Association between Choroidal Thickness and Ocular Perfusion Pressure in Young, Healthy Subjects: Enhanced Depth Imaging Optical Coherence Tomography Study

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Purpose. To investigate the correlation of choroidal thickness (CT) with ocular perfusion pressure (OPP) in young, healthy subjects using enhanced depth imaging optical coherence tomography (EDI-OCT).

Methods. A single horizontal section and a single vertical section of EDI-OCT scans in each eye of 69 young, healthy subjects were obtained at the macula. CT was measured at the fovea, and up to 3 mm, at intervals of 0.5 mm, away from the fovea in the superior, inferior, nasal, and temporal choroid. Univariable and multivariable analyses were performed to assess the association of CT with OPP while axial length (AL), refractive error (RE), sex, and/or body mass index (BMI), were taken into consideration.

Results. Mean subfoveal CT was 307.03 ± 91.27 μm (mean age, 22.3 ± 3 years; mean axial length, 25.35 ± 1.14 mm; mean refractive error, −3.89 ± 2.02 diopters; mean OPP, 44.18 ± 5.49 mm Hg). Multivariable regression analysis showed that in eyes with <6 diopters of myopia, subfoveal CT (325.92 ± 88.46 μm) changed most significantly in association with RE and mean OPP ($\beta = 25.941$, $P < 0.001$; $\beta = -3.551$, $P = 0.042$, respectively; adjusted $R^2 = 0.249$). In subjects with myopia of >6 diopters, subfoveal CT (225.17 ± 49.37 μm) was significantly thinner ($P < 0.0001$), and a significant correlation with OPP was not observed ($P > 0.05$).

Conclusions. In vivo subfoveal CT as measured by EDI-OCT was significantly associated with OPP in young, healthy subjects when adjusted for RE, suggesting that subfoveal CT may be indirectly indicative of subfoveal ocular perfusion status. This association was not observed in subjects with high myopia. (*Invest Ophthalmol Vis Sci.* 2012;53:7710–7717) DOI: 10.1167/iovs.12-10464

The choroid, one of the most highly vascularized tissues of the body, plays an important role in the nourishment of the outer retina with oxygen and nutrients, modulation of temperature in the retina, adjustment of the retinal position, and secretion of growth factors.[1] Being the most highly vascularized structure in the human body, the choroid is also involved in the pathophysiology of many ocular diseases associated with choroidal circulation such as age-related macular degeneration (AMD), central serous chorioretinopathy (CSC), and choroidal ischemia.

A recently developed technique known as enhanced depth imaging optical coherence tomography (EDI-OCT) enables in vivo cross-sectional imaging of the choroid.[2] Using this method, a few studies have described the characteristics of the choroid in normal as well as in certain pathologic states such as glaucoma, high myopia, and Vogt–Koyanagi–Harada syndrome.[3–7] Furthermore, correlations between choroidal thickness (CT) measured by EDI-OCT and various disease entities associated with choroidal circulation such as AMD, CSC, and polypoidal choroidal vasculopathy have also been recently suggested.[8–11]

Blood flow through a blood vessel relies on perfusion pressure[12] and, in the eye, ocular perfusion pressure (OPP) is thought to be the driving force of ocular blood flow.[13] OPP is important for efficient diffusive exchange of oxygen, nutrients, and metabolic waste across the relatively long distance between the choroid and the retina, in which the perfusion pressure in addition to vascularization of the choroid plays a vital role.[14,15] Low OPP can lead to a reduction in ocular blood flow, which may result in ocular ischemia and/or hypoxia.[13] Because there is no retinal vascular supply in the foveal avascular zone, choroidal blood supply plays a significant role in this region.[12] As a result, the fovea may become vulnerable to disturbances in choroidal circulation. By using EDI-OCT to measure CT noninvasively, discovery of correlations between subfoveal CT and OPP might be of clinical significance with regard to assessing the status of choroidal circulation based on in vivo CT, given that OPP is believed to be an indirect indicator of choroidal blood flow.[16] In the past, histologic studies have been performed in animal models to investigate the physiology of choroid and its blood flow,[16] but due to limitation in reflecting the in vivo choroid in humans, their interpretation and application to the human eye are limited. Using EDI-OCT, a recent study by Maul et al.[11] showed that diastolic OPP was significantly associated with CT in glaucoma suspects and glaucoma patients, whereas another group suggested no correlation.[5] Considering the high vascularity of the choroid, we hypothesized that OPP would be one of the major parameters associated with CT.

