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Choroidal thickness and high myopia: a case–control study of young Chinese men in Singapore

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ABSTRACT.

Purpose: **To determine the distribution of choroidal thickness (CT) and ocular factors associated with CT in high myopic eyes in comparison with emmetropic eyes of young healthy adults.**

Methods: **A case–control study of 648 young, male subjects, including 520 high myopes and 128 emmetropes. Choroidal imaging was performed using enhanced depth imaging spectral domain optical coherence tomography. Images were postprocessed using adaptive compensation for quality enhancement. CT was measured at nine locations, including subfovea and 1.5 and 3 mm nasal, temporal, superior and inferior to fovea.**

Results: **The CT at the subfovea was significantly thinner (mean ± standard error: 225.87 ± 5.51 μm) for high myopes compared to emmetropes (375.15 ± 6.58 μm, $p < 0.001$). Likewise, CT in high myopic group was significantly thinner than emmetropic control group at all locations (p for trend <0.001 for all locations). Distribution of CT showed a markedly different pattern in high myopic eyes (thickest superiorly at 3 mm, 265.97 ± 5.97 μm) and emmetropic eyes (thickest subfoveally, 375.15 ± 6.58 μm). Choroid was thinnest at nasal 3 mm location in both the myopic (108.85 ± 3.97 μm) and emmetropic (238.25 ± 6.72 μm) groups. Among the ocular factors studied, axial length, posterior staphyloma and chorio-retinal atrophy were the significant predictors of CT.**

Conclusions: **Highly myopic eyes have significantly thinner choroid and showed different distribution pattern, compared to emmetropes. Axial length, posterior staphyloma and chorio-retinal atrophy are the strongest determinants of CT.**

Key words: case-control study – choroidal thickness – EDI SD-OCT – high myopia

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Introduction

Pathological myopia or high myopia is one of the leading causes of visual impairment in the world (Fredrick 2002; Hayashi et al. 2010). Although the prevalence of high myopia (defined as −6.0 dioptres or more) varies with ethnic groups and countries, high myopia is more common in Asian populations with rates of 9–21%, (Wong et al. 2000; Lin et al. 2004) compared with 2–4% in white people (Hofman et al. 1991; Wang et al. 1994; Attebo et al. 1999).

In pathological myopia, excessive axial elongation of globe can cause biomechanical stretching and thinning of choroid and retinal pigmented epithelium layers, leading to increased risk of chorioretinal complications such as choroidal neovascularization, posterior staphyloma, lacquer cracks in Bruch's membrane and myopic foveoschisis, which may lead to visual loss (Curtin & Karlin 1971; Curtin 1982; Noble & Carr 1982; Avila et al. 1984; Ohno-Matsui & Tokoro 1996; Wu et al. 2001; Vongphanit et al. 2002; Hsiang et al. 2008; Cheung et al. 2013; Jonas et al. 2014).

As some of the earliest changes in pathological myopia begin in the

choroid, choroidal thickness (CT) could be an important parameter to study the pathogenesis of macular vision loss in high myopia. The thickness of the choroid can be measured by enhanced depth imaging (EDI) spectral domain optical coherence tomography (SD-OCT) (Spaide et al. 2008) in a variety of ocular diseases (Kim et al. 2013; Hashizume et al. 2014; Tan et al. 2014; Zhou et al. 2014). Using this method, studies have now shown that myopic eyes have thinner CT (ranging from: 93.2 ± 62.5 to 156.07 ± 86.39 μm) (Fujiwara et al. 2009; Ikuno & Tano 2009; Flores-Moreno et al. 2013; Ho et al. 2013) compared to emmetropes (normal range of subfoveal CT: 191 ± 74.2 to 354 ± 111 μm) (Margolis & Spaide 2009; Ikuno et al. 2010; Fujiwara et al. 2012; Wei et al. 2013). However, these studies were either conducted on small sample populations (Fujiwara et al. 2009; Ikuno & Tano 2009) or were mainly limited in their assessment of CT to horizontal locations only (Flores-Moreno et al. 2013; Ho et al. 2013). To the best of our knowledge, there are no studies which investigated CT by severity of myopia and the distribution of CT and assessed ocular factors associated with CT in Asian eyes. Knowledge of such factors is crucial before drawing inferences on how CT influences the development of pathological myopia.

The aim of our study was to compare the distribution of CT in different myopic groups based on the degree of myopia and to assess ocular determinants of macular CT measured by EDI SD-OCT. We used a case–control study approach of young, highly myopic and emmetropic healthy male adults in Singapore.

