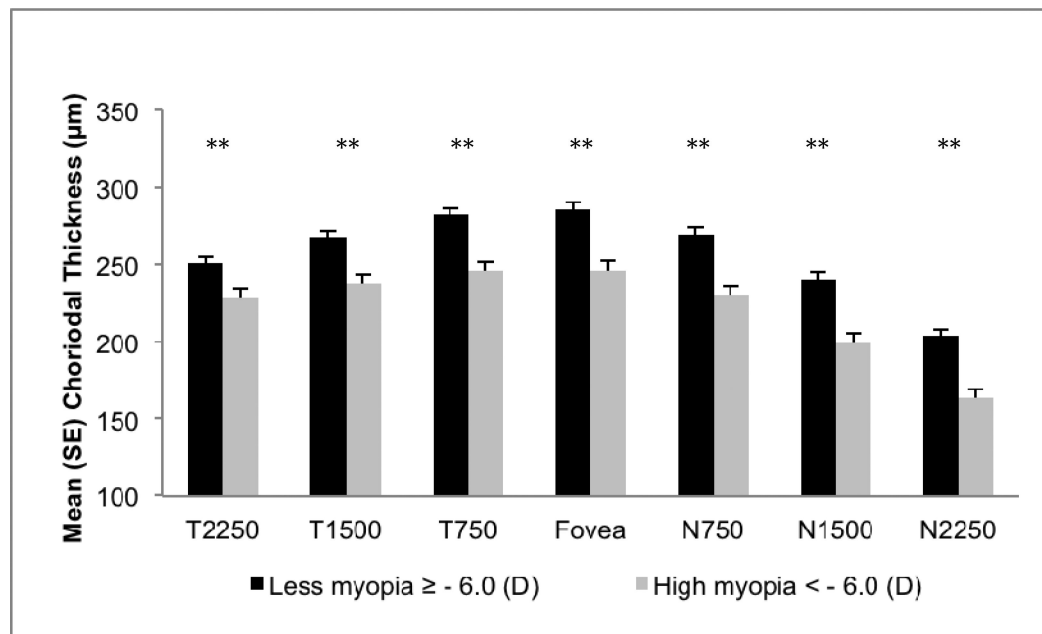
\*  $p \leq 0.05$ , \*\*  $p \leq 0.01$

**Figure 3. Ethnic variations in choroidal thickness in myopic eyes**

Mean choroidal thickness, by ethnic group, in the myopic participants of the Correction of Myopia Evaluation Trial cohort at each of the seven measured locations (N=nasal, T=temporal). Error bars represent SE. At N1500 and N2250, African Americans (white bars) had the thickest choroids and Asians (black bars) had the thinnest choroids.



\*  $p \leq 0.05$ , \*\*  $p \leq 0.01$



\*\*  $p \leq 0.01$

**Figure 4. Choroidal thickness in longer or highly myopic eyes**

**Top:** Mean choroidal thickness of myopic eyes with shorter (black bars) and longer (grey bars) axial length, based on a median split of 25.5 mm, at each of the seven measured locations (N=nasal, T=temporal). Error bars represent SE. **Bottom:** Mean choroidal thickness of eyes with high myopia (worse than -6.0 D, grey bars) and without high myopia