In the present study, we investigated the correlation between OPP and CT in healthy, young subjects using EDI-OCT.

Methods

Subjects

We initially recruited 69 consecutive, healthy, young volunteers with no previous history of ophthalmic disease. They were enrolled in a prospective manner from December 2010 to March 2011. Only one eye

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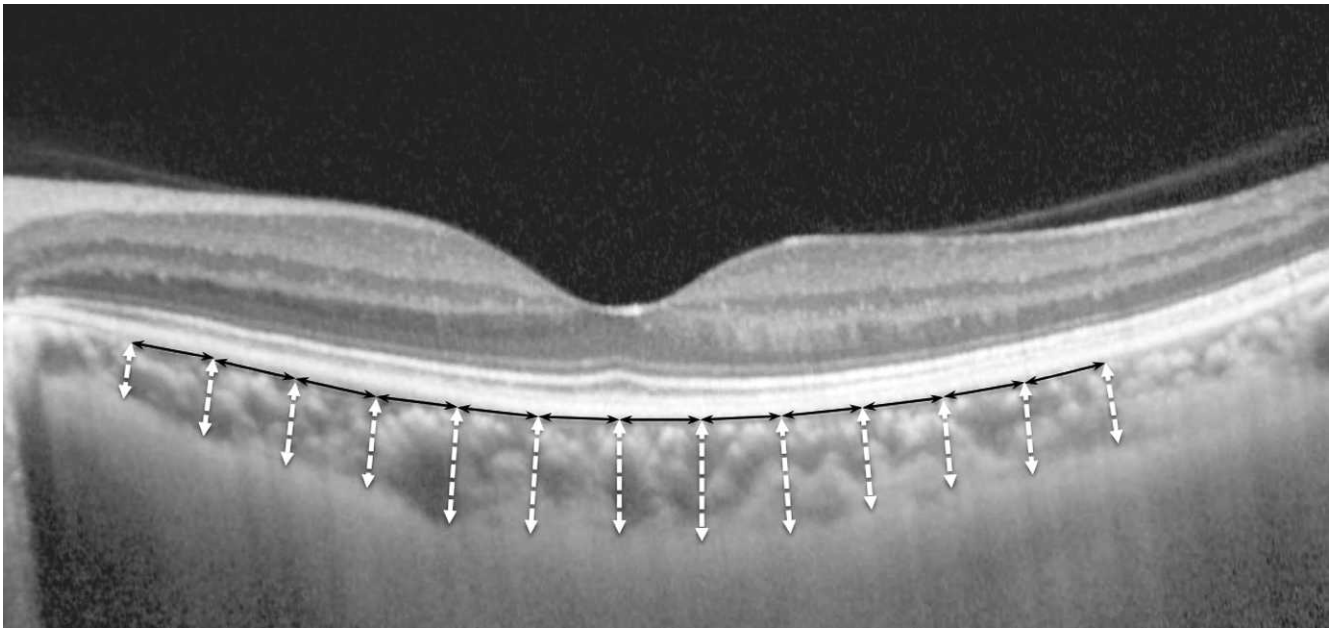

Figure 1. An illustrative horizontal EDI-OCT image from a 23-year-old subject showing choroidal thickness measurement taken perpendicularly from the hyperreflective line corresponding to the RPE to the chorioscleral interface. *Black solid arrows* represent an interval of 0.5 mm from the fovea up to 3.0 mm and *white dashed arrows* indicate choroidal thickness measurement. Choroidal thickness and the distance from the fovea to different locations were measured using the digital caliper provided by the software.

per subject was randomly selected for the study. All subjects were screened for the presence of any ocular disease. Slit-lamp examination was performed for examination of the anterior segment, and the posterior segment was evaluated using an indirect ophthalmoscope. Subjects were also screened for any medical condition that could potentially influence hemodynamic status such as hypertension, diabetes, or arrhythmia. Any subjects with retinal or choroidal pathology were excluded. Subjects were required to have a best corrected visual acuity of 20/25 or better, a refractive error of less than –9 diopters, or 3 diopters of cylinder. Exclusion criteria also included previous ocular surgery, high hyperopia, and poor image quality. The eyes in which the chorioscleral interface could not be clearly visualized were also excluded. The study was approved by the institutional review board of Yonsei University College of Medicine. It followed the tenets of the Declaration of Helsinki and informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study.