Materials and Methods

Study population

A total of 28 908 male adults were screened for myopia (mean age ± SD: 19.8 ± 1.2 years; range: 17–29 years) from 2009 to 2010 as part of a mandatory medical eye review for employment purposes. Measured using non-cycloplegic autorefraction (Huvitz MRK-3100P), 2584 persons were identified to have myopia with spherical equivalent (SE) of −6.0 dioptres (D) or worse. Of these 2584 persons, 719 were selected on the basis of a refractive error-stratified random sampling strategy and underwent a further comprehensive ophthalmologic examination at Singapore Eye Research Institute from December 2011 to June 2012. Their SE was further confirmed by subjective refraction, and those with SE >−6.0 D ($n = 96$) were excluded, leaving 623 subjects with high myopia (251 with SE between −6.0 and −8.0 D; 207 with SE between −8.0 and −10.0 D; 165 with SE −10.0 D or worse). In addition, 151 emmetropes who had SE < 0.5 D in both eyes measured using autorefraction were recruited as controls and went through a similar ophthalmologic examination. Subjects were further excluded if they did not give consent to take part in this medical review, had any previous ocular trauma or surgery, and those with other clinically significant ocular comorbidity.

Written informed consent was taken from the subjects and their parents/guardians (if they were 21 years old and below). Ethics approval was obtained from the Institutional Review Board of DSO National Laboratories, Singapore. The study was conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki.

Ophthalmic examination and measurements

Each subject underwent a standardized questionnaire and a complete ophthalmologic examination. The subjects were asked a series of questions, such as previous ocular trauma or surgery, history of ocular diseases.

Their refractive error screened with autorefraction (Canon Autorefractor RK-F1; Canon Inc. Ltd., Tochigiken, Japan) and confirmed with manifest refraction in which the best corrected visual acuity, which was measured monocularly using a logarithm of the minimum angle of resolution (LogMAR) chart (Lighthouse International, New York, NY, USA) at a distance of 4 m, was performed. Contrast sensitivity (CS) was measured using the Rabin super vision test (Davies et al. 2004), with and without a night vision goggle filter (SVT-NVG) and low and high luminance log CS were taken for this test. The NVG filter used was a dark green, low-luminance filter which slides in place in front of the illuminated chart, reducing chart luminance (from 100 to 4 cd/m^2) to simulate the low luminance (i.e. wearing NVG). To minimize memorization of optotypes, two different sequences were displayed for right and left eyes and measurement of CS was recorded by counting the number of letters correctly read by the subjects using the Conversion Table.

Biometry measurements, that is axial length (AL), anterior chamber depth, and K-readings, were obtained from the non-contact Zeiss IOL Master (V3.01; Carl Zeiss Meditec AG, Jena, Germany). Intraocular pressure (IOP) was measured using non-contact tonometry (Auto Non-Contact Tonometer, NT-3000; Nidek, Gamagori, Aichi, Japan), and if IOP was found to be 21 mmHg or more, a further IOP measurement using Goldmann applanation tonometry (Haag-Streit, Bern, Switzerland) was performed by study ophthalmologists.

Subjects underwent slit-lamp examination. Binocular indirect ophthalmoscopy was performed approximately 30 min after topical instillation of three drops of tropicamide and 2.5% phenylephrine, given 5 min apart. Dilated fundus examination was carried out by ophthalmologists. The presence and type of peripheral retinal degenerations and vitreous degenerations were systematically documented. Fundus photography was performed using non-mydriatic retinal camera (Canon CR-DGi with a 10-DSLR back, Tokyo, Japan).

OCT imaging

The retina, optic disc and choroidal architectural parameters were determined using SD-OCT (Spectralis, Wavelength: 870 nm; Heidelberg Engineering, Heidelberg, Germany). Choroid was imaged with EDI modality after pupil dilation. EDI is a method that improves resolution of choroidal detail by automatically setting the choroid closer to the zero-delay line and thus theoretically provides better visualization of the choroid scleral interface (CSI) than in standard retinal SD-OCT images. Radial scan consisting of six sections, each comprising 100 averaged scans (using the automatic averaging and eye tracking features of the proprietary device), was obtained in an angle of 30° centred onto the fovea (30° angles between the lines).

The horizontal and vertical sections passing through the centre of the fovea were selected for analysis. Following Spectralis user manual guidelines, subjects' keratometry readings and refraction were entered into the Spectralis' software before imaging choroid to estimate optical magnification, thus allowing for more accurate comparisons across individuals. However, Spectralis OCT does not allow AL to be input; our methods may still have residual errors (2–7%) (Garway-Heath et al. 1998) due to ocular magnification from methods that additionally uses AL. For each subject, only right eye was chosen for subsequent analysis.