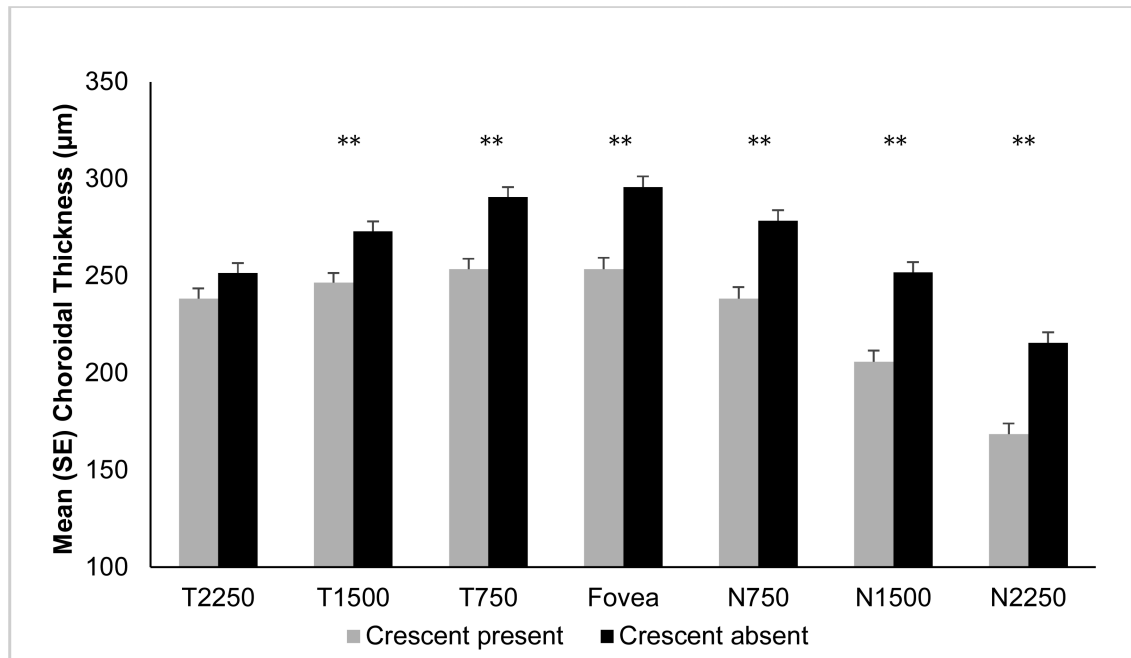
(black bars) at each of the seven measured locations (N=nasal, T=temporal). Error bars represent SE.

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\*\*  $p \leq 0.01$

**Figure 5. Choroidal thickness in eyes with and without crescent**

Mean choroidal thickness of myopic eyes with crescent (grey bars) and without crescent (black bars) at each of the seven measured locations (N=nasal, T=temporal). Error bars represent SE.

**Table 1**

Comparison of characteristics between participants with choroidal OCT scans that were gradable (n=294) and not gradable (n=49) for choroidal thickness.

Participant Characteristics	Scan gradable (N=294)		Scan not gradable (N=49)		p-value
	n	(%)	n	(%)	
<b>Gender</b>					0.59 <sup>a</sup>
Male	132	(86.8)	20	(13.2)	
Female	162	(84.8)	29	(15.2)	
<b>Ethnicity</b>					< 0.01 <sup>a</sup>
Asian	29	(100)	0	(0.0)	
Hispanic	41	(93.2)	3	(6.8)	
Mixed / Other	15	(83.3)	3	(16.7)	
White	142	(92.8)	11	(7.2)	
African American	67	(67.7)	32	(32.2)	
<b>Age (years)</b>					0.65 <sup>b</sup>
Mean (SD)	24.3	(1.4)	24.	2 (1.4)	
Median (min, max)	24.3 (20.7, 27.5)		24.2 (20.4, 26.9)		
<b>Refractive Error (D)</b>					0.01 <sup>b</sup>
Mean (SD)	-5.3 (2.0)		-4.5 (1.9)		
Median (min, max)	-4.9 (-13.1, -0.9)		-4.1 (-9.4, -0.9)		
<b>Axial Length (mm)</b>					0.01 <sup>b</sup>
Mean (SD)	25.5 (1.0)		25.1 (0.9)		
Median (min, max)	25.5 (22.0, 28.1)		25.0 (23.3, 27.6)		

<sup>a</sup>Based on chi-square test

<sup>b</sup>Based on t-test

**Table 2**

Linear mixed model<sup>a</sup> estimates of differences in choroidal thickness, by location, for participant axial length and presence of crescent in a myopic population.