Image Acquisition

A spectral-domain (SD)–OCT was placed close enough to the eye to obtain an inverted image as described by a previous report.[2] In our study, the EDI option allowed the chorioretinal interface to be placed adjacent to the zero delay, and an upright image of the retina and choroid was obtained. All subjects were imaged by the same experienced specialist (MK) through undilated pupils (Spectralis OCT, with software version 5.3; Heidelberg Engineering, Heidelberg, Germany). Briefly, this OCT protocol uses a 870-nm wavelength superluminescent diode (SLD) and is capable of obtaining 40,000 A scans/second with an axial resolution of 7 μm and transversal resolution of 14 μm. A horizontal section and a single vertical section were obtained within a $5 \times 30^{\circ}$ area at the fovea, in which 100 scans were averaged for each section. The signal-to-noise ratio was maximized using the automatic real-time averaging mode to ensure high-quality images, and only scans with signal-to-noise ratio >20 dB were used for analysis. CT was defined as the distance from the outermost layer of the retinal pigment epithelium (RPE) to the inner scleral border, presumed to be the chorioscleral interface, and it was measured using the caliper tools of the software. CT was measured at the fovea, and at 500-μm intervals up to 3 mm temporal and nasal to the fovea in horizontal sections, and up to 3 mm superior and inferior to the fovea in vertical sections using the manual segmentation method (Fig. 1). A mean overall CT was obtained by calculating average values of CT measurements at all eccentricities. The measurements were performed by two independent retinal specialists who were unaware of demographic information as well as the subjects' ocular parameters, and the measurements from the two observers were then averaged together for analysis. Measurements by the first examiner were performed three times for evaluation of intraobserver variability.

Measurement of IOP, OPP, and Systemic Hemodynamics

Intraocular pressure was measured three times using a noncontact tonometer at the time of the OCT imaging, and the average value was used in the analysis. The spherical equivalent of refractive error was measured by autorefractometry (RK-3; Canon, Tokyo, Japan) and the axial length was measured using interferometry (IOL-Master; Carl Zeiss Meditec, Dublin, CA) three times each, the average values of which were used in the analysis. For blood pressure (BP) measurement, subjects were asked to rest for at least 5 minutes to ensure a stable hemodynamic condition before BP was measured on the upper arm by an automated oscillometric device. It was measured twice to verify stable hemodynamic condition and the average value was obtained. The measurement was performed in a seated, resting position just before the EDI-OCT imaging was performed. Mean OPP was calculated using the following equation: mean ocular perfusion pressure (OPP) = $(2/3 \times$ mean arterial pressure [MAP] $-$ IOP),[17,18] where MAP = diastolic BP + $(1/3 \times$ [systolic BP $-$ diastolic BP]).[19] Systolic and diastolic OPP were calculated using the following equations: systolic OPP = systolic BP $-$ IOP and diastolic OPP = diastolic BP $-$ IOP, respectively.

Statistical Analysis

Commercial software was used for statistical analysis (SPSS 18.0; SPSS Inc., Chicago, IL). Variations in CT at each location were evaluated. In

Table 1. A Summary of Subject Demographics, Ocular Parameters, and Systemic Factors

Factor	Mean ± SD	Range
Age, y	22.25 ± 3.01	20 to 25
Visual acuity (Snellen)	1.263 ± 0.372	0.8 to 2.0
Subfoveal choroidal thickness, μm	307.03 ± 91.27	137 to 555
A mean overall choroidal thickness, μm	297.86 ± 76.02	151.36 to 516.44
Axial length, mm	25.35 ± 1.14	23.3 to 28.1
Spherical equivalent of manifest refraction, diopters	−3.89 ± 2.02	−0.13 to −8.63
Intraocular pressure, (IOP), mm Hg	14.05 ± 3.59	8 to 21
Systolic BP, mm Hg	122.34 ± 9.46	103 to 138
Diastolic BP, mm Hg	69.84 ± 8.39	52 to 90
Pulse rate, bpm	72 ± 10.59	54 to 100
Mean arterial pressure, (MAP), mm Hg	87.34 ± 7.49	72.33 to 103.33
Mean OPP, mm Hg	44.18 ± 5.49	31.78 to 56.89
Systolic OPP, mm Hg	108.29 ± 9.41	93 to 132
Diastolic OPP, mm Hg	55.79 ± 8.55	38 to 78
Body mass index, BMI	23.57 ± 2.33	19.45 to 29.98
Height, cm	175.66 ± 5.59	168 to 187
Weight, kg	72.66 ± 7.41	61 to 95