Measurement of choroidal thickness

As an accurate evaluation of the CT with EDI-OCT relies mainly on the visibility of CSI, which anatomically represents the junction between the choroid and the sclera and is a principal landmark for quantitative measurements of choroid. Therefore, in our study, To accurately determine CT, CSI was enhanced using our novel technique of adaptive compensation described in detail elsewhere (Girard et al. 2011; Mari et al. 2013; Gupta et al. 2014). Our method has shown higher intra- and intergrader reliability of CT measurements compared to conventional method (Gupta et al. 2014).

The CT in the enhanced images was measured as the perpendicular distance between the outer portion of the hyperreflective line corresponding to the RPE (automatically detected by the instrument) to the now clear hyporeflective line or margin corresponding to the CSI (manually drawn by an experienced grader, who was masked to subject characteristics and clinical diagnosis) at the following locations: subfovea and 1.5 and 3 mm nasal, temporal, superior and inferior to fovea. As there was no significant difference between the horizontal and vertical subfoveal CT (horizontal SFCT = 225.87 μm, vertical SFCT = 232.09 μm, p = 0.399), only horizontal CT was used for analysis. In addition, we evaluated the intra-observer reliability of CT measurements in both the myopic and emmetropic group. Forty randomly selected Spectralis images (20 from each group) were assessed again by the same grader (grader 1 versus grader 1) after an interval of 1 week.

Statistical analysis

Subjects were excluded from analysis if they had any history of anterior ocular diseases, previous ocular trauma, evidence of macular or vitreoretinal diseases or any form of refractive surgery performed in their eyes. However, conditions such as peripapillary atrophy, lacquer crack, posterior staphyloma or chorio-retinal atrophy were not excluded, as they are commonly seen in high myopic eyes. Statistical analysis was performed using SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA) and MedCalc version 12.3 (MedCalc Software, Ostend, Belgium).

The demographics and ocular parameters between myopic and control eyes were compared using independent *t*-tests. The intrasession repeatability of the CT was measured by the absolute agreement model of the intraclass correlation coefficient (ICC) (Fleiss & Cohen 1973). For the purpose of analyses, myopic eyes were divided into three groups based on SE: <−6 to −8 D, <−8 to −10 D and <−10 D. Generalized linear model was used to assess the mean CT across different locations in eyes with varying degree of myopia, and conditions such as posterior staphyloma and chorio-retinal atrophy were included to adjust for potential residual confounding. Repeated-measures analysis of variance (ANOVA) with Bonferroni post-test was used to compare mean thickness at various locations within each group. Univariate and multiple linear regression analyses were performed to determine the association of ocular factors (independent variables) with CT measurements (dependent variables). For multiple linear regression, age and factors which showed significant association in univariate analysis ($p < 0.05$) were included.

Results

Of the 623 eligible high myopes (SE ≤ −6.0 D), we further excluded 103 subjects because either their choroidal images were not successfully attained ($n = 69$) or the available images were not of optimal quality to perform accurate measurements ($n = 31$) or they did not meet the inclusion criteria ($n = 3$), leaving 648 subjects (520 high myopes and 128 emmetropes) with complete data on CT for analysis.

The mean age of included myopic and emmetropic subjects was 21.59 ± 1.15 years and 22.06 ± 0.97 years, respectively. The mean SE was −8.68 ± 2.05 dioptres (range, −6 to −23 D) for myopic group and 0.12 ± 0.24 dioptres for emmetropic group. Among the myopic group, all our subjects had peripapillary atrophy, 35.6% had posterior staphyloma, 6.5% had chorio-retinal atrophy and 2% had lacquer cracks. The demographics and ocular characteristics of the study population are shown in Table 1. In terms of reliability of CT measurements, the intra-observer reliability for myopic (ICC: 0.95–0.98) and emmetropic group (ICC: 0.95–0.97) was excellent for all locations of CT (Table 2).

CT varied significantly across the myopic subgroups and the emmetropic control group at all the locations (p for trend <0.001 for all locations, Table 3). It was significantly thinner in the more myopic eyes over a range of eccentricities, and the pattern of distribution was different from emmetropes (Fig. 1A,B). Across the three myopic subgroups, CT was found to be thickest at the superior location, followed by the temporal, subfoveal, inferior and the nasal locations ($p < 0.001$ by repeated-measures ANOVA). In comparison, the choroid in emmetropic eyes was thickest at the fovea, followed by the superior, inferior, temporal and the nasal locations ($p < 0.001$ by repeated-measures ANOVA). However, in both the myopia and emmetropic groups, choroid was thinnest at the nasal location being 108.85 μm and 238.25 μm in myopic and emmetropic group, respectively (Fig. 1A,B).