Location	Axial Length (mm)		Crescent		
	Model Estimate ( $\mu\text{m}$ ) (SE)	p-value <sup>b</sup>	Yes No	Model Estimate ( $\mu\text{m}$ ) (SE)	p-value <sup>b</sup>
<b>T2250</b> (n=291)	-9.7 (3.8)	0.01	Yes No	-8.0 (7.7) Reference	0.30 .
<b>T1500</b> (n=291)	-12.0 (3.7)	0.001 <sup>*</sup>	Yes No	-19.7 (7.5) Reference	0.01 .
<b>T750</b> (n=292)	-13.3 (3.8)	0.0005 <sup>*</sup>	Yes No	-29.9 (7.7) Reference	0.0001 <sup>*</sup> .
<b>Fovea</b> (n=294)	-14.3 (4.1)	0.0005 <sup>*</sup>	Yes No	-34.7 (8.3) Reference	<0.0001 <sup>*</sup> .
<b>N750</b> (n=292)	-14.8 (4.1)	0.0004 <sup>*</sup>	Yes No	-33.3 (8.4) Reference	0.0001 <sup>*</sup> .
<b>N1500</b> (n=292)	-16.4 (4.0)	<0.0001 <sup>*</sup>	Yes No	-35.0 (8.2) Reference	<0.0001 <sup>*</sup> .
<b>N2250</b> (n=292)	-14.9 (3.8)	<0.0001 <sup>*</sup>	Yes No	-33.7 (7.7) Reference	<0.0001 <sup>*</sup> .

<sup>a</sup>Linear mixed model includes axial length, crescent and ethnicity as covariates. Although included in the model, results are not presented for ethnicity since there was only one location that had a significant overall (main effect) relationship to choroidal thickness (T2250).

<sup>b</sup>Uncorrected p-values are presented.

\* p-values less than 0.007 (0.05/7) after adjustment for multiple comparisons based on Bonferroni correction are considered statistically significant and noted.

**Table 3**

Summary table of OCT studies investigating choroidal thickness and associated factors in young adult myopic eyes.

STUDY	n	PARTICIPANT CHARACTERISTICS		Ethnicity	DEVICE	Mean Subfoveal Choroidal Thickness (um)	CHOROIDAL THICKNESS PATTERN BY FACTOR			
		Age (yrs)	Mean Refractive Error (D)				Location	Axial Length	Refractive Error	Ethnicity
COMET (2015)	n-294	24.3 ± 1.4 (21-28)	-5.3 ± 2.0D (-1.00 to -13.00)	AA, W, H, A, M	RTVue	273.8 ± 70.9	F > T > N	S > L	M > HM	AA > W > A
Li (2011) <sup>18</sup>	n-93	24.9 ± 2.6 (20-33)	-1.43 ± 2.9 (-4.50 to -11.25)	W	Spectralis	342.0 ± 118.0		S > L	NM > M > HM	
Chen (2011) <sup>26</sup>	n-64	NM= 34.8 ± 10.83 M= 28.37 ± 7.74 HM= 28.8 ± 12.61	NM= -0.26 ± 0.43 M= -3.9 ± 1.29 HM= -9.29 ± 3.10	A	Spectralis	NM=271.0 ± 88.5 M=198.4 ± 53.4 HM= 156.1 ± 86.4			NM > M > HM	
Sogawa (2012) <sup>44</sup>	n-25	30.1 ± 2.8 (25-34)	-3.4 ± 3.1 (+1.00 to -11.00)	A	Spectralis	241.3 ± 91.4		S > L	NM > M	
Kim (2012) <sup>27</sup>	n- 64	22.3 ± 3.0 (20-25)	-3.89 ± 2.00 (-0.13 to -8.63)	A	Spectralis	307.0 ± 91.3	T=F > N	S > L	M > HM	
Tan (2013) <sup>30</sup>	n-124	23.0 ± 1.9 (21-33)	-4.0 ± 2.7 (+0.50 to -11.5)	A	Spectralis	322.2 ± 98.2*	T=F > N*	S > L	NM > M > HM	

AA=African American W=White H=Hispanic A= Asian M= Mixed

N= Nasal L=Longer S=Shorter M= Myopes NM= Non-myopes HM = High-myopes F=Foveal T=Temporal

\* Central 1mm subfield

\* Based on ETDRS quadrants