univariable analysis, all variables (sex, BMI, refractive error, axial length, IOP, BP, and OPP) were fitted in a model. Subgroup analysis based on the refractive error in highly myopic eyes (≥6 diopters) was performed. Independent Student's *t*-test was used for comparison of CT between the two subgroups. Stepwise multivariable linear regression analysis was performed to investigate the independent associations of CT with systemic and ocular parameters and to identify clinically significant factors for CT. Because axial length and refractive error were correlated with each other, each variable was tested separately in regression models adjusted for IOP, BP, and/or OPP variables. Subfoveal CT and a mean overall CT were regressed against OPP to verify the hypothesis that CT may vary as a function of OPP. To evaluate intraobserver and interobserver agreement, intraclass correlation coefficient (ICC) and Pearson's correlation coefficient were calculated. A value of $P < 0.05$ was considered to be statistically significant and a value of P between 0.05 and 0.10 was considered to be of borderline statistical significance.

Results

A total of 64 eyes from 64 subjects (35 males, 29 females) were analyzed in this study. Five eyes were excluded because of poor OCT image quality ($n = 1$) and obscure chorioscleral interface ($n = 4$). Figure 1 shows a representative EDI-OCT measurement of CT. Enrolled subjects' demographic and clinical characteristics are summarized in Table 1. The mean subfoveal CT was 307.03 ± 91.27 μm (range: 137–555) and the mean overall CT was 297.86 ± 76.02 μm (range: 151.36–516.44). The mean axial length was 25.35 ± 1.14 mm (range: 23.3–28.1) and the mean refractive error was –3.89 ± 2.02 diopters (range: –0.13 to –8.63). The mean OPP was 44.18 ± 5.49 mm Hg (range: 31.78–56.89). When classified into two groups based on sex, there was no significant difference in subfoveal CT, refractive error, or the mean OPP between the two groups (all values of $P > 0.05$; data not shown). Figure 2 shows the geographical distribution of choroidal thickness of both horizontal and vertical 3-mm sections across the macula. The SD was the largest at the fovea in both the horizontal and vertical sections. In the vertical section, the SD of CT decreased toward the superior part of the measurements, and less so in the inferior part.

Table 2 summarizes the results of univariable linear regression analysis of subfoveal CT. Refractive error was significantly and positively correlated with subfoveal CT ($\beta = 26.29$, $R^2 = 0.337$, $P < 0.0001$). There was a significant negative correlation between subfoveal CT and axial length ($\beta = -33.7$, $R^2 = 0.177$, $P = 0.001$). The mean OPP showed a negative correlation with low regression of borderline significance ($\beta = -3.63$, $R^2 = 0.048$, $P = 0.082$). Using the mean overall CT value as the outcome variable instead of the subfoveal CT value, univariable linear regression analysis showed a similar trend of statistical significance for refractive error ($\beta = 26.29$, $R^2 = 0.358$, $P < 0.0001$) and axial length ($\beta = -27.386$, $R^2 = 0.169$, $P = 0.001$).

When eyes were classified into two groups according to refractive error, there were 14 eyes with high myopia of >6.0 diopters. The mean subfoveal CT thereof was 225.17 ± 49.37 μm (range: 137–284), and the mean overall CT was 226.85 ± 36.88 μm (range: 151.36–290.48). The choroid was significantly thinner in this group than those with <6.0 diopters of myopia (the subfoveal CT, 325.92 ± 88.46 μm and the mean overall CT, 314.26 ± 73.38 μm; all $P < 0.0001$, independent Student's *t*-test). The mean refractive error was 6.93 ± 0.88 diopters (range: –6.0 to –8.63) and the mean axial length was 26.96 ± 0.82 mm (range: 25.79–28.09), which were significantly different from those with <6.0 diopters of myopia (–3.18 ± 1.47 diopters and 24.97 ± 0.84 mm, respectively; all $P < 0.0001$). In the univariable analysis of highly myopic eyes (>6 diopters), no statistically significant correlation for subfoveal CT with refractive error, axial length, and mean OPP was observed (Table 3, all $P > 0.05$). In subjects with <6.0 diopters of myopia, the statistical significance of mean OPP increased from borderline significance to a statistically significant level ($\beta = -4.733$, $R^2 = 0.087$, $P = 0.03$, Table 3).