In the univariate analysis, SE, AL, corneal curvature, presence of posterior staphyloma and chorio-retinal atrophy were significantly associated with SFCT (all $p < 0.05$, Table 4 and Fig. 2). For each mm increase in AL and corneal curvature, SFCT on average decreased by 32.31 μm ($p < 0.001$) and 84.31 μm ($p < 0.001$), respectively. A decrease in mean SFCT by 13.10 μm was observed for each myopic dioptre increase ($p < 0.001$). Presence of posterior staphyloma and chorio-retinal atrophy decreased the mean SFCT by 22.69 μm and 26.91 μm respectively.

Both AL and SE influenced CT but a larger extent from AL. The results remained similar after adjusting for age (data not shown).

Because of collinearity between AL and SE (correlation coefficient = −0.65), only AL was selected and retained in the multivariate analysis as it had a greater explanatory power on CT change than did SE (standardized β, −0.489 versus 0.348). In the multiple linear regression analysis, AL, presence of posterior staphyloma and chorio-retinal atrophy remained significantly associated with CT (all $p < 0.05$), whereas the association with corneal curvature was abolished ($p = 0.975$). However, there was no change in results after adjusting for age.

In addition, SFCT correlated negatively with the logMAR visual acuity ($r = -0.085$, $p = 0.054$) and log low luminance CS ($r = -0.115$, $p = 0.009$) although the association was not statistically significant in multivariate analysis (Fig. 3).

Table 1. Baseline characteristics of study subjects.

	Myopes (n = 520)	Emmetropes (n = 128)	p-value
Age, years	21.59 (1.15)	22.06 (0.97)	<0.001
Axial length, mm	27.32 (1.16)	23.69 (0.62)	<0.001
Anterior chamber depth, mm	3.74 (0.25)	3.46 (0.27)	<0.001
Corneal curvature, mm	7.76 (0.25)	7.85 (0.41)	0.137
Spherical equivalent, D	−8.68 (2.05)	0.12 (0.24)	<0.001
Best corrected visual acuity Log MAR	0.01 (0.08)	−0.09 (0.06)	<0.001
Log low luminance contrast sensitivity	0.36 (0.28)	0.50 (0.20)	<0.001
Log high luminance contrast sensitivity	0.66 (0.33)	0.88 (0.21)	<0.001
Intraocular pressure, mmHg	16.12 (2.94)	15.26 (2.74)	0.002

Data are mean (SD).

Table 2. Intragrader reliability of choroidal thickness measurements in myopic and emmetropic group at different locations.

	Myopes		Emmetropes	
Locations of measurement	ICC (95% CI)	Mean difference (μm)* (SD)	ICC (95% CI)	Mean difference (μm)* (SD)
Choroidal thickness				
Subfoveal	0.98 (0.96–0.99)	9.9 (11.3)	0.97 (0.95–0.99)	11.5 (17.7)
Nasal, 1.5 mm	0.96 (0.93–0.98)	9.6 (14.8)	0.96 (0.93–0.98)	10.1 (20.6)
Nasal, 3 mm	0.94 (0.87–0.97)	8.0 (14.4)	0.96 (0.93–0.98)	−15.0 (20.8)
Temporal, 1.5 mm	0.97 (0.93–0.98)	9.1 (14.8)	0.97 (0.94–0.98)	14.3 (19.4)
Temporal, 3 mm	0.97 (0.94–0.98)	10.8 (13.0)	0.96 (0.91–0.98)	11.1 (18.5)
Superior, 1.5 mm	0.96 (0.93–0.98)	−7.5 (16.2)	0.95 (0.90–0.98)	13.2 (20.4)
Superior, 3 mm	0.95 (0.90–0.98)	9.2 (17.8)	0.97 (0.94–0.99)	−14.9 (17.2)
Inferior, 1.5 mm	0.97 (0.95–0.99)	11.0 (13.5)	0.96 (0.92–0.98)	14.7 (18.0)
Inferior, 3 mm	0.96 (0.93–0.98)	−8.6 (17.0)	0.97 (0.94–0.99)	13.1 (18.5)

ICC = intraclass correlation coefficient; CI = confidence interval; SD = standard deviation.
* Mean difference was determined from the 1st measurement minus 2nd measurement.

Discussion

Although the understanding of the characteristics of the *in vivo* choroid has increased substantially in recent years, to date, only a few studies have examined CT in high myopia. To our best knowledge, this study measured CT directly with EDI SD-OCT in the largest group of young, high myopic Asian subjects. CT in the myopic group was significantly lower than that of the emmetropic control group at any locations. We demonstrated further decrease in CT with increase in degree of myopic refractive error. CT distribution follows a different profile in

Table 3. Distribution of mean adjusted choroidal thickness at nine different locations across the myopic and control groups using generalized linear model.

						Changes in choroidal thickness across 3 myopic groups	
Location	Emmetropes (N = 128)	Myopia, 6−8 (D) (N = 233)	Myopia, <−8–10 (D) (N = 169)	Myopia > 10 (D) (N = 118)	All myopes (N = 520)	Beta†	p for trend†
Subfoveal	375.15 (6.58)	241.54 (6.63)	223.90 (7.14)	210.60 (7.13)	225.87 (5.51)	−15.74	<0.001
Nasal, 1.5 mm	324.01 (6.59)	187.01 (6.17)	165.27 (6.66)	150.70 (6.64)	168.35 (5.18)	−18.60	<0.001
Nasal, 3 mm	238.25 (6.72)	121.19 (4.76)	106.90 (5.13)	97.13 (5.12)	108.85 (3.97)	−12.30	<0.001
Temporal, 1.5 mm	359.27 (6.51)	249.52 (6.38)	235.82 (6.87)	223.47 (6.85)	236.64 (5.27)	−13.10	<0.001
Temporal, 3 mm	328.41 (6.04)	251.51 (6.02)	243.83 (6.49)	235.77 (6.47)	243.88 (4.94)	−07.84	<0.001
Superior, 1.5 mm	365.01 (5.66)	263.84 (7.05)	250.70 (7.59)	238.81 (7.57)	251.47 (5.81)	−12.59	<0.001
Superior, 3 mm	358.03 (5.74)	278.23 (7.25)	263.61 (7.81)	254.64 (7.79)	265.97 (5.97)	−12.14	<0.001
Inferior, 1.5 mm	358.93 (6.14)	243.27 (6.32)	219.94 (6.81)	202.87 (6.79)	222.74 (5.32)	−20.59	<0.001
Inferior, 3 mm	339.41 (6.30)	232.76 (6.25)	214.86 (6.74)	199.84 (6.72)	216.32 (5.21)	−16.63	<0.001
	p < 0.001*	p < 0.001*	p < 0.001*	p < 0.001*	p < 0.001*		

Data are mean (standard error) in μm, adjusted for presence of posterior staphyloma and chorio-retinal atrophy.
† Adjusted for presence of posterior staphyloma and chorio-retinal atrophy.
* Repeated-measures ANOVA, comparing the distribution of choroidal thickness across fovea, nasal (3 mm), temporal (3 mm), superior (3 mm) and inferior (3 mm) locations.

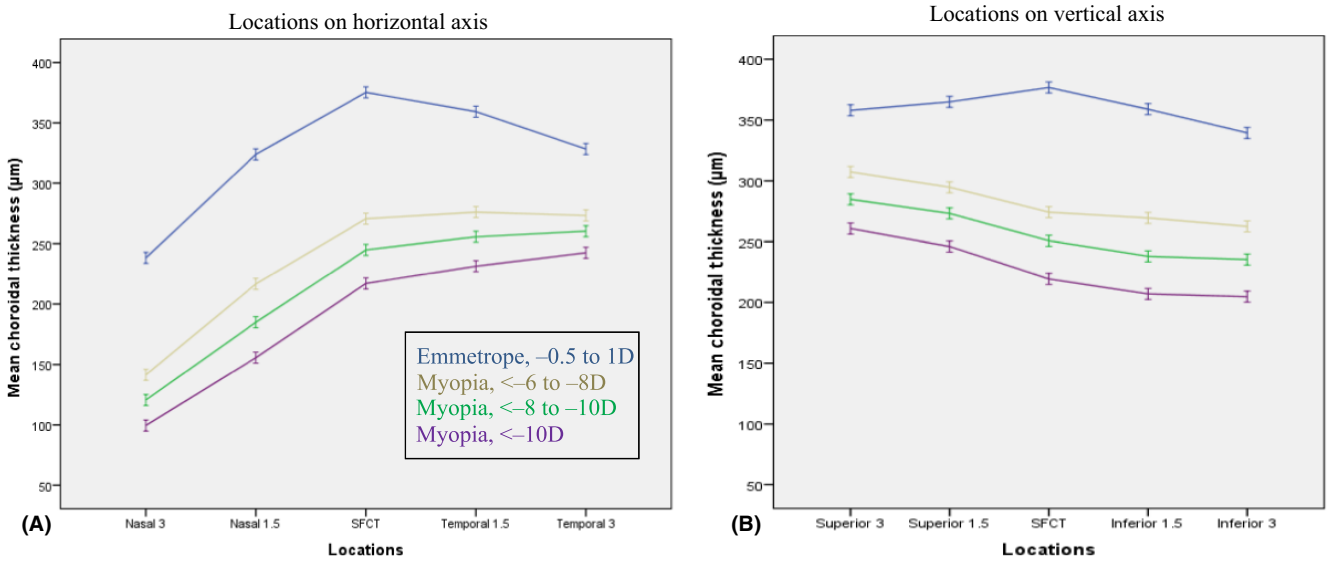

Fig. 1. Graph showing the differences in macular choroidal thickness (CT) in the high myopic groups and emmetropic group along the horizontal axis (A) and vertical axis (B). Mean thickness at each of the nasal, temporal, superior and inferior locations measured at 1.5 and 3 mm intervals eccentric to the subfoveal area. Error bars indicate standard error. SFCT is subfoveal CT.