Multivariable linear regression of explanatory variables with subfoveal CT using forward stepwise variable selection resulted in five different sets of models after adjusting for either refractive error or axial length (Table 4). For eyes with <6 diopters of myopia, the subfoveal CT changed most significantly in association with refractive error and mean OPP ($\beta = 25.941$, $P < 0.001$; $\beta = -3.551$, $P = 0.042$, adjusted $R^2 = 0.249$, respectively). When these two variables were excluded, none of the variables showed any significant association with subfoveal CT or with overall mean CT. When only refractive error was excluded, axial length and mean OPP were the two most significant variables associated with subfoveal CT ($\beta = -26.998$, $P = 0.046$; $\beta = -4.435$, $P = 0.037$, respectively), but the adjusted R^2 values (the goodness of fit) were only 0.123, compared with 0.249 when refractive error and the mean OPP were included in the model. Since axial length and refractive

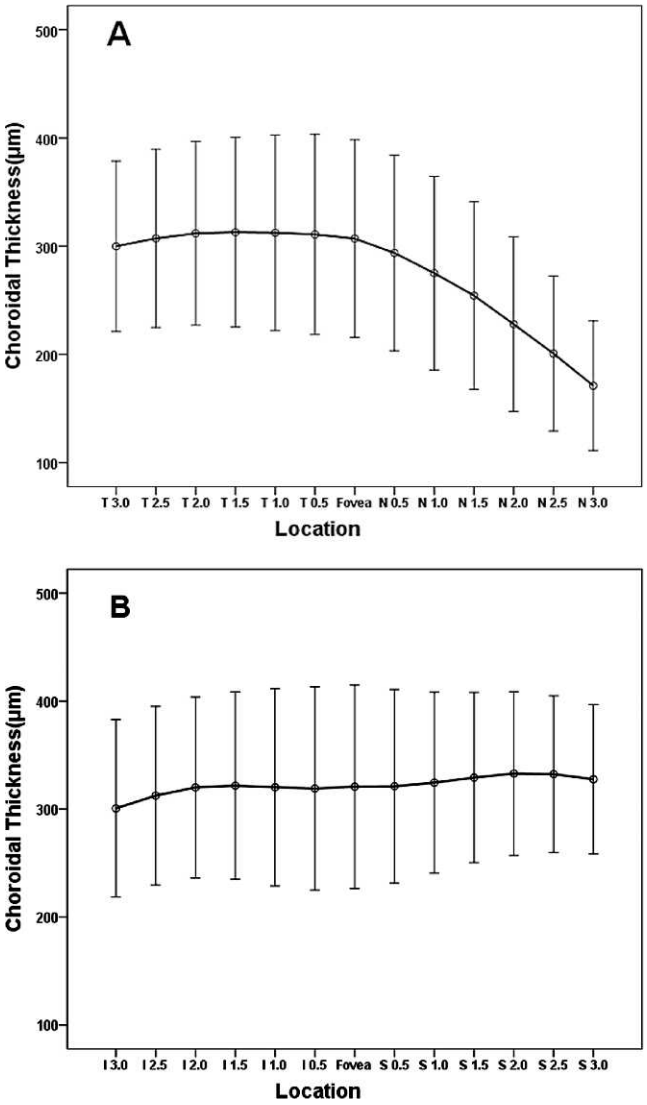

Figure 2. Graphs showing choroidal thickness measured at multiple locations across a horizontal section through the fovea with a 500-μm interval up to 3 mm temporal (T) and nasal (N) to the fovea (**A**) and across a vertical section through the fovea with a 500-μm interval up to 3 mm inferior (I) and superior (S) to the fovea (**B**). *Error bars* indicate the SD of the mean choroidal thickness.

error are closely related to each other, they were not included in the multivariable analysis at the same time. When the overall mean value of CT at all eccentricities was used in multivariable analysis, none of the parameters showed any statistical significance, except for refractive error (all $P > 0.05$; data not shown). None of the models was statistically significant for eyes with >6 diopters of myopia (data not shown; all $P > 0.05$).

Discussion

In this study, we showed that mean OPP exhibits a significant association with subfoveal CT after adjusting for refractive error and other potential clinical parameters that could be associated with CT. Subgroup analysis performed according to the refractive errors demonstrated that this relationship was not significant in highly myopic eyes with myopia of >6.0 diopters.