Table 4. Association of ocular factors with subfoveal choroidal thickness in all myopes (n = 520).

	Univariate analysis			Multivariate analysis		
	Unstandardized beta coefficient	Standardized beta coefficient	p-value	Unstandardized beta coefficient	Standardized beta coefficient	p-value
Ocular factors						
Spherical equivalent, D	13.109	0.348	<0.001	–	–	–
Axial length, mm	−32.319	−0.489	<0.001	−24.232	−0.370	<0.001
Corneal curvature, mm	−84.318	−0.279	<0.001	0.397	0.001	0.975
Anterior chamber depth, mm	−8.200	−0.027	0.541	–	–	–
Intraocular pressure, mmHg	0.714	0.027	0.535	–	–	–
Posterior Staphyloma	−22.698	−0.443	<0.001	−15.642	−0.306	<0.001
Chorio-retinal atrophy	−26.910	−0.289	<0.001	−10.585	−0.114	0.003

high myopia (thickest CT superiorly), compared to emmetropia (thickest CT subfoveally). Among the range of ocular factors studied, AL, presence of posterior staphyloma and chorio-retinal atrophy were the significant predictors of CT.

Our study provided new data on CT and severity of myopia. There were significant differences in the mean CT among myopic subgroups and the emmetropic group at various eccentricities (p for trend <0.001 for all locations). Myopes had significantly thinner choroid compared to emmetropes at all eccentricities. Our findings are consistent with previous experimental animal studies (Wallman et al. 1995; Shaikh et al. 1999; Troilo et al. 2000) which have shown that chicks developing experimentally induced myopia show profound thinning of choroid (Troilo et al. 2000). The mean SFCT in myopic group was 225.87 ± 5.51 μm, which is much thicker than those reported in previous studies that showed a mean CT of 93.2 (Fujiwara et al. 2009) to 115.5 (Flores-Moreno et al. 2013) μm (Table 5). In Table 5, on performing a metaregression on various studies to quantify the change in mean CT with SE adjusting for age, we found no significant association between SE and mean CT (β = 0.429, p = 0.952) indicating AL to be a more important predictor of CT than SE. The mean SFCT in emmetropes was 375.15 μm which is also thicker than previous studies that reported a mean thickness of 272–354 μm (Spaide et al. 2008; Margolis & Spaide 2009; Esmaeelpour et al. 2010; Manjunath et al. 2010).

The differences in CT in our study compared to other studies could be because of differences in participants' characteristics, such as age, refractive error and ethnicity. Our study participants are twice as young, mean age 21.63 years compared to other studies (Fujiwara et al. 2009; Ikuno & Tano 2009; Margolis & Spaide 2009; Esmaeelpour et al. 2010; Manjunath et al. 2010; Flores-Moreno et al. 2013). In addition, there were variations in OCT device characteristics such as wavelength, eye tracking method and averaging software among studies. In our results, CT decreased with increase in severity of myopic refractive error. The findings suggest that thinning or abnormalities of choroid play a role in the pathogenesis of myopic degeneration and thus visual impairment.

We found that CT in highly myopic eyes was thickest superiorly and thinnest nasally. In comparison, the choroid in normal eyes was thickest at the fovea and thinnest nasally. The observed pattern of CT distribution in our study is similar to the previous studies, in both myopes (Ikuno & Tano

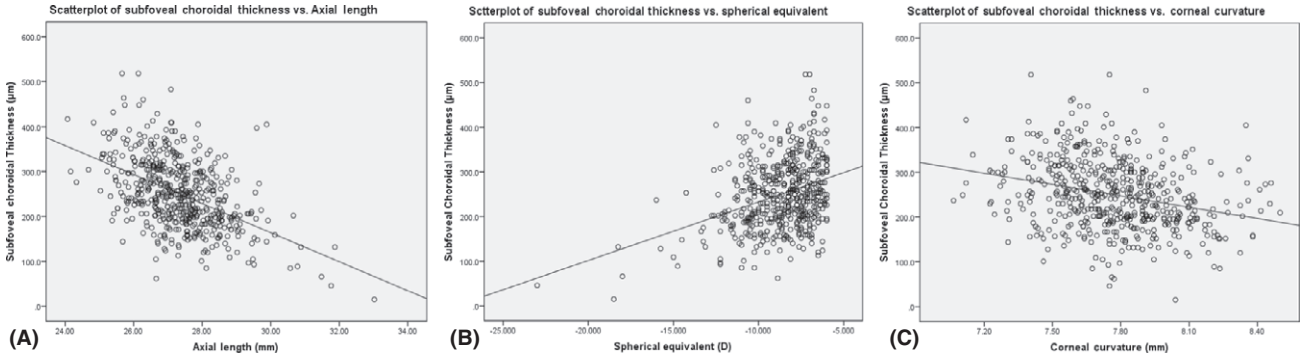

Fig. 2. (A) Scatterplot showing negative correlation between subfoveal choroidal thickness (CT) and axial length in all myopes. (B) Scatterplot showing positive correlation between subfoveal CT and spherical equivalent in all myopes. (C) Scatterplot showing negative correlation between subfoveal CT and corneal curvature in all myopes.

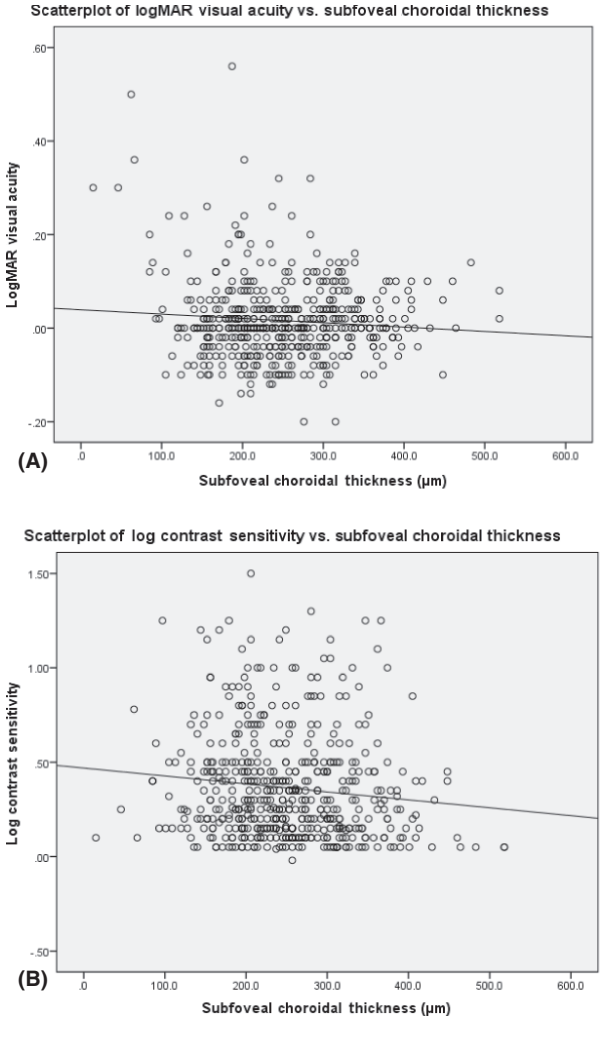

Fig. 3. (A) Scatterplot showing negative correlation between LogMAR visual acuity and subfoveal choroidal thickness (CT) in all myopes. (B) Scatterplot showing negative correlation between Log contrast sensitivity and subfoveal CT in all myopes.

2009; Goldenberg et al. 2012) and emmetropes (Margolis & Spaide 2009). Fujiwara et al. (2009) measured CT in high myopes only in the horizontal meridian and reported CT to be thickest temporal to the fovea (Hsiang et al. 2008). Two possible reasons for the relative choroidal thinning nasally and inferiorly in normal eyes are the choroidal watershed and the fetal choroidal fissure, which closes inferiorly at 7 weeks (Sadler 2006). In summary, the current thickness data agreed with the previous studies.

We found a significant negative association of SFCT with AL. In high myopia because of axial elongation, both the retina and choroid are stretched (Yanoff & Fine 1989; Lim et al. 2005; Lam et al. 2007) leading to thinning (Fujiwara et al. 2009; Ikuno & Tano 2009; Margolis & Spaide 2009). However, thinner choroid is still adequate to nourish proportionally thin retina which is consistent with fairly normal visual functions in adolescents and young adults with high myopia than their aged counterparts which undergoes further age-related reduction in choroid (Fujiwara et al. 2009). In contrast, in non-myopic elderly eyes, thinner choroid may not be adequate to supply the relatively thick retina which might in turn influence visual function. We therefore speculate that the relatively thin choroid in young myopes may be physiologically sufficient, although the same CT may be considered pathologic in older eyes without myopia.