Although the primary role of the choroid in the regulation of ocular physiology is well known, the clinical association of in vivo CT with ocular perfusion status remains unknown, despite the potential clinical significance that choroidal blood flow is known to be one of the highest in the human body[20] and choroidal thinning is reported to be associated with lack of vessels and choriocapillaris thinning in the high myopia group.[21,22] Anatomically, the fovea has an area that lacks inner retina, called a foveal avascular zone due to the absence of retinal capillaries. This area of the outer retina is nourished solely by the choroidal blood vessel.[12] Since the fovea contains densely packed metabolically active photoreceptors requiring high oxygen tension, choroidal blood supply needs to be rich in the subfoveal area to nourish the high energy consumption of the fovea. Thus, this area can be particularly vulnerable to compromised choroidal circulation. Choroidal thinning may lead to a relative decrease in choroidal circulation, eventually leading to a reduced level of necessary oxygen and nutrient delivery to the most metabolically active foveal region.[23] This suggests that, since blood flow through a blood vessel depends on perfusion pressure, any significant correlation between subfoveal CT and OPP could be of potential clinical value in indirectly estimating ocular perfusion status by measurement of CT using EDI-OCT.

In multivariable analysis, after adjusting for the influence of refractive error on CT, mean OPP became the second most important factor associated with subfoveal CT, next to refractive error in eyes with <6 diopters of myopia (Table 4).

Table 2. Univariable Linear Regression Analysis of Subfoveal Choroidal Thickness Measured by EDI-OCT

	Subfoveal Choroidal Thickness			A Mean Overall Choroidal Thickness*		
Factor	**Coefficients (95% CI†)**	R^2	***P* Value**	**Coefficients (95% CI)**	R^2	***P* Value**
BMI	−1.45 (−11.41, 8.49)	0.001	0.771	−2.316 (−10.587, 5.956)	0.005	0.578
Sex	−4.45 (−20.24, 17.84)	0.003	0.591	−12.18 (−30.78, 5.323)	0.013	0.139
Axial length	−33.7 (−52.13, −15.27)	0.177	*0.001*	−27.386 (−42.815, −11.957)	0.169	*0.001*
Refractive error	26.29 (16.93, 35.66)	0.337	*<0.0001*	26.29 (14.916, 30.263)	0.358	*<0.0001*
IOP	8.26 (2.16, 14.37)	0.106	*0.009*	6.421 (1.295, 11.547)	0.092	*0.015*
Systolic BP	−0.072 (−2.52, 2.38)	0.0005	0.953	0.186 (−1.853, 2.225)	0.001	0.856
Diastolic BP	−0.059 (−2.82, 2.70)	0.0003	0.966	0.511 (−1.783, 2.805)	0.003	0.658
MAP	−0.088 (−3.18, 3.01)	0.0005	0.955	0.527 (−2.045, 3.099)	0.003	0.684
Mean OPP	−3.63 (−7.75, 0.48)	0.048	0.082	−2.085 (−5.557, 1.388)	0.023	0.235
Systolic OPP	−1.274 (−3.716, 1.167)	0.017	0.301	−0.746 (−2.788, 1.297)	0.009	0.468
Diastolic OPP	−1.511 (−4.193, 1.171)	0.020	0.264	−0.637 (−2.888, 1.613)	0.005	0.573

Italic numbers represent *P* values that are statistically significant values.

* A mean overall choroidal thickness = average of choroidal thickness measured at all eccentricities.

† CI, confidence interval.

Table 3. Subgroup Analysis Based on Refractive Error by Univariable Linear Regression Analysis of Subfoveal Choroidal Thickness Measured by EDI-OCT

	Myopia of <6.0 Diopters (n = 50 Eyes)			Myopia of >6.0 Diopters (n = 14 Eyes)		
Factor	**Coefficients (95% CI)**	**R^2**	***P* Value**	**Coefficients (95% CI)**	**R^2**	***P* Value**
BMI	−1.151 (−11.41, 8.49)	0.001	0.771	−7.116 (−25.786, 11.554)	0.088	0.405
Sex	−5.41 (−21.34, 15.83)	0.017	0.383	−3.54 (−10.51, 13.28)	0.037	0.321
Axial length	−29.006 (−56.364, −1.648)	0.08	*0.038*	4.147 (−36.853, 45.148)	0.007	0.821
Refractive error	28.114 (13.766, 42.462)	0.229	*<0.0001*	25.193 (−10.710, 61.097)	0.247	0.144
IOP	8.472 (2.175, 14.77)	0.123	*0.009*	−10.778 (−22.012, 0.457)	0.380	0.058
Systolic BP	−0.151 (−3.984, 1.681)	0.013	0.418	−1.018 (−4.075, 2.040)	0.069	0.465
Diastolic BP	−0.376 (−3.333, 2.581)	0.001	0.800	−1.509 (−5.813, 2.796)	0.076	0.442
MAP	−0.864 (−4.231, 2.503)	0.005	0.609	−2.047 (−6.693, 2.599)	0.114	0.339
Mean OPP	−4.733 (−8.995, −0.472)	0.087	*0.03*	−0.171 (−7.696, 7.355)	0.0003	0.96
Systolic OPP	−2.504 (−5.173, 0.165)	0.064	0.065	−0.601 (−4.091, 2.888)	0.019	0.701
Diastolic OPP	−1.938 (−4.193, 1.171)	0.035	0.178	−0.410 (−4.682, 3.863)	0.006	0.831

Italic numbers represent *P* values that are statistically significant values.