In contrast to Nishida's study (Nishida et al. 2012) that demonstrated CT to be an important predictor of visual acuity in high myopes, we did not find a significant correlation between SFCT and visual acuity. They speculated that a thin choroid may deliver decreased amounts of oxygen and nutrients to the retina, thus potentially affecting signal generation from the photoreceptors or cause loss of the overlying photoreceptors as a consequence (Nishida et al. 2012). The discrepancy may be due to differences in age groups and CT between our study and Nishida's study. The mean age of the participants in Nishida et al. study was 57 years, and with the advancing age, the choroid may undergo further age-related attenuation (Fujiwara et al. 2009; Margolis

Table 5. Summary of CT and other variables in various studies in high myopia.

Study	No of eyes	Mean Age, years	AL, mm	SE, dioptres	OCT Machine	EDI (yes/no)	Mean CT,* μm
Current study	520	21.59	27.32	−8.68	Spectralis SD-OCT	Yes	225.87 (5.51)
Flores-Moreno et al. (2013)	120	54.4	29.17	−14.34	Topcon 3D-2000 OCT	No	115.5 (85.3)
Fujiwara et al. (2009)	55	59.7	–	−11.9	Spectralis SD-OCT	Yes	93.2 (62.5)
Ikuno & Tano (2009)	31	51.7	29.6	−15.5	Cirrus SD-OCT	No	99.3 (58.8)
Takahashi et al. 2012;	20	63.4	28.37	−10.8	Cirrus SD-OCT	No	68.1 (10.5)
Chen et al. (2012)	20	28.8	–	−9.29	Spectralis SD-OCT	Yes	156.07 (86.3)

EDI = enhanced depth imaging; SD-OCT = spectral domain optical coherence tomography; AL = axial length; CT = choroidal thickness; SE = spherical equivalent; "–"not available.
* Data are mean (SD) except current study which is mean (standard error).

& Spaide 2009). A substantially thinner choroid (113.3 μm) observed in Nishida's study suggests that the magnitude of thinning is likely the reason for the observed relationship with visual acuity, that is there is a threshold level of choroidal thinning, beyond which retinal function becomes compromised. Thus, available supply from choroid may not be sufficient to support outer retina, the RPE and even the choroid itself, which may explain why vision was affected. In contrast, our young participants with thicker choroid (225.87 μm) retained their retinal function and therefore enjoyed better vision. In addition, their results may be confounded by other ocular comorbidities due to ageing, while our study involved younger subjects with few ocular comorbidities, and thus, the results are less complicated by confounding factors.

Presence of posterior staphyloma, a hallmark of high myopia, was significantly associated with choroidal thinning. Similar results were reported in the previous studies which demonstrated posterior staphyloma formation as a key factor in choroidal thinning in highly myopic eyes (Fujiwara et al. 2009; Ikuno & Tano 2009). This association is probably because in myopic eyes with posterior staphyloma, choroidal circulation is altered with marked attenuation and reduction in number of large choroidal vessels (Quaranta et al. 1996). In addition, there is a shift in the entry site of the posterior ciliary arteries towards the staphyloma's border leading to scarce choroidal arterial network in the area occupied by staphyloma (Moriyama et al. 2007). Thus, all these changes lead to choroidal thinning in eyes with staphyloma.

The study has several strengths. Our study has a relatively large sample size, and EDI SD-OCT images were enhanced using adaptive compensation (Wang et al. 1994) to improve CSI visibility. Therefore, the CT measurements obtained in our study are likely more reliable and accurate. Unlike other studies, our study included an emmetropic group, and therefore, we could examine the differences between highly myopic eyes and non-myopic eyes in our case–control study. The study also has some limitations. First, due to our cross-sectional study design, we were unable to determine the causal relationships between the various risk factors and CT. Second, all of our study subjects were males, and thus, some of our findings may not be generalized to females. Previous studies have shown higher CT in men than in women adjusting for age and AL (Li et al. 2011). Third, by not taking into account AL to correct for ocular magnification, there may still be some residual error. Lastly, only horizontal and vertical scan lines were used to determine the CT profile. A denser scanning protocol is likely to provide further insights regarding the thickness profile across the posterior pole. While denser scanning protocols may not be feasible with manual segmentation and large subject numbers, the development of automated choroidal segmentation methods opens the door for potential future studies to use denser scanning protocols to determine the topographical thickness profile of the choroid, which will likely provide additional insights into the changes in the choroid associated with myopia.

Conclusion

Our study shows that CT is significantly lower in high myopic eyes. Macular CT distribution follows a different profile in high myopia compared to emmetropes. AL, presence of posterior staphyloma and chorio-retinal atrophy are the significant predictors of CT in high myopia and must be taken into account when interpreting the data on CT. Given the large number of people with myopia in the world, these findings seem to have widespread implications.

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