Based on the highly vascular nature of the choroid, it is reasonable to assume the CT could vary in association with OPP, in addition to previously known significant parameters such as refractive error. Correlation between CT and ocular parameters associated with ocular hemodynamic status has been explored previously in a number of studies. Association between OPP and CT has been reported by Maul et al.,[11] who showed choroidal thinning in glaucoma patients with lower diastolic OPP. In glaucomatous eyes, it has been hypothesized that a decreased number of choroidal vessels in a thin choroid could lead to a reduction in blood flow, resulting in an increase of pressure with an increase in CT.[24] With regard to systemic hemodynamic parameters, a recent study reported no significant correlation between arterial blood pressure and subfoveal CT,[25] whereas another group found a positive correlation between changes in CT and changes in systolic blood pressure.[26] In our study of healthy subjects, the negative association between OPP and subfoveal CT may be explained by the role of the choroid in vasomotor control of blood flow, because OPP is thought to be an important determinant of ocular blood flow.[27] We postulated that in eyes with a relatively thick choroid, the perfusion pressure may not need to be as high to maintain constant blood flow. Likewise, a relatively thin choroid may require higher OPP to compensate for potential decreases in choroidal blood flow, but since blood flow through a blood vessel depends not only on the perfusion pressure, but also on the resistance generated by the blood vessels,[12] this remains only speculative at the present moment without direct measurement of choroidal blood flow and choroidal vascular resistance.

A potential association between CT and choroidal circulation has been investigated previously. An animal study documented an increase in choroidal blood flow before an increase in CT during recovery from deprivation myopia.[28] There is also a report of the potential role of sildenafil citrate on choroidal thickness, due to its vasodilatory effect.[29] However, a recent study by Sogawa et al.[30] suggested a lack of any relationship between choroidal thickness and circulation in healthy young subjects. Choroidal autoregulation has been demonstrated in several studies during changes in OPP,[31–37] and neural input into the choroid, as well as intricate interaction between myogenic and metabolic mechanisms during OPP changes have been implicated as potential mechanisms of choroidal autoregulation.[38] At present, considering the findings from our study and past studies, the autoregulatory process involved in controlling OPP and ocular blood flow seems very complex; the interaction of multiple systemic and local control mechanisms is thought to affect the tone of the smooth muscles in the choroid, thereby influencing choroidal thickness and choroidal blood flow, although it is beyond the scope of this study to elucidate the precise mechanism.

The significant association between the mean OPP and the subfoveal CT was lost in the high myopia group with >6 diopters of myopia. The lack of association between CT and OPP suggests potentially different choroidal anatomic and physiologic features in high myopia, compared with the other group with <6 diopters of myopia. We speculated that high myopia with >6 diopters might display different associations with OPP and CT based on the following study, and that is why further analysis with respect to refractive error at 6 diopters has been chosen for subgroup analysis. A previous study by Fujiwara et al.[4] suggested the attenuation of the choroid with increasing myopia and speculated that choroidal thinning might be an important feature in the pathophysiology of high myopia due to relative ischemia of the outer retina. Evidence also suggests thinning of choriocapillaries,[21] decreased choroidal circulation,[39–41] and stretching of retinal tissue by axial elongation may lead to retinal dysfunction[42,43] in high myopia. Ocular volume in addition to axial length has also been suggested to play a role in ocular pressure pulse generated by choroidal blood flow.[44] Collectively, relative thinning of the choroid underneath the fovea, relative thinning of the sclera in high myopia with different and abnormal organization of collagen fibers,[45,46] and decreased choroidal circulation may contribute to differences in the association of CT and mean OPP. Nevertheless, this remains only speculation, given the small number of eyes with high myopia and our limited data, which did not provide conclusive evidence or an adequate explanation for ocular anatomy and physiology in high myopia other than the lack of association between subfoveal CT and the mean OPP. Further studies directly correlating choroidal blood flow, OPP, oxygen concentration level, and in vivo CT are needed because many pathophysiologic features of vision loss in high myopia may be associated with the oxygen and nutrient supply provided by the choroid.[23]

The findings of our study suggest that subfoveal CT measured by EDI-OCT might be used as a simple, convenient, noninvasive method to examine the choroid and might be of clinical value because, in addition to refractive error, mean OPP is significantly associated with subfoveal CT in eyes with <6 diopters of myopia. Nevertheless, given the known findings that age, refractive error, and/or axial length other than OPP could significantly influence CT, the use of CT as an indirect

TABLE 4. Multiple Linear Regression Model for Subfoveal Choroidal Thickness in Eyes with <6 Diopters of Myopia

	Model 1		Model 2		Model 3		Model 4		Model 5	
	B* (SE)	*P* Value	B (SE)	*P* Value	B (SE)	*P* Value	B (SE)	*P* Value	B (SE)	*P* Value
Intercept	1194.514 (337.288)	0.001	564.677 (85.888)	<0.0001	325.107 (57.245)	<0.0001	611.637 (130.585)	<0.0001	503.212 (73.922)	<0.0001
Refractive error			25.941 (7.093)	0.001	23.967 (7.411)	0.002	26.524 (7.132)	<0.0001	27.527 (7.120)	<0.0001
Axial length	−26.998 (13.218)	0.046								
Mean OPP	−4.435 (2.067)	0.037	−3.551 (1.936)	0.042						
Systolic OPP							−1.857 (1.204)	0.129		
Diastolic OPP									−1.625 (1.264)	0.204
IOP					5.294 (3.049)	0.089				
Systolic BP										
Diastolic BP										
Adjusted R^2	0.123		0.249		0.244		0.235		0.224	

* B, coefficients.

assessment of ocular perfusion status might be of limited clinical application at the present moment. A future prospective study is needed to investigate temporal associations among changes in choroidal blood flow, OPP, and CT.

We used a different approach using mean overall CT, which was calculated from the average of CT measurements of both horizontal and vertical scans across the macula, but the average CT approach did not show a significant correlation with the mean OPP; subfoveal CT alone showed better correlation with OPP than the mean overall value of CT. In this study, CT was measured between 9:00 AM and 12:00 PM to ensure consistency and minimize any influence from potential diurnal fluctuation in CT, because studies have shown that the choroid thickens the most around midnight and thins the most around noon.[47–49] The reliability and repeatability of the SD-OCT scan at our institute seemed to be within an acceptable range; there was good agreement for CT between intraobserver and interobserver variations (a mean ICC of 0.991 and Pearson correlation coefficient of 0.985 for all measured locations, respectively). Sex-associated differences in axial length, IOP,[50] and CT[25] have been reported previously, but in our study, there was no significant sex-associated difference in CT, refractive error, or axial length.

Our emphasis on young and healthy subjects is both a strength and a weakness of this study. In this study, the association between age and CT at all measured locations was not statistically significant because the subjects were mostly young, healthy patients, 20 to 25 years of age. In multivariable linear regression analysis with the forward stepwise variable selection method, age was not taken into consideration as one of the confounding factors, considering the homogeneous age composition of our subjects. Because age was shown to be one of the most important factors in CT in recent reports,[6,7,51–53] the advantage of evaluating in vivo anatomy in a young population is that it minimizes any variation in CT potentially related with age. However, it also limits its relevance, because the choroidal physiology of young healthy people is not likely to be relevant to that of older people, especially those with systemic vascular disease.

The strength of our study includes its prospective design, subjects of young age minimizing possible age-dependent changes in CT, inclusion of 3-mm sections of both horizontal and vertical choroidal imaging, and evaluation of various ocular parameters. As a limitation of this study, variations in ocular parameters such as IOP and BP were not large, implying that the findings of our study might not be relevant to those with ocular as well as systemic vasculopathy. The use of a noncontact tonometer was also a weakness of this study. Also, subjects enrolled in this study were mainly of Asian ethnicity, and might exhibit choroidal features different from those of the Western population.

In the future, automated software algorithms delineating the choroidal border would be of great value in consistently tracking choroidal changes and better visualization of the choroidal structure. Also, more extensive studies, involving a larger population of normal, as well as subjects with chorioretinal pathology, on the correlation of CT with choroidal blood flow would help our clinical understanding of the association between CT and choroidal circulation.

In conclusion, we found that in addition to refractive error, mean OPP was significantly associated with subfoveal CT in eyes with <6 diopters of myopia. This association became insignificant in eyes with high myopia of >6 diopters. Our findings suggest that in vivo subfoveal CT may be indicative of OPP in healthy young subjects, but future prospective studies involving more subjects with a wider range of age are warranted.

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